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Self-Organization of Quantum Entropy in Evolutionary Studies in Mammalian Brain Networks

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Abstract

Characterization of complex brain connectomic datasets and feature extraction thereof is progressively being attempted over the last decade. Intra-class evolutionary layout of such networks is regarded as one of the upcoming research domains of high importance. However, appropriate evolutionary profile generation requires thorough exploration of classical as well as non-classical graph theoretic properties. In this study, scaling parameter associated to graph community-wise distribution of quantum von Neumann entropy was found to be unambiguously correlated ($R^2 \approx 0.99$) to two phylogenetic markers (long non-coding genes and gene transcripts). Segmental connectivity datasets of different brain regions pertaining to six mammalian species were considered for this purpose. Furthermore, two classical network properties (clustering coefficient and closeness centrality) were demonstrated to fail in generating such an intra-mammalian evolutionary profile. Outcomes of this investigation justifies the efficacy of complex graph theoretic property in development of quantitative brain connectivity locus according to evolutionary selection.

Keywords: brain network, quantum entropy, self-organization, phylogeny, centrality, clustering-coefficient

1. Introduction

Improving social interaction environment emphasizes changing of cognitive features on different neurobiologically meaningful complex brain network segments [1]. Brain networks integrate multiple regions, sub-regions, scales and many other dissimilar structural attributes. Fortunately, these networks share a number of common and non-trivial topological traits with other networks of biological, physical and social origins [2]. Structurofunctional analysis of brain networks yields reliable outcomes in terms of small set of non-redundant, 'neurobiologically meaningful' parameters [3]. Across different brain networks, extensive comparisons of these parameters may help to categorize neurological and psychiatric disorders of clinical importance [4]. Sequentially, a large number of interdisciplinary research efforts, combining state of art knowledge of evolutionary neuroscience and complex network model are gradually being undertaken by several groups [5, 6].

Connectivity analysis and between-subject comparison in biological network studies requires a set of customized graph theoretic parameters, which is supposed to be functionally equivalent to different biomarkers used in cellular, molecular and evolutionary biology [7]. Several evolutionary profile studies were introduced over time. In searching for methods to determine phylogenetic relationships, many techniques now allow molecular comparisons among species [8]. Nevertheless, in order to develop even the simplest intraclass evolutionary layout, researchers must explore key traits involved in conservation biology, graph theory, health science, environmental science, natural resource exploitation and many other diverse domains [9]. In the present investigation, we have explored classical as well as non-classical graph theoretic properties to trace out the evolutionary layout of mammalian class. Our study clearly demonstrates the effectiveness of quantum entropy of brain network for this purpose.

Entropy measures have played a central role in classical and quantum information theory [10, 11, 12]. In essence, entropy is a measure of degeneracy inherent within any information source. Shannon and von Neumann formalisms provide the theoretical framework of this degeneracy estimate in classical and quantum paradigms respectively [13]. Quantum information entropy of a complex graphs, brain connectivity network for example, may reveal some of its attributes in evolutionary analysis beyond the scope of its classical counterpart. Present work has been undertaken to explore any hidden evolutionary signature associated to von Neumann entropic measure of complex brain connectomic datasets belonging to mammalian class. Six species of different phylogenetic locations (*Felis catus, Rattus norvegicus, Mus musculus, Macaca mulatta, Pan troglodytes and Homo sapiens*) were investigated for this study. Outcomes of present investigation are expected to be highly useful in quantitative evolutionary studies.

2. Materials and Methods

2.1 Construction of brain networks

Neural connection matrices pertaining to 65 cortical regions of cat mixed species (*Felis catus*), 503 of rat (*Rattus norvegicus*), 213 regions of mouse brain (*Mus musculus*), 242 cortical regions of macaque rhesus (*Macaca mulatta*), 72 regions of chimpanzee brain (*Pan troglodytes*) and 638 brain regions of human species (*Homo sapiens*) were considered as baseline data (Dataset available at https://networkrepository.com, https://sites.google.com/site/bctnet/datasets).
Undirected and unweighted graphs of aforementioned brain networks were constructed from the aforesaid datasets and analyzed in Wolfram Mathematica 11.3 platform.

