The Impact of Persistence Length on the Communication Efficiency of Microtubules and CNTs

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Abstract. There are similarities between microtubules in living cells and carbon nanotubes (CNTs). Both microtubules and carbon nanotubes have a similar physical structure and properties and both are capable of transporting information at the nanoscale. Microtubules and carbon nanotubes can also self-organize to create random graph structures, which can be used as communication networks. The behavior of microtubules can be understood by investigating the behavior of their synthetic counterparts, namely, carbon nanotubes (CNT). At the same time, networks of CNTs may be used for molecular-level transport in the human body for treatment of diseases. This paper seeks to examine the basic properties of the networks created by CNTs and microtubules. This behavior depends strongly on the alignment of bond segments and filaments, which in turn depends on the persistence length of the tubes. Persistence length is also important in analyzing other structures such as DNA; however, the focus in this paper is on nanotube structures and microtubules. We use graph spectral analysis for analyzing a simulated CNT network in which a network graph is extracted from the layout of the tubes and graph properties of the resultant graphs are examined. The paper presents the results of the simulation with tubes of different persistence lengths.

Keywords: Biology, Networks, Microtubules, Molecular Communication, Carbon Nanotubes, Communication Networks, and Sensor Networks.

1 Introduction

One of the most promising applications of nanotechnology is nanomedicine in which nanoscale devices are used for improved therapy and diagnosis. Nanodevices have the potential to deliver therapeutic agents, serve as detectors for disease, and correct metabolic pathways to prevent diseases. Given their size, they can also seek out specific cells or invading viruses, release localized drugs to minimize potential side effects of generalized drug therapy, or bind to a target preventing further activity. Significant research is being conducted to examine the impact of nanomaterials in biological applications [1], [2], [3], [4], [5], [6]. Despite the significant investment in this research, use of nanotechnology for therapeutic applications still lags the promise. Fundamental properties of such structures need to be established prior to conception of practical applications. One of the most promising nanostructures is the carbon

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nanotube (CNT). Unique mechanical and electronic properties of these materials have enabled a variety of applications ranging from novel composites [7] to electronic circuits [8] and sensors [9]. Due to their small size, nanotubes can reach deep into their environment without affecting the natural behavior of the environment. For example, a single CNT is small enough to penetrate a cell without triggering the cell's defensive responses.

Networks of CNTs can be used as a substrate to generate, route, and transport information when a subset of tubes are functionalized (e.g. with quantum dots) just as networks of microtubules serve as a substrate for the transportation of molecular motors (where molecular motor cargo is considered as information) within the body. Microtubules are cytoskeletal biopolymers, which are a close biological counterpart to nanotubes that perform these functions in living organisms. Microtubules and CNTs have [10] similar structures; both are hollow, thin-walled tubes with a high aspect ratio and are very efficient for bearing loads. Microtubules provide mechanical stability for the cell, including holding its shape during cell migration, and providing tracks for intracellular transport. Microtubules are one hundred times stiffer than other cellular components and have a high degree of resilience. CNTs are extremely stiff, with a Young's Modulus five times higher than steel. Similar to microtubules, they are also highly resilient. While the chemical composition of microtubules, which is comprised of proteins and non-covalent bonds, differs from CNTs, which are comprised of carbon and covalent bonds, their mechanical behavior is quite similar. Both microtubules and CNTs spontaneously assemble into bundles. In addition, microtubules and CNTs share electrical properties, namely, both have conductances that have been carefully measured. The flow of current through microtubules and CNTs is a different process, namely microtubules use an ion channel while CNTs are either semi-conducting or metallic. Current flow through microtubules was measured in [11] to be approximately 9 nS (nano-Siemens) at a rate of approximately 1.0 m/s and exhibits an amplification effect. Also, both are impacted by magnetic fields and free-floating microtubules can be steered via a magnetic field. Microtubules naturally self-assemble, while controlled self-assembly of CNTs is possible by amino acid coating [12], [13].

