Growing random networks under constraints

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We study the evolution of a random graph under the constraint that the diameter remain constant as the graph grows. We show that if the graph maintains the form of its link distribution it must be scale-free with exponent between 2 and 3. These uniqueness results may help explain the scale-free nature of graphs, of varying sizes, representing the evolved metabolic pathways in 43 organisms.

In recent years measurements on a wide variety of networks such as the world wide web [3,4], the internet backbone [4], social networks [12,20] and metabolic networks [14,21] have shown that they differ significantly from the classic Erdos-Renyi model of random graphs [17]. While the traditional Erdos-Renyi model has a Poisson link distribution, with most nodes having a characteristic number of links, these networks have scale-free link distributions following a power law \( p(x) \sim x^{-\gamma} \). To account for these observations, the traditional Erdos-Renyi growth process [17] has been replaced by newer processes [5,6,20,19,22] relying on the intuitively appealing idea of preferential attachment. These processes, have been extensively studied in [21,23].

While models of preferential attachment provide an explanation of the prevalence of scale-free networks, the models are largely endogenous and do not take account of global exogenous selection pressures which might shape the form of evolving and growing networks. Such selection pressures would be especially relevant in a biological context. Recent measurements of the topological properties of graphs representing the metabolic networks of 43 organisms have demonstrated their scale-free nature [14]. These metabolic networks are a rare example of different graphs of varying size shaped by similar selection pressures, and allow the testing of explanations for their generic features.

The main selection-based explanation [14,22] for the metabolic network topologies relies on the fact that scale-free networks are robust with respect to random malfunction of nodes [1]. Robustness is identified with the diameter of the network, and scale-free networks maintain their diameter when nodes are eliminated at random. However, while scale-free graphs are robust in this sense, it has not been shown that robust graphs must be scale-free. This leaves lingering the question of why metabolic networks are scale-free.

In this paper we consider the evolution of random graphs under the constraint that the diameter remain constant as the graph grows. We show if the graph maintains the form of its link distribution it must be scale-free with exponent between 2 and 3. These uniqueness results may help explain the (apparently universal) scale-free nature of graphs, of varying sizes, representing the evolved metabolic pathways of different organisms. Our assumptions and results are consistent with experimental findings.

We first present a brief introduction to the study of metabolic networks, review the findings of previous investigations, and present the basic definitions necessary for the rest of the paper.

A cell is a complex system composed of numerous organic constituents thickly interwoven in a web of reactions. The processes underlying the life of the cell, which include the generation of mass and energy, and information transfer, are a result of this network of complex interactions [3].

Much work has been done on understanding the control processes underlying the workings of a cell [1,10]. However there are many open fundamental questions. While it is of importance to uncover the fundamental design principles underlying the organization of a cell, progress in this direction has been limited because of the immense complexity and the lack of good abstractions which capture certain aspects of the large scale organization.

One possible abstraction of this web of interactions is to represent the gamut of chemical reactions by a graph, where each node represents a chemical constituent of the cell and a directed edge from one chemical constituent to another constituent B implies that B is a product of a reaction between A and other chemical constituents. Such a graph representation is referred to as a metabolic network.

Large scale sequencing projects have furnished integrated pathway-genome databases [8,15,9] from which metabolic networks can be inferred.

Recently, such databases have been used [14,22] to analyze the topological properties of the metabolic networks of 43 different organisms including E-coli (bacterium) and Caenorhabditis elegans (eukaryote). They found remarkable similarities in these properties. In short they found that these networks were uniformly scale free with exponents between 2 and 3.

We present now a brief recap of basic definitions necessary to understand our results.

A Directed Graph \( G(V,E) \) is a collection of points V connected by edges E such that each edge points from one point to another. We will also use the word node to denote a point in the graph.

The \textit{degree} of a node is the number of edges attached to it.

The outgoing degree is the number of edges going out and the incoming degree is the number of edges coming in.

