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A Review of Polymer Physics and Potential Applications to Radiation Biophysics and Neurodegenerative Disorders

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Abstract

Polymers are an essential aspect of molecular biology and biochemistry. The most significant of macromolecules involved in biological processes and phenomena are polymers. In this article, we provide a comprehensive summary of the proposed physical models for the configuration of polymers. Such physical models include the freely-jointed chain, freely-rotating chain, worm-like chain, and the Gaussian chain model. We then connect these models to the existing models regarding the radiation biophysics of DNA damage, as well as to the damage of RNA molecules, and provide an insight into future areas of research in the subject areas. The conclusion is that polymer physics and the Linear-Quadratic model can be used for future biophysical research in cancer and neurological disorders. Through such connections, we hope to provide a potential future insight with regards to biophysical research in cancer and neurodegenerative disorders.

1 Introduction

1.1 A Brief Introduction to Polymers in Biology

A polymer is a molecule that consists of many repeated molecules in a “chain-like” manner. Each one of these repeated units are called *monomers* ([3], [5]). In biological processes, polymers are produced through a *dehydration reaction*, and

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split through the process of *hydrolysis*. All of nucleic acids, proteins, and carbohydrates are polymers. Nucleic acids are made up of monomers called nucleotides. Proteins are made up of monomers called amino acids. And carbohydrates are made up of monomers called monosaccharides. Polymers have a vast range of applications in biological research, including genomics, proteomics, toxicology, and also have applications in the bioengineering industry.

1.2 Overview of DNA and RNA

Source [5] serves to give a solid overview of DNA and RNA molecules. DNA, which fully stands for *deoxyribonucleic acid*, is a polymer consisting of a repeated chain of many monomers called *nucleotides*. An individual nucleotide consists of three main aspects:

1. A nitrogenous base, which can be any of Adenine (A), Thymine (T), Cytosine (C), and Guanine (G)
2. Deoxyribose pentose sugar
3. A phosphate group

Together, the deoxyribose sugar and phosphate group serve to make up the backbone of a nucleotide. The nucleotides are bonded to each other through *phosphodiester bonds* between the sugar and phosphate in the backbones of adjacent nucleotides, which make up the overall backbone of DNA. This proves to be significant when discussing DNA damage and radiation biophysics in Section 3.1. In general, there are two strands of DNA that are joined together through hydrogen bonds between the nitrogenous bases. Together, these two strands of DNA gives the overall DNA molecule a double-helix shape. While DNA is double-stranded, only single-stranded breaks for a DNA molecule are discussed in this paper. RNA, which stands for ribonucleic acid, is quite similar to DNA, but has slight differences. Perhaps the biggest difference is that RNA is a single-stranded molecule. Therefore, only single-stranded breaks can occur in RNA molecules. Furthermore, thymine from DNA is replaced by a nitrogenous base called *uracil* in RNA. Also, while DNA contains the deoxyribose sugar in its backbone, RNA is made up of ribose sugar. RNA is significant in a variety of neurodegenerative disorders ([9]), and is therefore significant in research regarding the pathology of such disorders.

2 A Review of Core Concepts in Polymer Physics

Here, we provide a comprehensive summary, along with the derivations, of some of the main theoretical model regarding the physics of polymers. They are best described in sources [6], [7], and [8].

2.1 The Freely Jointed chain

The freely-joined chain (FJC) is the simplest mathematical model for a polymer. Comprehensively, the FJC consists of N segments, each segment denoted as $\vec{r_i}$, each of a fixed length b. Furthermore, $\vec{R_i}$ denote the position vectors for the nodes of the polymer. From this:

$$\vec{r_i} = \vec{R_i} - \vec{R}_{i-1}. \tag{1}$$

Furthermore:

$$|\vec{r_i}| = b. \tag{2}$$

Since each position vector can point in a random direction, letting $\vec{R}$ denote the overall end-to-end vector:

$$< \vec{R} >= \sum_{i=1}^{N} < \vec{r_i} >= 0. \tag{3}$$

Looking at the mean-squared end-to-end distance gives:

$$< R^2 >=< \left(\sum_i \vec{r_i} \right) \left(\sum_j \vec{r_j} \right) > . \tag{4}$$

