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Conformational Study of Macromolecular Systems

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ABSTRACT

A numerical solution of the sedimentation coefficient is obtained using three three-dimensional lattice models and has been applied to a variety of macromolecular systems; in particular, polysome, single and double stranded DNA, protein polypeptide chains, and polystyrenes. Attention has been directed to their flexibility. In order to understand the flexibility of the above-mentioned macromolecules, a comparison of the exponents of the molecular weight is made except for the polysome, where the calculated I_n values are compared with the experimental values. It is concluded that the coiled configurations are too extended to fit the experimental polysome values of rat liver, whereas the ring configurations of tetrahedral models are too open and on cubic-four and cubic-five choice models are too compact. The single-stranded DNA, which is supposed to be more flexible than the double-stranded DNA, has the flexibility of excluded volume configurations, while the double-stranded DNA possesses the flexibility of excluded volume configurations with exclusion of second order or possibly higher order nearest neighbor interactions. The protein polypeptide chains and polystyrenes assume the behavior of the excluded volume configurations.

INTRODUCTION

Hydrodynamic properties, such as sedimentation coefficient, diffusion coefficient, rotational diffusion coefficient, and intrinsic viscosity, provide vital information regarding the structure, shape, size, and molecular weight of macromolecules. The hydrodynamic properties which are the macroscopic properties cannot yield definite information about the nature of macromolecules. Macromolecules in solution are of a statistical nature. In other words, macromolecules in solution, even under standard conditions, undergo a dynamic motion due to their configurational free energy which leads to continuous configurational change. Hence, it is impossible to obtain accurate information about the nature of macromolecules due to their dynamic motion. Therefore, one is forced to seek the help of macroscopic properties such as hydrodynamic properties or thermodynamic properties which give the best statistical average of the microscopic properties.

In order to interpret such properties as hydrodynamic properties and their dependence on size and shape, a model closely related to the structure actually under investigation must be understood. The commonly used models are the ellipsoid of revolution, the rigid rod, and the random coil [1, 2]. The possibilities also extend to cylindrically symmetric models with rigidities intermediate between the flexible coil and the rigid rod [3-6]. All these models are based on the original work of Kirkwood [7, 8] on the theory of irreversible processes in solutions of macromolecules. These studies neglect the effect of excluded volume or the effect of chain stiffness. However, recently Gray et al. [9] have studied the Kratky-Porod workcoil model with the excluded volume effect. The excluded volume effect is usually scaled by the exponent of the molecular weight in the following equation which relates the hydrodynamic properties and molecular weight:

$$X = a + b\,M^{\delta} \tag{1}$$

where X is the sedimentation coefficient at infinite dilution or the intrinsic viscosity, and a and b are constants. For excluded volume systems, the parameter δ deviates from the Gaussian value of 0.5.

According to Kirkwood and Reisman [10], the sedimentation coefficient is given by

$$S^0 = M_0\,(1 - \bar{v}\rho)\,f^{-1}\left[1 + \frac{a}{2nb}\sum_i\sum_j (1 - \delta_{ij})\,\langle r_{ij}^{-1}\rangle\right] \tag{2}$$

where M_0 is the mass per frictional element; $a = f/3\pi\eta_0$, the effective Stokes diameter of an element; η_0 is the solvent viscosity; $r_{ij} = R_{ij}/b$ is the reduced distance between elements i and j; δ_{ij} is the Kronecker δ function; and n is the number of identical structural units in a macromolecule (chain or ring).

Due to the ordered structure of macromolecules in solution the lattice models can be used to study their hydrodynamic properties. Recently Filson and Bloomfield [11] carried out the Monte Carlo study of tetrahedral and cubic-five choice lattice models as applied to polysomes. In the present investigation we are mainly concerned with the application of our numerical results to a variety of protein systems. Such a study may yield valuable information about the nature of the macromolecules, especially their flexibility.

NUMERICAL SOLUTION

A numerical solution to Eq. (2) is obtained by using three types of three-dimensional lattice models; namely, tetrahedral, cubic-four choice, and cubic-five choice. We have studied these three models with and without exclusion of first nearest neighbor interactions. A direct enumeration technique which is well known [38] has been utilized and programmed for the CDC 3600 computer housed at Adelphi University. The functions

$$I_n = \frac{1}{n} \sum_k \sum_j \langle r_{ij}^{-1} \rangle \quad \text{and} \quad J_n = (2/n) I_n$$

have been utilized for the purpose of computation of sedimentation and diffusion coefficients, respectively. The numerical values of I_n and J_n for chain and ring molecules with no exclusion have been tabulated in Tables 1, 2, and 3, respectively, for tetrahedral, cubic-four choice, and cubic-five choice lattice models. In Tables 4, 5, and 6 the I_n and J_n values with exclusion of first nearest neighbor interactions are given for tetrahedral, cubic-four choice, and cubic-five choice, respectively.