2.2 Measures of von-Neumann entropy

Idea of network's von Neumann entropy was first introduced by Braunstein et al. [12], which was further extended in a number of subsequent works [13, 14]. Precisely, a graph Laplacian, the combinatorial replica of Laplace-Beltrami operator was used. Quantum von Neumann entropy is hypothesized to be functionally related to the spectra of network Laplacian. Mathematical details are elaborated as under:
Let G be a directed graph with a set of vertices V and a set of edges $E \subseteq V \times V$. Note that the adjacency matrix of a graph G is represented with the following elements

$$A_{uv} = \begin{cases} 1, if(u,v) \in E \\ 0, otherwise \end{cases} \quad (1)$$

Let D be the diagonal matrix with elements $d_u = \sum_{v=1}^{n} A(u,v)$, where d_u is the degree of node u. Graph Laplacian is defined as $L \equiv D - A$, which, is regarded as the combinatorial analogue of Laplace-Beltrami operator [13]. Passerini and Severini [15] proposed a different measure of von Neumann entropy for a graph created on normalized Laplacian, defined as $L = D^{-1/2} L D^{-1/2}$. Given a graph G with n number of nodes and normalized Laplacian L, the corresponding density matrix was formulated as $\rho(L) = \frac{L}{tr(L)} = \frac{L}{n}$. On the other hand, for a quantum mechanical system given by density matrix ρ, the quantum von Neumann entropy [16] is expressed as

$$S(\rho) = -tr(\rho ln \rho) \quad (2)$$

Presently, to formulate the functional relation between community entropy and community size (= number of vertices) following normalized forms were used:

$$\Gamma_{1\to k}^{j} = \frac{s^k(\rho_k)}{S(\rho)},\ \vartheta_{1\to k}^{j} = \frac{v_k}{V} \quad (3)$$

where, v_k and $s^k(\rho_k)$ are the number of vertices and quantum von Neumann entropy respectively for k^{th} community pertaining to brain networks for j^{th} species. V and $S(\rho)$ represent the number of vertices and von Neumann entropy of whole network respectively. Naturally, $\Gamma_{1\to k}^{j}$ be a probability distribution of entropy from level 1 (initial network) to related community levels (marked by distinct values of k) i.e., probability distribution of entropy from initial network into corresponding communities of j^{th} species. It is imperative to note that distribution of normalized entropy in each community with respect to normalized community volume was found to satisfy the following power law type scaling relation:

$$\Gamma_{1\to k}^{j} \propto \vartheta^{\eta} \tag{4}$$

where,ϑ represents the normalized community size and η is the scaling exponent. In essence, the functional relation between von Neumann entropy and community volume of the graph is formalized through η.

2.3 Measures of clustering coefficient

Structural analysis of complex brain network has revealed important "small-world" feature, commonly recognized by increased clustering coefficient and low mean path length [17, 18]. Mathematically, clustering coefficient (C) is cited as the fraction between mean number of edges amongst neighbors of any node and mean of probable edges between the same neighbors [17, 19]. Therefore,

$$C \equiv \frac{3\times numberoftriangles}{numberofalltriples} \tag{5}$$

Formally, the measures of isolation not only represent the presence of unified clusters of regions, but also find the precise size and conformation of these individual groups. This composition, recognized as network's modular assembly (community structure), is exposed by dividing the network into collections of nodes, with a maximally possible sum of within-group edges, and a minimally conceivable sum of between-group links [20, 21]. In the present study, well-known clustering-based 'Newman-Girvan modularity' [21] approach was used for community identification.

2.4 Measures of centrality

The above description had allowed looking into structure and functional connectivity of brain topology in relations to a network of interrelated segments. Among several nodes inside a network, few exhibit a critical role and are recognized via centrality measures, with betweenness, degree, eigenvector and closeness centrality are the most popular metrics. Throughout this work, we have investigated the closeness centrality metric[$= C_{cl}(u)$]. The closeness centrality measure is

important in cases where a change in local pathways often affect the overall network connectivity [3]. The chosen centrality measure is defined as:

$$C_{cl}(u) = \frac{(n-1)}{\sum_{v \in V} d(u,v)} \tag{6}$$

where n is number of vertices and $d(u,v)$ is measured the shortest path covered between a pair of vertices u and v. Evidently, if any node has smallest cumulative path distance, then that node takes maximal closeness centrality.
Scaling behaviour analysis and evaluation of corresponding exponents in relation to von Neumann entropy, clustering coefficient and closeness centrality for all mammalian species are considered as the entry point towards the development of intra-mammalian class evolutionary profile.