Individual CNTs are weak and unable to perform complex tasks, however, through self-organization; networks of CNTs can exhibit sophisticated behavior and perform complex tasks. Self-organization typically occurs in microtubules and CNTs through supra-molecular interactions, which are short-range forces between the molecules that are too weak to cause intermolecular changes or bond formation, but sufficient to cause elastic deformations of microtubules and CNTs [14], [15]. The persistence length and isotropy of nanotubes is directly correlated to such forces and is a major factor in determining graph properties resulting from self-organization of CNTs. CNT networks can be used as a substrate to transmit information across nano-sensors and thus, provide connectivity across sensors. Analogously, microtubule structures are used for transport of molecules across the network. In a cell, small molecules such as gases and glucose diffuse to where they are needed. Large molecules synthesized in the cell body, intracellular components such as vesicles, and organelles such as mitochondria, are too large to diffuse to their destinations. Motor proteins transport these large structures to their required destinations. Motor proteins such as kinesins walk along microtubule tracks carrying their cargo.

The stepping motion of molecular motors on microtubule rails is due to a small conformational change in a molecular complex powered by ATP hydrolysis. In simple terms, the motor has two heads (more like feet, but they are known as heads) that alternately bind and release from microtubule binding sites. The binding sites are like steps on a ladder. When a head releases from the microtubule binding site, it swings forward, landing on the next binding site on the microtubule. The process is then repeated with the other head releasing and swinging forward while the current head remains attached. More specifically, a head is bound to the microtubule via ATP. The loss of the γ-phosphate group from ATP leaves a space of approximately 0.5 nm. This is thought to cause a rearrangement of structural elements flanking the ATP-binding site [16]. Ultimately, this loosens the head from its binding to the microtubule allowing it to swing forward along a lever comprised of an α-helix of variable length. The lever swings the head through an angle of up to 70˚. The lever swing is believed to be the ultimate cause for the working stroke; motors with longer necks take larger steps and move faster.

By investigating the behavior of these networks, we hope to understand the behavior of naturally occurring microtubule networks within the human body. Understanding the nanotube network properties within the context of individual nanotube attributes will assist in the design of nanotube networks. For instance, changing the persistence length of the tubules can control the connectivity of nanotube networks. Such custom-designed networks will help us control the latency and bandwidth of transmission of information in nanotube network applications. We are examining the behavior of general nanotube networks, both CNT and biological microtubules with regard to information transport. The next section describes the simulation results that examine the nanotube network properties in context of the attributes of individual nanotubes.

There are several interesting applications associated with CNT networks and nano-bio applications such as detection of cancer cells, delivery of drugs, and slowing propagation of diseases. We investigate four specific problems associated with the design of CNT networks and through them the behavior of microtubule networks. 1) The impact of network topology (whether CNT or microtubule) on the efficiency of information flow, i.e. maximizing bandwidth. We specifically examine properties such as isotropy and persistence length of individual CNTs on the behavior of the resultant network. This will help in design of ad-hoc nanoscale networks and understanding the behavior of microtubule communication networks within the human body. 2) Maximizing sensitivity to change, i.e. making a sensitive detector. We envisage using a CNT network as a substrate to nano-sensors for transmitting sensor information. The expectation is that an activated sensor will release energy that will alter the resistance of the CNT network preferentially in a localized area within the substrate. By analyzing the behavior of the CNT network, we will be able to discern the activation of different sensors. The change in transport of molecular motors based upon changes to microtubule topology can also be used for detection of mitotic catastrophe in cancer treatment (microtubule malfunction). We look at the rate of change of measurable network properties (resistance and graph walks of molecular motors) corresponding to the persistence length of the nano-networks. 3) Information capacity of a CNT network with a given topology. A CNT network can be used to encode and store information within the network topology. This information could be use to process the sensor information obtained by the network and perhaps

for computation of self-organization based upon the information content of the topology. For this, we introduce a graph entropy measure. 4) Latency of transport within a network. The goal is to understand the behavior of molecular motors such as kinesin on microtubules within the cell with a goal to use these molecular motors as part of a nanoscale Internet within the human body. The topology of the network will have an impact on the latency and rate of delivery of information as well as targeted drugs in the body.