Since the position vectors have a fixed magnitude b, equation (4) can then be written as:

$$< R^2 >= \sum_{i=1}^{N} < \vec{r_i}^2 > + \sum_{i \neq j} < \vec{r_i} \cdot \vec{r_j} >= Nb^2. \tag{5}$$

From this, the final value is given:

$$\boxed{R = b\sqrt{N}.} \tag{6}$$

From equation (6), R therefore denotes the extension of the polymer chain, a principle known as the *ideal scaling law.* We now look at the FJC through a diffusion-based point of view. Introducing a time t:

$$t = N\tau, \tag{7}$$

where τ denotes the stepping time, the mean-squared distance is given:

$$< R^2 >= 2dDt. \tag{8}$$

Here, D denotes the diffusion constant:

$$D = \frac{b^2}{2\tau}, \tag{9}$$

and d denotes the spatial dimension. In general, a polymer has correlations between the distinct bond vectors present. However, at larger distances, the correlation becomes void, and such polymers are referred to as *ideal polymers.* Therefore, the overall sum of these correlations converges to a finite value when taken to infinity. Therefore, this gives:

$$< R^2 >= b^2 \sum_{i=1}^{N} \sum_{j=1}^{N} < cos(\theta_{ij}) >= C_x N b^2 \tag{10}$$

$$\lim_{x \to \infty} C_x N b^2 \to \boxed{C_\infty N b^2.} \tag{11}$$

Here, C_∞ is *Flory's characteristic ratio*, and has been determined experimentally for many ideal polymers. Next, defining a value L:

$$L = N \cdot b. \tag{12}$$

It can be written:

$$< R^2 >= N \cdot b^2 = b \cdot L. \tag{13}$$

From this, the Kuhn Length for polymers is defined:

$$b = \frac{< R^2 >}{L}, \tag{14}$$

$$N = \frac{L^2}{< R^2 >}. \tag{15}$$

2.2 Freely Rotating Chain

In the freely-rotating chain (FRC) model, both the monomer length and bond angle are kept constant. Therefore:

$$< \vec{r_i} \cdot \vec{r_j} >= b^2 \cos(\theta)^{|j-i|}. \tag{16}$$

Due to the fact that $cos(\theta) < 1$, the series therefore decays in an exponential manner. This can be denoted as:

$$e^{-\frac{b|j-i|}{l_p}}, \tag{17}$$

where l_p denote the *persistence length*, the scale over which the correlations between the bond vectors decay:

$$l_p = -\frac{b}{\ln(cos(\theta))}. \tag{18}$$

Therefore, the exponential decay can be used to find the mean-squared end-to-end distance for the vector. Through mathematical calculations, this mean end-to-end distance can be written as:

$$< R^2 >= b^2 N + b^2 \sum_{i=1}^{N} \left(\sum_{k=1}^{i-1} (cos(\theta))^k + \sum_{k=1}^{N-i} (cos(\theta))^k \right). \tag{19}$$

Since at larger distances, the correlation is decayed essentially entirely, k can be taken to infinity, giving the infinite series:

$$\sum_{k=1}^{\infty} (cos(\theta))^k. \tag{20}$$

Since this is simply a geometric series, the formula $\frac{a}{1-r}$ is applied, giving the sum:

$$\frac{cos(\theta)}{1 - cos(\theta)}. \tag{21}$$

This yields to the final mean-squared end-to-end distance:

$$< R^2 >= N b^2 \left(\frac{1 + cos(\theta)}{1 - cos(\theta)} \right). \tag{22}$$

Therefore, the extension of the FRC finally becomes:

$$\boxed{R = b \sqrt{N \left(\frac{1+cos(\theta)}{1-cos(\theta)} \right)}.} \tag{23}$$