3. Results and Discussions

Anatomical brain connectivity layouts were independently constructed from the available baseline datasets mentioned in "method section". Corresponding community structures are displayed in figure 1. All communities were found to be disjointed without sharing any common set of vertices, as usual.
In the following, some of the general features associated with six mammalian brain networks are thoroughly investigated with the primary objective to trace out the intra-mammalian evolutionary layout.

3.1 Scaling behavior of brain networks

Evaluated community structure of six networks clearly indicates the existence of highly packed interacting communities with few distributed nodes (fig. 1). It is important to note that self-organization can be formally justified through scaling behaviour of individual network property according to community hierarchy. Scaling property of quantum von-Neumann entropy was primarily explored for all six brain networks considering their community structure in each level of organization for all six species. Eqn. 4 indicates self-organization of information degeneracy in all community levels resulting from respective network. In order to verify the self-repeated feature in all scale, double logarithmic profiles of $\Gamma_{1\to k}^{j}$ vs. ϑ dataset for all species were investigated (fig. 2). Individual profiles of each species have showed appreciable linearity, which indicates non-trivial self-organizing feature [22]. This is justified in terms of high correlation coefficients (0.98 to 1.00) of respective linear fit (fig. 2). Consequently, quantum von Neumann entropy is inferred to follow one parameter scaling relation in its community distribution of respective network structure. This may be otherwise established by associated scaling parameter (η) of brain information entropy relative to community volume of different species. Nonetheless, the scaling parameter was found to be nearly equal (≈ 0.03) in homologous species.

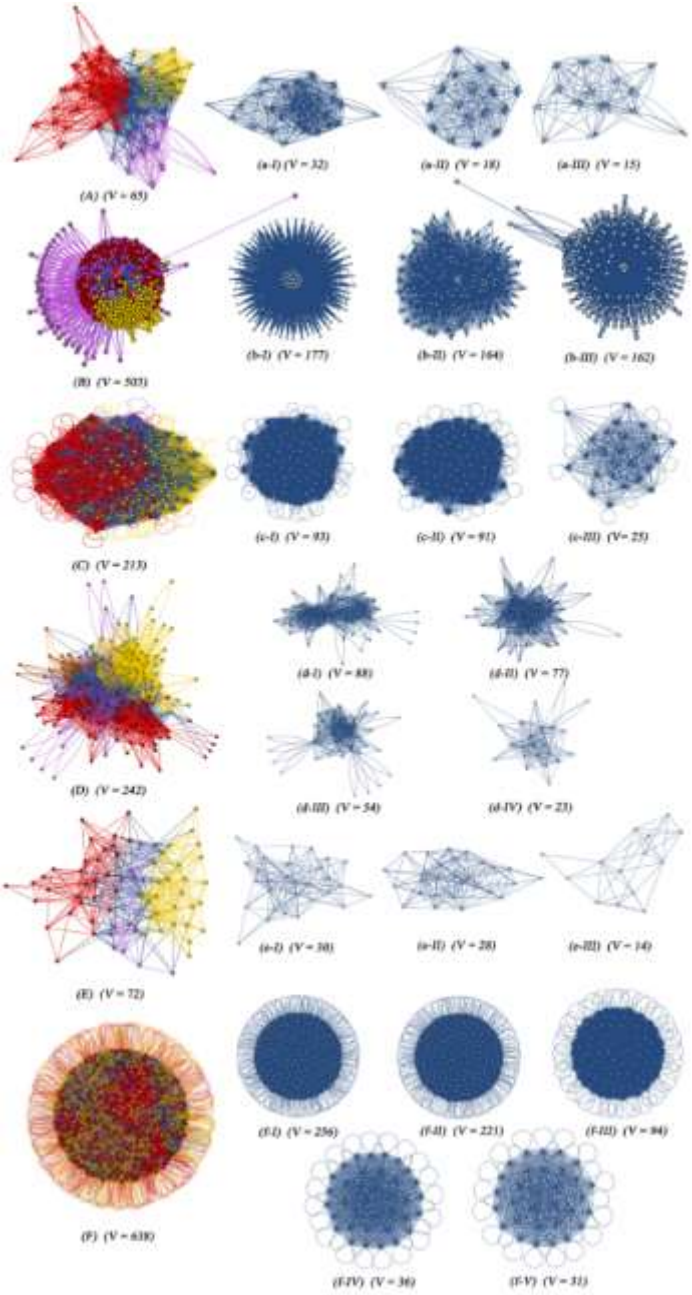

Figure 1. Brain networks and their respective community structures for (a*) Felis catus*, (b) *Rattus norvegicus*, (c) *Mus musculus*, (d) *Macaca mulatta*, (e) *Pan troglodytes* and (f) *Homo sapiens.*