2 The Nanotube Network Simulation

In this work, the impact of persistence length and isotropy of CNTs on graph properties is initially examined and subsequently latency and bandwidth of such networks in molecular transport. Metrics, namely autocorrelation and persistence area are proposed to help characterize and analyze nanotube network structures. This work is based upon prior work by Bush and Goel [17] that shows the impact of random tube characteristics of location and angle on the behavior of a CNT network. In the previous work, single-walled carbon nanotubes (SWNT) are modeled as linear tubes positioned in two dimensions via central coordinates with a specified angle. A network graph is extracted from the layout of the tubes and the ability to route information at the level of individual nanotubes is considered. A similar approach for examining the impact of CNT properties on the graph attributes is used here.

Persistence length quantifies the degree of bending in microtubules. Briefly, the persistence length is the rate at which the tangents taken along each segment of a microtubule become decorrelated from one another. If *R(s)* is a point on a segment *s*, then let *u(s)* be the unit tangent vector,

$$u(s) = \frac{\partial R}{\partial s} \ . \tag{1}$$

The orientations of the unit tangent vectors for all segments *s* is quantified by the inner product,

$$\langle u(s) \cdot u(0) \rangle = e^{-s/\xi_p} \ , \tag{2}$$

where ξ_p is the persistence length. For longer persistence lengths, or for shorter tubes, the microtubules will be straighter. For longer tubes or shorter persistence lengths, the impact of de-correlation along the chain tangent becomes more significant. We can approximate the curved microtubules as many smaller random chains that happen to be connected end-to-end, but with de-correlated alignment. Thus, shorter persistence lengths will tend to decrease the percolation threshold, which is important in the explanation of network conductance that follows. Persistence length becomes important in applications of nanotubes in photovoltaics, fuel cells and electronic components such as transistors, primarily due to longer lengths having greater electrical resistance. The persistence length of a microtubule has been estimated to range from 0.2 to 5.2 mm, while the persistence length at the tip of a microtubule has been found to be much shorter [18]. The rigidity and persistence length of microtubules has been found to be sensitive to various chemicals and related to various diseases [19], [20], [21].

In Figure 1, networks of tubes with different persistence lengths have been simulated. Networks of tubes with low persistence length tend to be tightly curled and contain a high density of tube segments. Networks comprised of tubes with higher persistence lengths cover a larger area and the tube segments are less dense. The tubes are positioned on a two-dimensional coordinate system. The mean persistence length of each tube is used to characterize the entire network. A source contact in green (vertical line at $x = 0$) and drain contact in blue (vertical line at $x = -10$) are also shown. The electrical resistance from the source to the drain is measured for each nanotube network. As shown in the figures, the position of the source and drain remain constant in each network. The tubes are positioned randomly within an area centered between the source-drain contacts. When the tubes are perfectly straight, they are parallel to one another across the source-drain contacts.

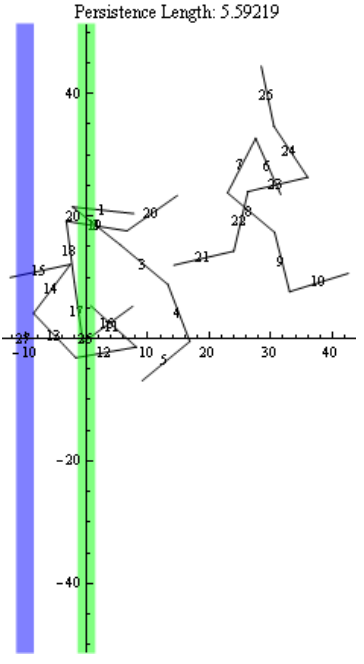
In the network simulation, tubes that overlap in two-dimensional space create a network vertex. Figure 2 shows the number of vertices in the graph due to intersecting tubes as a function of persistence length. An observation of interest is that our simulations show a decreasing trend for connectivity versus persistence length.