2.3 Worm-Like Chain

In the limit $\theta \to 0$, the persistance length and Flory's characteristic ratio both diverge. Therefore, the Worm-Like Chain (WLC) model is defined in such cases. The mean-square end-to-end distance of the WLC is calculated through the exponential decay of correlations between tangent vectors in the polymer chain:

$$< R^2 >= b^2 \sum_j \sum_i e^{-\frac{b|j-i|}{l_p}}. \tag{24}$$

Taking this in the continuum limit gives:

$$\int_0^L du \int_0^L e^{\frac{-|u-v|}{l_p}} dv. \tag{25}$$

Solving the absolute-value integral through adding the integral with regards to both sides of the absolute value gives:

$$\int_0^L du \int_0^u e^{\frac{v-u}{l_p}} dv + \int_0^L du \int_u^L e^{\frac{u-v}{l_p}} dv, \tag{26}$$

which finally gives the final solution to be:

$$< R^2 >= 2l_pL - 2l_p^2 \left(1 - e^{\frac{-L}{l_p}}\right). \tag{27}$$

Therefore, the extension of the WLC is given to be:

$$\boxed{R = \sqrt{2l_pL - 2l_p^2 \left(1 - e^{\frac{-L}{l_p}}\right)}.} \tag{28}$$

2.4 Bending Elasticity of Polymers

The bending energy of a polymer is denoted as:

$$\boxed{E_{polymer} = \tfrac{YI}{2} \int_0^{L_c} \left[\tfrac{\partial \vec{u}}{\partial s}\right]^2 ds.} \tag{29}$$

Here, $\vec{u}$ denotes the unit vector for $\vec{b}$:

$$\vec{u} = \frac{\vec{b}}{|\vec{r_i}|}. \tag{30}$$

Y is Young's Modulus, and I denotes the moment of inertia:

$$I = \int y^2 dA. \tag{31}$$

Above, y denotes the distance in the direction of curvature, and dA denotes the area. Together, I and Y give the *bending resistance* (also known as *flexural rigidity*) of the polymer.

2.5 Gaussian Chain Model

The Gaussian Chain Model (GCM) serves to give the comprehensive probability distribution for a polymer, making use of the FJC model, and it therefore represents a random walk model for the polymer chain. Letting our chain still have N units, this therefore gives the probability distribution for the segments to be:

$$P(\vec{r_1}, \vec{r_2} ... \vec{r_N}) = \prod_{i=1}^{N} \frac{1}{4\pi b^2} \delta(|\vec{r_i}| - b). \tag{32}$$

From this, the probability distribution for the end-to-end vector can be written as:

$$P(\vec{R}) = \prod_{i=1}^{N} \int P(\vec{r_1}, \vec{r_2}, ... \vec{r_N}) \delta(\vec{R} - \sum_{i=1}^{N} \vec{r_i}) d\vec{r_i}. \tag{33}$$

In the above, equation, it should be noted:

$$\delta(\vec{R} - \sum_{i=1}^{N} \vec{r_i}) = \frac{1}{(2\pi)^3} \int e^{i\vec{k}(\vec{R} - \sum \vec{r_i})} d\vec{k}, \tag{34}$$

is the Fourier integral for the delta function, and is required in order to solve the integral. From this, the end-to-end distribution now becomes:

$$P(\vec{R}) = \frac{1}{(2\pi)^3} \int e^{i\vec{k}\vec{R}} d\vec{k} \left[\int e^{-i\vec{k}\vec{r_i}} \frac{1}{4\pi b^2} \delta(|r_i| - b) d\vec{r_i} \right]^N. \tag{35}$$

Solving the integral inside the brackets gives:

$$\int e^{-i\vec{k}\vec{r_i}} \frac{1}{4\pi b^2} \delta(|r_i| - b) d\vec{r_i} = \frac{1}{4\pi b^2} \int_0^\infty \vec{r_i}^2 d\vec{r_i} \int_0^{2\pi} d\phi \int_0^1 e^{-i\vec{k}\vec{r_i} cos(\theta)} \delta(\vec{r_i} - b) d(cos\theta). \tag{36}$$