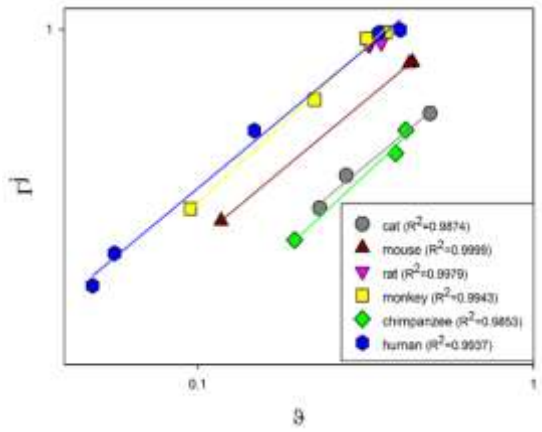

Figure 2. Double logarithmic plot and corresponding linear fit of $\Gamma^{j}_{1\to k} - \vartheta$ power law relation for brain networks of the six species: cat ($\eta = 0.0340$), mouse ($\eta = 0.0342$), rat ($\eta = 0.0056$), monkey (η =0.0381), chimpanzee (η =0.0384) and human($\eta = 0.0341$).

In what follows, we try to further explore how scaling coefficient might play a significant role on tracing the respective evolutionary pathways over the restricted domain of aforementioned collection of six mammalian brains.

3.2 Evolutionary mapping of scaling parameter

The scaling parameter η was found to be almost equal in evolved species, as shown in figure 2. Therefore, correlation study of η with selected markers (molecular markers, DNA sequences, etc.) that closely represent phylogenetic identity of respective species is worth exploring. For this reason, we have primarily chosen the number of nucleotides as the numerical marker for phylogenetic classification. Definitely, number of nucleotides is a primitive way of species differentiation in evolutionary frame. There also exists a set of updated procedures to construct the phylogenetic scale. Moreover, the selected species of present investigation are of close taxonomic ranks, which eventually lead to numerical proximity in their respective nucleotide numbers. Number of nucleotides in *Felis catus* is approximately 2.49×10^9, for rodent species it is around 3.04×10^9 (*rattus norvegicus*) to 3.49×10^9 (*mus muculus*), whereas for humanoid to human it spans between 3.39×10^9 (*pan troglodytes*) to 3.61×10^9 (*homo sapiens*). However, only within mammalian class, considerable variation exists because of their built-in difference. Figure 3 depicts the profiles of η vs. number of nucleotides along with the corresponding linear fir for six brain networks. Respective correlation coefficient (R^2 = 0.6567) indicates moderate applicability of linear fit only within closely related mammalian class members (*macaca mulatta, pan troglodytes and homo sapiens*) (fig. 3b). Rodent class member (rat) was apprehended to be diverged out due to their deviant genomic features as they might have unusually rapid chromosome alterations [23]. Nevertheless, the linearity observed in semi-logarithmic plot clearly specifies the validity of exponential growth type functional

relation between entropy vs. community volume scaling parameter and number of nucleotide sequences. However, relatively inferior correlation (R^2 = 0.2038) was recorded in gross entropy measures of brain networks (fig. 3a) with the same phylogenetic marker. In case of closely related mammalian species, relatively higher correlation coefficient was expected because of its superior scaling property (fig. 3b). Additionally, for all six mammalian species, much inferior correlation (R^2 = 0.0305) exists between η and nucleotide number.