Specifically, with very low persistence length, the total network connectivity is high due to a tendency for the individual tubes to coil up. As the persistence length increases, it reaches a point where the tubes are nearly linear and aligned, the networks lose connectivity again. The impact of persistence length on connectivity becomes important when designing CNT networks to control the rate of dissemination and transmission within the network. It's interesting to note the relationship between persistence length and the autocorrelation function, which is shown in Equation 3 where τ represents lag. Note that with zero lag and without the denominator, the autocorrelation reduces simply to the variance. In relation to persistence length, the random variable is the tube segment angle. As the variance is reduced, the tubes become longer, spread out over a larger area, and there is a lower density of tube segments per unit area.

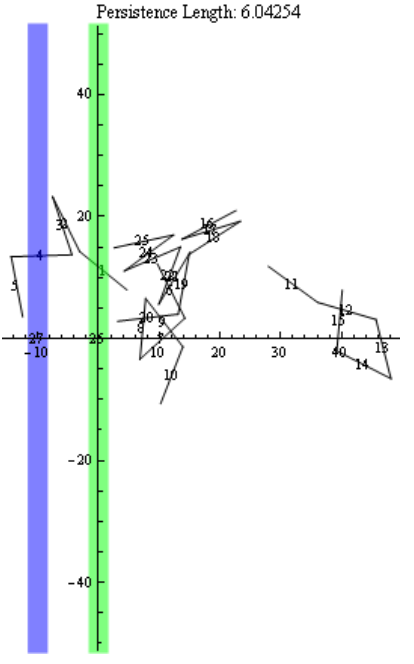
$$R(\tau) = \frac{E\left[(X_t - \mu)(X_{(t+\tau)} - \mu)\right]}{\sigma^2} . \tag{3}$$

The autocorrelation of one of the tube's angles is shown in Figure 3. The exponential decline in the autocorrelation as the lag is increased corresponds to the mean change in angle correlation as distance increases, where the distance is as defined in persistence length.

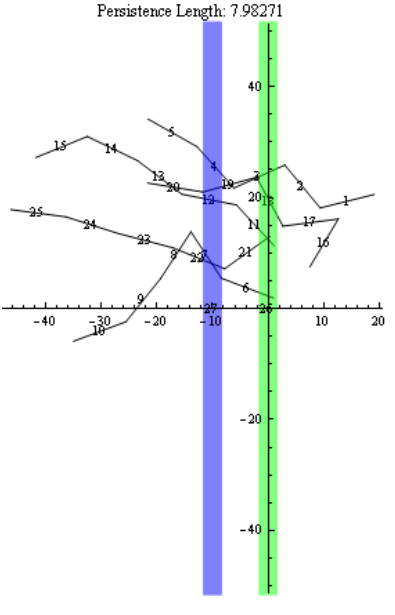
A key component of the tube layout is the overall directionality of the tubes, that is, the angle of each tube relative to all other tubes. Isotropy is a global measure of this directionality. Isotropy quantifies the directionality of the tubes and is defined in Equation 5, where l is the tube length and α is the tube angle. Tubes that are almost aligned have a high isotropy and tubes that are randomly oriented have a low isotropy. Isotropy measures the alignment of all segments within the network and differs from persistence length, which was developed to measure the alignment of segments comprising individual tubes. In this paper, we introduce a new measure, known as persistence area, which is similar in nature to persistence length, but operates in two-dimensions instead of one. Persistence area is defined as shown in