The \textit{link distribution} \( p(k) \) of a graph is the probability
that a given node chosen at random has \( k \) edges going into it or going out. Note that there are two different link distributions ingoing and outgoing.

The diameter of a graph is the average number of steps in takes to go from a node to any other node. The quantity \( E \) from a node the resulting node is a high degree node is higher than if following a link chosen at random, the probability that this is because high degree nodes have more links. Thus, a node \( A \) on a graph, the expected degree of a node \( B \), found by a random edge traversal, will in general be different from the average degree of the graph. This is because high degree nodes have more links. Thus, following a link chosen at random, the probability that the resulting node is a high degree node is higher than if the node was chosen at random.

We now impose the constraint that the diameter is constant as the graph grows. This amounts to demanding that \( D \) be independent of \( N \) in equation (3). This would be constant with respect to \( N \) if the denominator scales as \( \log N \), i.e.

\[
\log E = \alpha \log N
\]

where \( \alpha \) is a constant. Equation (4) implies

\[
E = N^\alpha
\]

Note that \( \alpha \leq 1 \). This is because no node can have degree greater than the total number of nodes, \( N^\alpha \leq N \) or \( \alpha \leq 1 \).

Now we have because of (4) and (3)

\[
\frac{\int_{k_c}^{k} k^2 p(k) \, dk}{M_1} = N^\alpha
\]

where \( k_c \) is the largest degree in the graph.

Since \( N \) is a variable here, we can differentiate both sides of (1) with respect to \( N \) in order to say something about the relationship between the various quantities. Note that \( k_c \) is dependent on \( N \) in some way. This differentiation gives an equation entirely in terms of \( k_c \), since the derivative of the integral depends only on the value of the integrand at the endpoints.

Differentiating the left-hand side of (1) gives

\[
\frac{\partial}{\partial N} \left( \frac{M_2}{M_1} \right) = \frac{1}{M_1} \left( \frac{\partial M_2}{\partial N} - \frac{M_2}{M_1^2} \left( \frac{\partial M_1}{\partial N} \right) \right) \tag{7}
\]

For a normalizable distribution \( M_2 \geq M_1^2 \) by definition. In the worst case, when \( M_1 \) is the largest it can be, \( M_2 = M_1^2 \). Substituting into (7), the first term is \( 2 \frac{\partial M_1}{\partial N} \) and the second term is \( \frac{\partial M_1}{\partial N} \). Thus, in the worst case, neglecting the second term does not change the scaling of the left-hand side of (1) with respect to \( N \). We may thus simplify our equation by dropping the derivatives of the integrand at the endpoints.

The resulting equation is:

\[
k_c^2 p(k_c) \frac{\partial k_c}{\partial N} = \alpha a N^{\alpha-1} \tag{8}
\]

To derive the nature of \( p_k \) we need to know something about the dependance of \( k_c \) on \( N \). We observe that the expected degree \( E \) of a node chosen at random will always be smaller than the largest degree \( k_c \). Also note that the largest degree \( k_c \) will be smaller than the total number of nodes \( N \). Thus \( k_c \) is bounded below and above by power laws

\[
E \approx N^\alpha \leq k_c \leq N \tag{9}
\]

which means that \( k_c \) itself will scale with \( N \) as a power law according to some intermediate exponent \( \beta \) as \( k_c = bN^\beta \) where \( \alpha \leq \beta \leq 1 \).

Putting this into (6) we get an equation describing the function \( p(\cdot) \) in terms of \( N \).

\[
p(bN^\beta) = \left( \frac{a}{b^\beta} \right) \frac{1}{N^{\beta - \alpha}} \tag{10}
\]

Substituting \( bN^\beta = x \) we get

\[
p(x) = \left( \frac{ab^{1+\frac{\alpha}{\gamma}}}{x^\gamma} \right) \frac{1}{x^\gamma} \tag{11}
\]

where \( 2 \leq \gamma = 3 - \frac{\alpha}{\beta} \leq 3 \). This shows that under the constraint that a growing graph has a constant diameter the probability distribution assumed constant in functional form \( p(x) \) must have a power law distribution where the probability of a node having \( x \) links is inversely proportional to \( x \) with an exponent \( \gamma \) between 2 and 3.