Solving equation (36) further yields:

$$\frac{sin(kb)}{kb}. \tag{37}$$

The overall equation now becomes:

$$\left[\frac{sin(kb)}{kb}\right]^N. \tag{38}$$

Taking the limit of N to infinity gives:

$$e^{-\frac{N\vec{k}^2b^2}{6}}, \tag{39}$$

which therefore gives the end-to-end distribution to be:

$$P(\vec{R}) = \frac{1}{(2\pi)^3}\int e^{i\vec{k}\vec{R}}e^{-\frac{N\vec{k}^2b^2}{6}}d\vec{k}, \tag{40}$$

which represents the Gauss integral. Therefore, the final end-to-end distribution for the GCM is given to be:

$$\boxed{P(\vec{R}) = \left(\tfrac{3}{2\pi Nb^2}\right)^{\frac{3}{2}}\exp\left(-\tfrac{3\vec{R}^2}{2b^2N}\right).} \tag{41}$$

The free energy of the chain can be written to be:

$$G = \frac{3\vec{R}^2k_BT}{2b^2N} + c, \tag{42}$$

where c is simply a constant. Assuming that the polymer chain is a Hookean Spring, the potential energy of the chain can be written as:

$$U = \frac{1}{2}kx^2, \tag{43}$$

where k denotes the spring constant. Therefore, the free energy for the polymer chain can now be denoted as:

$$G = \frac{1}{2}kx^2 + c. \tag{44}$$

From this, the *spring constant* for the chain can be denoted as:

$$\boxed{k_{chain} = \tfrac{3k_BT}{Nb^2},} \tag{45}$$

and for a single bond:

$$\boxed{k_{bond} = \tfrac{3k_BT}{b^2}.} \tag{46}$$

3 Potential Applications of Polymer Physics to Radiation Biophysics

3.1 Linear-Quadratic Model of DNA Damage

The Linear-Quadratic Model is a model for the damage of certain critical molecules in a cell, which in our case, is double-stranded DNA molecules. Source [1] serves to provide a detailed explanation of the model with regards to single-stranded and double-stranged breaks in molecules of DNA. In the model, radiation serves to damage the molecules of DNA, known as *lesions*. Suppose that we have n_1 bonds in the first strand of a DNA molecule, and n_2 bonds in the second strand of the DNA molecule, where $n_1 = n_2$. Furthermore, let k denote the probability of bond rupture per bond per unit dose of radiation, and let f_1 and f_2 denote the unrestored fraction of bonds in the first strand and second strand respectively. Letting q denote the number of bonds broken per cell, the number of broken bonds on strand 1 per cell, q_1, is given to be:

$$\boxed{q_1 = f_1 n_1[1 - e^{-kD(1-\Delta)}],} \tag{47}$$

where D denotes the dose of radiation, and Δ denotes the fraction of dose D due to which both strands are broken by one event. From q_1, the number of broken bonds in strand 2 is equal to:

$$\boxed{q_1 = f_2 n_2[1 - e^{-kD(1-\Delta)}].} \tag{48}$$

While the source focuses on double-stranded breaks in the DNA molecules present in a cell, it would be more reasonable to look at each DNA strand individually, since the physical models described for polymers are for one chain individually ([2]). We now provide potential applications of the physical models for polymers discussed previously to such breaks in DNA strands due to radiation.