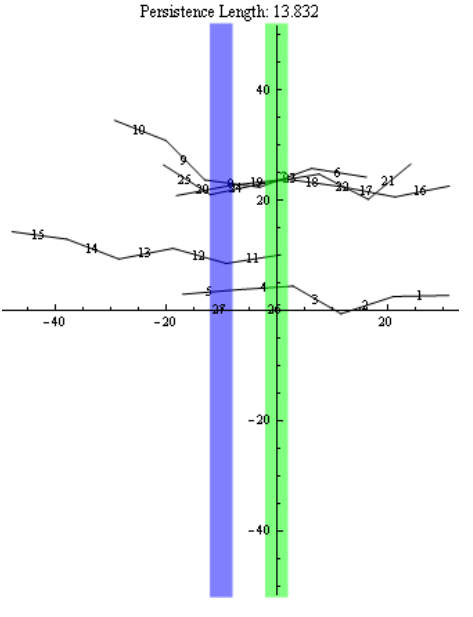
(a) Low persistence length



(b) Moderate persistence length



(c) High persistence length



(d) Very high persistence length

Fig. 1. Networks as a function of increasing persistence length

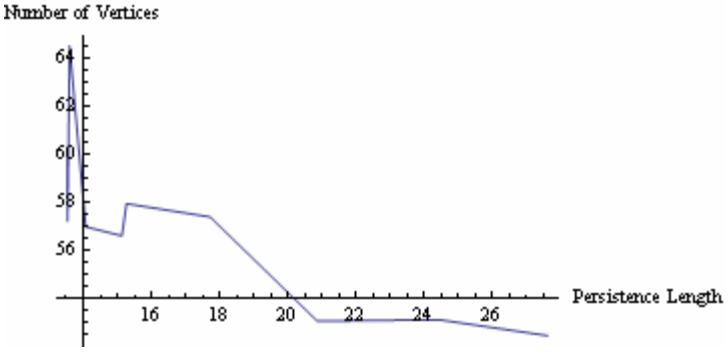


Fig. 2. Number of network vertices as a function of persistence length

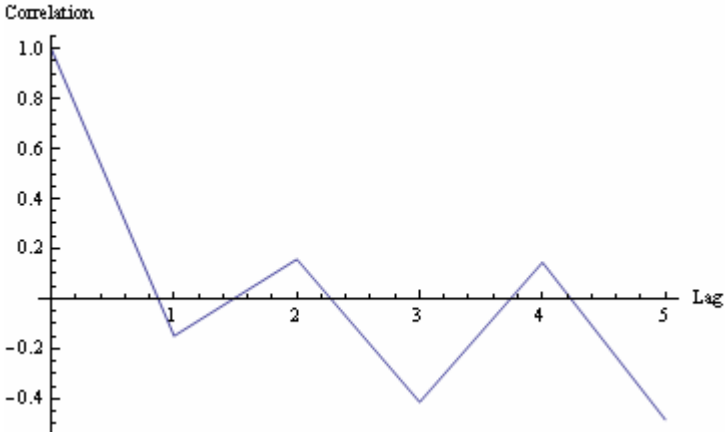


Fig. 3. The autocorrelation of a tube's angles

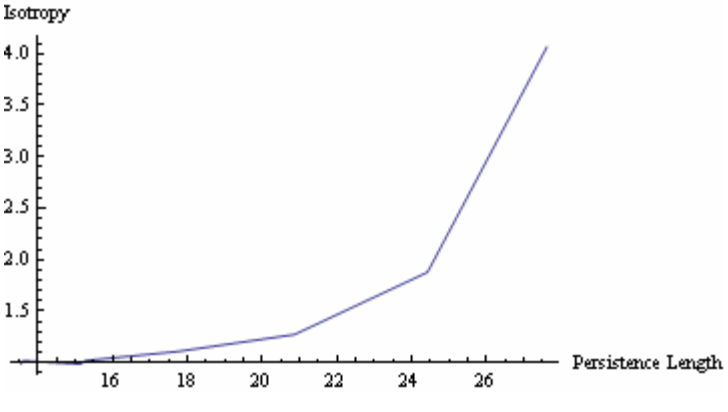


Fig. 4. Isotropy as a function of persistence length

Equation 4, where both r and α_v are radii of circular areas extending from each point in the area of interest.

$$\langle u(r) \cdot u(0) \rangle = e^{-r/\alpha_p} \ . \tag{4}$$

$$isotropy = \frac{\sum l \cos(\alpha)}{\sum l \sin(\alpha)} \ . \tag{5}$$

A combination of isotropy and persistence length can be used for controlling the connectivity of the CNT network. The number of network vertices, due to connected or overlapping tube segments is shown in Figure 5 as a function of both persistence length and isotropy. Having two measures of control makes manufacturing of CNT networks to specification easier.