We next consider our results in the context of evolved metabolic networks. Jeong, et. al. [14] have measured
link distribution, average degree and diameter for the metabolic networks of 43 different organisms. That they found the link distributions to be uniformly scale-free with exponents between 2 and 3. Furthermore, they found that the diameter was constant with respect to size (see Figure 2).

The fact that the metabolic network diameter is constant across sizes suggests an evolutionary selection pressure on the organism as it evolved. Our results suggest that such a constant diameter constraint (the possible biological reasons for which we discuss later) leads to a scale-free link distribution with exponents between 2 and 3, as has been observed. Thus, our results help to explain why such networks are likely to be scale-free.

We now justify the various formulae and assumptions used in the derivation. Figure 1 shows the metabolic network diameters as a function of the size of the network. As is evident, the diameter is constant across sizes at around 3.4. According to the Newman, et. al. formula 29, the diameter for these graphs should be around 3.29. Since these quantities are close it means that the Newman et. al formula applies.

For further validation of our underlying assumptions, Figure 2 demonstrates that for these data, the cutoff \( k_c \) does scale algebraically with \( N \) (consistent with our assumption that \( k_c \approx N^{\beta} \)). In the figure \( k_c \) has been obtained from the graph data by using the average degree \( d \) and the exponent of the power law \( \gamma \), which are all related by the formula \( d = \sum k p_k \approx \frac{1}{\gamma - 2} \left(1 - \frac{1}{k_c^{\gamma - 3}}\right) \).

Figure 3 shows the variation of the average outgoing degree for the metabolic networks on a log-linear plot. Because the data is approximately linear on a log-linear scale, we conclude that the average outgoing degree is proportional to \( \log(N) \), confirming that the variation of the average degree \( (M_1) \) is weak as we have assumed in the proof.

Figures 1-3 show that the formulae and the assumptions used to derive the scale-free nature hold true for metabolic networks. Our reasoning for the scale-free link distribution observed is consistent with measurements.

Further we provide some biological reasons as to why metabolic networks might be constrained to have small constant diameters. With more steps in the network, pathways are longer. For \( A \) to be converted to \( B \) it takes more steps. Because the driving force at each reaction in the cell gets smaller on average, under this scenario (long pathways) the cell would be inefficient at doing its job. It has been shown that certain metabolic paths (ie routes leading from a chemical \( A \) to a chemical \( B \)) are the shortest possible to carry out a transformation; other pathways can be designed, but involve more steps and intermediates.

According to Fell 25 minimizing transition times between different states, and reducing the time for perturbations to die out, is a consideration. Watts 24 has shown that perturbations die out rapidly in networks with small diameters. Thus having small diameters would reduce transition times between different states, suggesting a selective advantage to maintaining the network diameter.

Another reason for maintaining network diameter relates to the minimization of metabolite concentrations 4. With hundreds of metabolites in cells, their average concentration must be kept low to avoid osmotic and solvation problems. Some metabolites are even toxic if allowed to accumulate. A small diameter leads to quick dissipation.

We have presented a plausible reason for the scale-free
distribution observed in metabolic networks, with our assumptions and conclusions being consistent with experiments and with other biological facts. Our argument addresses the issue of why robust networks are likely to be scale-free. Combined with endogenous models of preferential attachment, and the error tolerance of scale-free networks, our results help explain the prevalence of scale-free networks in selective environments.

FIG. 3. Showing the average degree vs $N$ on a log-linear plot. The figure shows that the average outgoing degree is logarithmic with respect to $N$.

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