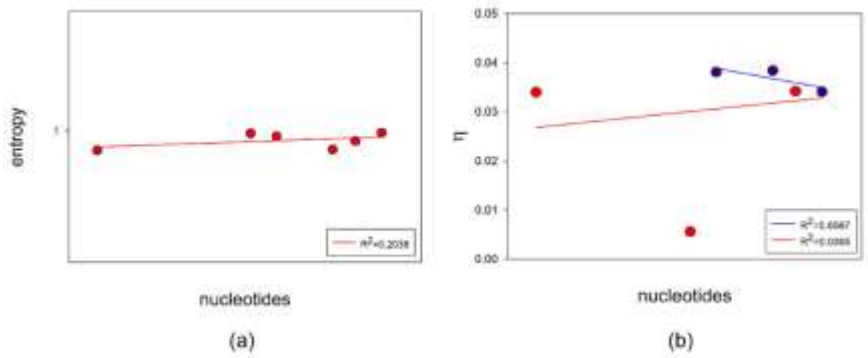

Figure 3. Variation of quantum entropy and scaling parameter η on nucleotide sequences of six mammalian species: (a) entropy vs nucleotides, (b) η vs nucleotides.

Phylogenetic analyses of closely related species are reported to be highly dependent on marker selection and the nature of functional dependence is quite different from that of more distant species [24]. It is formally evident that the nucleotide sequences generally have large variability inside and between the investigated species to find a satisfactory resolution in their phylogenetic position. Subsequently, we have chosen to explore a new set of quantitative parameters that includes nuclear introns (long), exons, gene transcripts and body to brain mass ratio (kg/g) [25]. Large number of introns, verified experimentally exhibited perfect extension and appreciable inconsistency in most species, signifying that this nuclear marker could be quite effective in representing the multi-locus phylogenetic traits in mammals [26]. With lower variability and robust stochastic nature of nuclear markers with respect to mitochondrial genes, intron markers may be apprehended to be served as excellent phylogenetic markers in evolutionary study of mammalian species. Accordingly, present correlation study of scaling parameter associated with quantum entropy with mixed set of evolutionary markers would be worthwhile in evolutionary layout formulation. To the best of our knowledge, the role of scaling parameter associated to entropic measures of complex brain networks as a viable candidate in evolutionary analysis of mammalian species is not being explored so far.

Figure 4 displays the corresponding regression analysis with the new set of phylogenetic markers and the same procedure was separately investigated for three closely related species (*macaca mulatta, pan troglodytes, homo sapiens* respectively). Appreciably high correlation coefficient (R^2=0.9871) of the corresponding linear fit was noted for gene transcripts. Similar traits (R^2=0.9773)

were found to exist for long non-coding genes in case of closely related species. Much lower correlation coefficients of the scaling parameter in relation to nucleotide sequences (R^2=0.6567) (fig. 3 b) as well as with coding genes (R^2=0.5130) (fig. 4 c) were observed for three closely related species. Besides, we have also explored conceivable correlations, if any, between η and relevant cognitive parameters. Recent reports on cognitive ability also suggests that the so-called 'rudimentary' estimate of brain-to-body mass ratio is literally a good predictor of problem-solving ability within the mammalian carnivores [27]. Interestingly, for all six species, an improved correlation (R^2=0.3448) was noticed with respect to a non-genetic marker of body-to-brain mass ratio compared to other genetic markers. Furthermore, gene transcripts and long non-coding gene counts possibly will also provide an important insight in evolutionary analysis of closely related species and also expected to facilitate characterization of the genetic basis underlying this information entropic trait of neural networks.