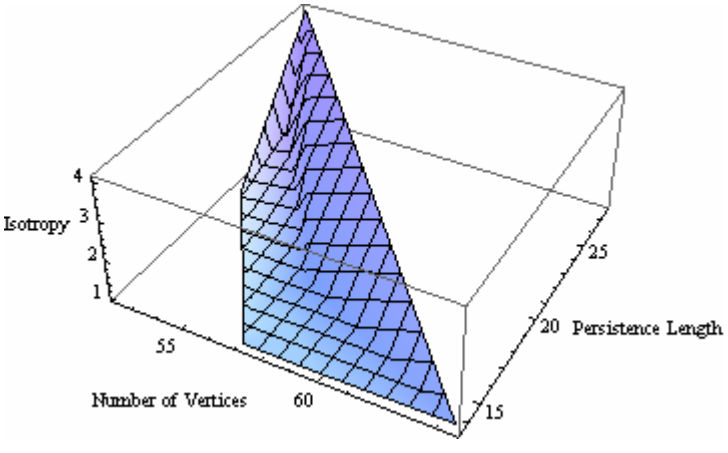


Fig. 5. Number of network vertices as a function of persistence length and isotropy

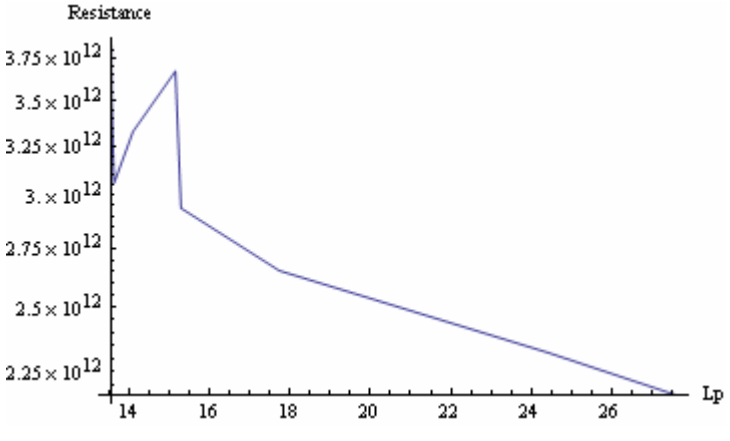


Fig. 6. Resistance as a function of persistence length (Lp)

Resistance is another key attribute for a CNT network since it is often used as a measure of change in sensor devices. Especially important is the rate of change of resistance to stimuli in the network, which determines the resolution of network. In Figure 6, the resistance to current flow is plotted as a function of the persistence length and shows an almost linear monotonically decreasing function (except for an initial spike). This makes the sensing more accurate and reliable.

The resistance of the network as a function of persistence length and the isotropy is shown in Figure 7. Again these two levers can be used to effectively control the resistance range of the CNT network.