3.2 Connecting Polymer Physics and Radiation-Based DNA Damage and RNA Damage

From 3.1, the number of bonds that are broken in a DNA strand due to radiation is given mathematically. Such broken bonds in the DNA strands can result in an alteration of the DNA strand's shape, which can be linked to a number of diseases and disorders, the primary one being cancer ([4]). Therefore, using the physical models of polymers discussed in Section 2 would allow to mathematically determine the alterations in the shape of the DNA strands affected, which then lead to cancer. Upon being exposed to radiation, the affected DNA strand would be broken into two or more segments, due to the fact that the bond between the nucleotides are broken. Therefore, equation (6) can be used to approximate the change in the extension of the segments of the DNA strand due to the broken bonds. This would therefore allow researchers to gain a further insight into the changes of the extension of the DNA strand in certain types of cancers. From equation (10), setting a correlation between the distinct bonds in the affected DNA strand could allow to mathematically determine Flory's characteristic ratio for the broken segments of the DNA strand, since the value of Nb^2 can be found by simply finding the square of the strand's extension. Fixing the angle in the affected strand would allow researchers to use the FRC model for polymers discussed in 2.2, which would allow for an alternative solution to approximate the extension of the affected strand. In the case for $\theta \to 0$, the WLC model can also be used, which would also provide a means to determine the extension for the segments of the broken DNA strand. The bending elasticity of the segments can be calculated through equation (29), and the spring constants for each of the overall segments can be calculated through equation (45). **Comprehensively, connecting the polymer physics discussed in Section 2 to the radiation biophysics of DNA damage would give a further insight into the mathematical and theoretical aspects regarding the physics of disorders such as cancer.** The polymer physics can also be used to determine mathematical and theoretical alterations in the shape of RNA molecules upon damage. RNA is essential to many biological processes, the main ones being transcription and translation in central dogma. RNA is susceptible to damage from a variety of endogenous and exogenous sources. Agents including reactive oxygen species and alkylating chemicals can lead to RNA damage. Such RNA damage has potential roles in a variety of neurodegenerative disorders, and can also have detrimental effects on the overall fitness of a cell ([9]). Therefore, using the physical models of polymers could give an insight into the polymer biophysics of such neurodegenerative disorders, as well as into the effects of different chemical substances on the physical properties of RNA molecules. Finally, the GCM, discussed in 2.5, could potentially allow for the stochastic modeling of the configuration of DNA strands during cancer, as well as of RNA molecules in a variety of neurodegenerative diseases. The derivation laid out for the GCM can be used for an exhaustive derivation of the end-to-end distribution with regards to the spatial orientation of DNA and RNA strands in such disorders. **In general, the physical models of polymers could give an insight into the physics of a variety of neurodegenerative disorders, and their correlation to the spatial arrangements and configurations of various nucleic acid molecules. It would also allow researchers to determine the impact of certain chemical substances on the configuration of RNA strands, which marks future applications to research in biochemistry and biophysics.**

4 Concluding Remarks

The physical models of polymers, reviewed in Section 2, serve to provide theoretical means for researchers to denote the configurations and spatial orientations of polymers in space. Furthermore, the Linear-Quadratic Model serves as a mathematical means to denote the damage to strands of DNA molecules by radiation. The radiation biophysics of DNA gives an insight into the biophysical mechanisms of disorders such as cancer. Therefore, connecting polymer physics to the Linear-Quadratic Model would give a mathematical, and therefore theoretical insight as to how the physical orientation of polymers is altered in cancer, and can also allow to determine the values for physical quantities of the segments of a broken DNA strand in cancer, such as extension, Flory's characteristic ratio, Kuhn length, bending elasticity, and the entropic spring constant. Polymer physics can also have applications to the biophysical research of a variety of neurodegenerative disorders, which are marked by RNA damage. Mathematically and theoretically modeling the changes in the physical orientation and quantitave physical values of the original RNA molecules in such neurodegenerative disorders can give future researchers an insight with regards to how the configuration of RNA polymers could potentially be linked to the pathology of such disorders, further marking a biophysical application of the polymer physics discussed. Finally, the Gaussian Chain Model can be used for the stochastic modeling of a variety of cancers and neurodegenerative disorders as discussed, since equation (41) provides the probability distribution of the end-to-end vector in a polymer chain. Comprehensively, the physical models of polymers have multitudinous applications in research regarding radiation biophysics, cancer, neuroscience, mathematical/theoretical biophysics, biochemistry, and a variety of other fields in biological research.

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