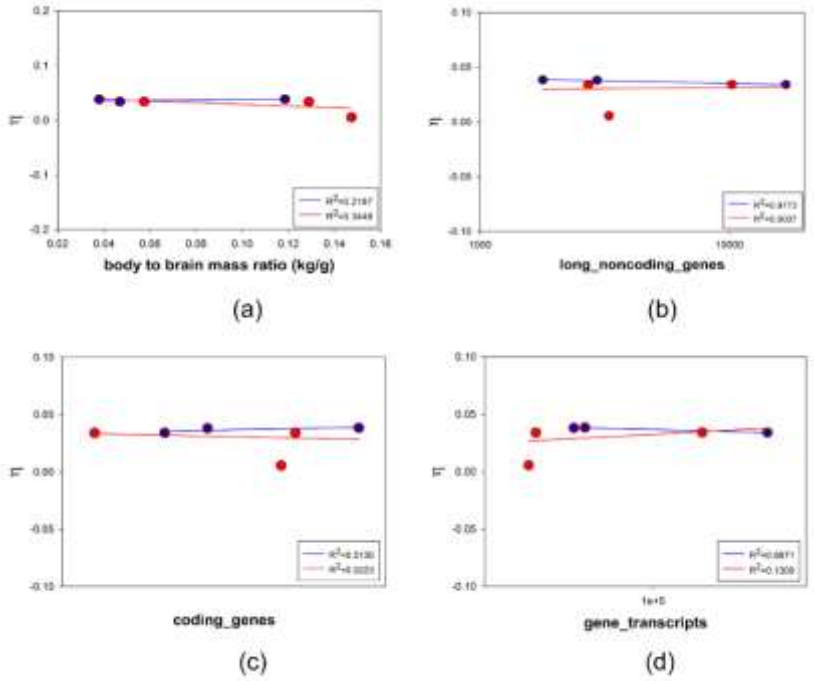

Figure 4. Variation of scaling parameter η on different genetic parameters of six species: (a) η vs. body-to-brain mass ratio (kg/g), (b) η vs. number of long noncoding genes, (e) η vs number of coding genes, (f) η vs gene transcripts

3.3 Classical graph theoretic properties (clustering coefficients and centrality measures)

In addition to scaling features of quantum graph theoretic property, other network measures of classical origin were also investigated. Evolutionary pattern of mean clustering coefficient and mean closeness centrality measures were also investigated using number of nucleotides as phylogenetic marker (fig. 5), similar to the case of entropy-community volume scaling parameter (fig. 3a). Collectively, the mean clustering coefficient profiles were noted to decrease from cat (=0.5222)

to mouse (=0.4853), however, from mouse to rat, there was a jump (= 0.6531). This was further followed by an abrupt drop from rat to macaque rhesus (= 0.4501). Subsequently, there was an increase as we move towards chimpanzee (=0.6001) and finally reaching a maximum in case of human (= 1.000). Similar zig-zag type profile was also recorded in case of mean closeness centrality. C_{cl} for cat was found to be 0.5503, followed by mouse (= 0.6697), rat (= 0.5309), macaque rhesus (= 0.4585), chimpanzee (= 0.4950) and finally human (= 1.0000).

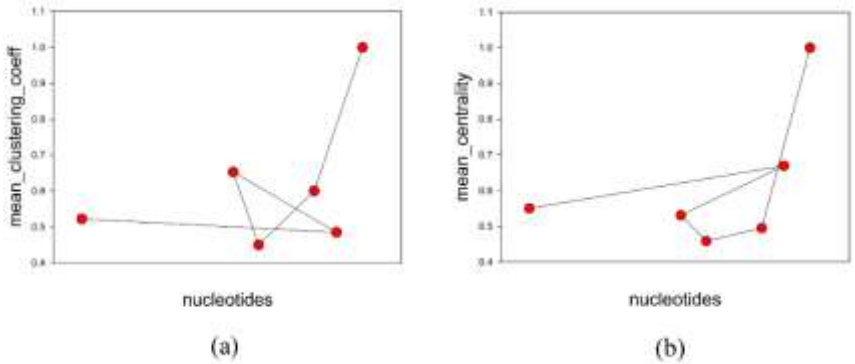

Figure 5. Profiles of (a) mean clustering coefficient and (b) mean closeness centrality with respect of number of nucleotides of six brain networks.

Evolution is a tactic process with non-sequential locus. Some of the beneficial neuro-functional attributes and corresponding network segment of distant phylogenetic member may be directly included in advanced species instead of successive upgradation from one species to the next. Highest average closeness centrality found in mouse brain (= 0.6697) model compared to other mammalian brain network is rather justified through the non-sequential form of evolutionary process. Moreover, increasing degree of neural clustering from one species to the higher is generally recognized as a signature of evolutionary process. Neural networks of rat, mouse, macaque rhesus and chimpanzee have been widely studied over decades to understand the working principle of human brain. However, there exists a wide scale of structural dissimilarities in addition to apparent differences in size and in weight. Abstract quantum properties may be apprehended to be suitable to create relatively simpler evolutionary layout compared to classical graph theoretic measures. Appreciably high correlation between scaling parameter of quantum von Neumann entropy and suitably chosen evolutionary marker is thus quite expected, whereas classical network measures fail to generate such evolutionary layout.

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