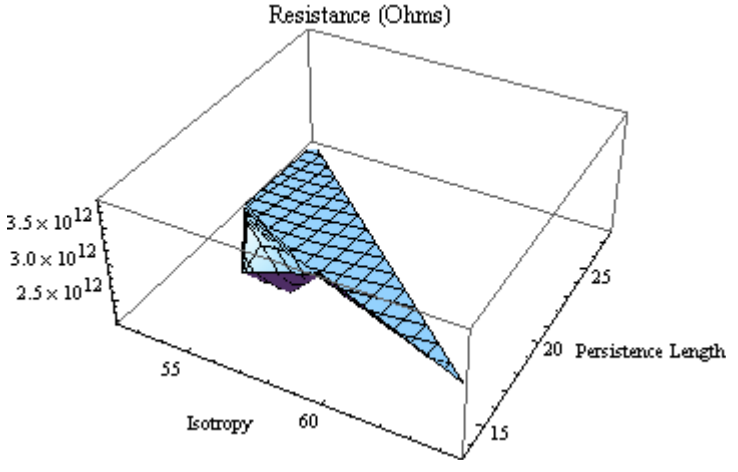


Fig. 7. Resistance as a function of persistence length and isotropy

Let us switch our focus from resistance to molecular motors operating on the same set of networks that were used to obtain the resistance measurements. The operation of molecular motors was discussed in the introduction. However, we should note here that a precise understanding of how molecular motors choose which direction to take when confronted with an intersection is still an open research problem. We choose to take a maximum entropy approach (that is, assume as little a priori knowledge as possible) and simulate the motors with a random walk. The motor chooses whether to proceed forward or turn at any road of intersection with equal likelihood. In Figure 8, a molecular motor performs a random walk along the network. The initial location of the motor is randomly chosen from a set of vertices at one end of the network, and the target destination for the motor is randomly chosen from a set of nodes at the opposite end of the network. A highly connected network should allow for a rapid traverse of the distance from source to destination. The expected percent distance from source to destination is shown after 1000 steps, where a step is a movement from one intersection to another. Clearly, shorter persistence length networks allowed for more efficient transport.

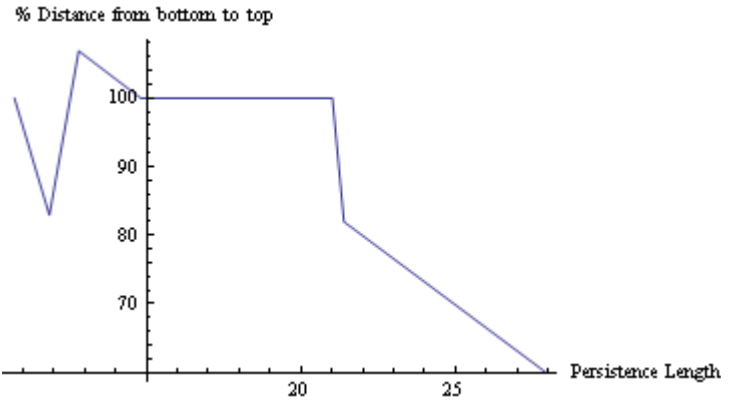


Fig. 8. The percent of distance traveled from the source to the target as a function of persistence length

3 Graph Information Theory

A network contains information within its structure, as well as potentially transports information over its structure. A new field of graph information theory has been suggested in the past and could provide useful techniques for reasoning about and analyzing the information content of network structures. There have been attempts to define graph entropy in the past via different approaches, namely, Korner's graph entropy [22] and others based upon the Shannon capacity of a graph [23]. However, these approaches are primarily based upon using graphs as an aid to advancing information theory. Here we suggest the reverse, using information theory to aid the understanding of graph structure. As we mentioned, there is information embodied within the structure of a graph that could reveal better insight into the topics we've examined in this paper.

Let us assume the tractable case of a normal distribution of tube angles. Equation 6 shows the information entropy of a normal distribution. It should be noted that a maximum entropy probability distribution is a probability distribution whose entropy is at least as great as that of all other members of a specified class of distributions. Thus, if little is known about a distribution, then, by default, the maximum entropy distribution is often chosen. This is known as the principle of maximum entropy. Maximizing entropy minimizes the amount of a priori information assumed by the distribution and it's interesting that physical systems tend to move toward maximal entropy configurations over time, which is perhaps a form of self-organization.

$$H_{normal}(\sigma) = \ln(\sigma\sqrt{2\pi e}) \tag{6}$$

It is conjectured that the information entropy within the tube chain and network structure can be captured in this manner. In this case, σ is the standard deviation of the tube angles. The information content of each tube is its variance from the mean, or its amount of decorrelation from neighboring tubes. As the graph entropy as defined here approaches zero, a network becomes unlikely to exist, as tubes are not likely to

overlap as they become parallel. As the graph entropy increases, more tubes are likely to overlap and the network structure becomes more complex (see Figure 9). As the graph entropy defined here increases further, the information in the graph begins to level out, that is, as the graph becomes fully connected, each additional tube connection adds less overall information.

This includes the notion that information may not only be conveyed in the tube network, but also hidden via steganographic means. The autocorrelation of a signal can reveal hidden periodic signals, thus autocorrelation of a tube chain can reveal hidden information within the tube angles.

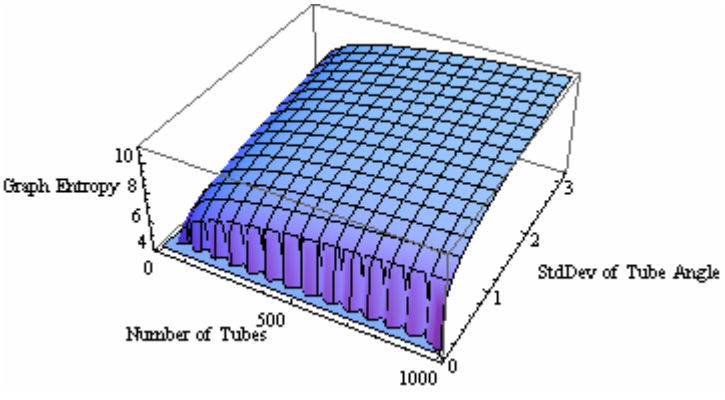


Fig. 9. Graph entropy of network versus number of tubes and tube angle

In Figure 10, Equation 6 is used to compute the entropy of the graphs simulated in this paper versus the expected persistence length of the tubes in each graph. As expected, the entropy is greater for shorter, more tightly curled – thus, random networks, and decreases as the tubes align.

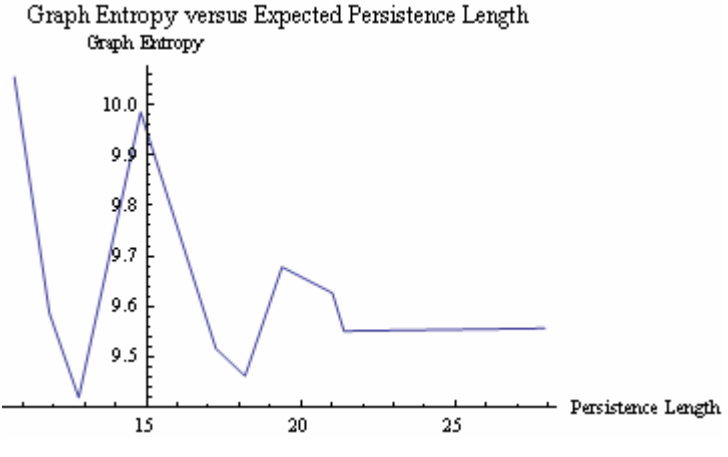


Fig. 10. Graph entropy of networks used in this paper

4 Conclusion

Rapid advances in nanotechnology have enabled science to operate at the cellular level with promise for improved therapy and diagnosis. There is remarkable similarity between nanostructures and cellular components. Fields of cellular biology and nanotechnology can both benefit from shared congruent objectives of human medicine. In this paper, we examine the analogy between microtubules, which form the skeletal structure of cells, and carbon nanotube networks. By examining the behavior and properties of CNT structures we seek to understand the natural behavior of microtubules and also develop artificial structures for sensing and drug delivery in the human body. We extract a network graph from a random CNT structure to examine its properties such as connectivity and resistance in relation to the persistence length and isotropy of CNTs that are used to construct these networks. We also examine the behavior or molecular motors in a random walk along CNT structures analogous to the locomotion of kinesin across microtubules in a living cell. Finally, we examine the information capacity of CNT networks in relation to individual CNT properties. We believe that computation, storage, and transmission will all come embedded in the CNT network. Understanding the behavior of individual CNT properties in relation to the resultant CNT network will assist in development of novel applications based on CNT networks.

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