In order to analyze the data for chain molecules we have assumed as a first approximation the following forms for I_n and J_n.

$$I_n = a_1 n^{\gamma_1}$$

$$J_n = a_2 n^{-\gamma_2} \tag{3}$$

TABLE 1. The Values of I_n and J_n for a Tetrahedral Lattice Model with No Exclusion

No. of structural elements	I_n		J_n	
	Chains	Rings	Chains	Rings
2	1.00000			
3	1.74158		1.16104	
4	2.35268		1.17634	
5	2.88872		1.15548	
6	3.38031	3.74698	1.12675	1.24898
7	3.81700		1.09055	
8	4.22493	4.79170	1.05623	1.19792
9	4.60238		1.02274	
10	4.95454	5.60196	0.99190	1.12039
11	5.29318		0.96235	
12	5.61310	6.38452	0.93547	1.06404
13	5.91526		0.91000	

TABLE 2. The Values of I_n and J_n for a Cubic-Four Choice Lattice Model with No Exclusion

No. of structural elements	I_n		J_n	
	Chains	Rings	Chains	Rings
3	1.80474		1.20315	
4	2.53235	2.70711	1.26617	1.35355
5	3.16482		1.26592	
6	3.76777	4.09723	1.25591	1.36573
7	4.29582		1.22735	
8	4.79974	5.30666	1.19993	1.32666
9	5.25325		1.16737	
10	5.68507		1.13701	
11	6.08601		1.10649	

TABLE 3. The Values of I_n and J_n for a Cubic-Five Choice Lattice Model with No Exclusion

No. of structural elements	I_n		J_n	
	Chains	Rings	Chains	Rings
3	1.77712		1.18473	
4	2.4520	2.70711	1.22603	1.35355
5	3.03507		1.21403	
6	3.57926	4.05930	1.19307	1.35308
7	4.06039		1.16009	
8	4.51661	5.13687	1.12915	1.28421
9	4.95605		1.10133	
10	5.34973		1.06994	

TABLE 4. The Values of I_n and J_n for a Cubic-Five Choice Lattice Model with Exclusion of First Nearest Neighbor Interaction

No. of structural elements	I_n		J_n	
	Chains	Rings	Chains	Rings
4	2.40348	2.70711	1.20174	1.35355
5	2.94166		1.17666	
6	3.40743	3.99156	1.13579	1.33050
7	3.83019		1.09432	
8	4.21171	4.79617	1.05292	1.19904
9	4.56661		1.01479	
10	4.91432	5.61436	0.98286	1.12287
11	5.22170		0.94935	

TABLE 5. The Values of I_n and J_n for a Tetrahedral Lattice Model with Exclusion of First Nearest Neighbor Interactions

No. of structural elements	I_n		J_n	
	Chains	Rings	Chains	Rings
6	3.35098	3.74698	1.11698	1.24898
7	3.77132		1.07750	
8	4.14508	4.79170	1.03627	1.19792
9	4.49617		0.99913	
10	4.82021	5.50236	0.96404	1.10047
11	5.12641		0.93203	
12	5.41315	6.11954	0.90215	1.01988
13	5.68675		0.87484	

TABLE 6. The Values of I_n and J_n for a Cubic-Four Choice Lattice Model with Exclusion First Nearest Neighbor Interactions

No. of structural elements	I_n		J_n	
	Chains	Rings	Chains	Rings
4	2.47409	2.70711	1.23704	1.35355
5	3.06314		1.22525	
6	3.56435	4.06201	1.18810	1.35398
7	4.01877		1.14820	
8	4.43078	5.15385	1.10769	1.28846
9	4.81110		1.06912	
10	5.16491	6.17418	1.03298	1.32483
11	5.49770		0.99953	
12	5.80656	6.75159	0.96772	1.12522
13	6.10190			

It is of interest to evaluate γ_1 and γ_2. The exponents are obtained by applying the ratio method [39]. Accordingly γ_1 and γ_2 are given to a first approximation by

$$\gamma_1 \approx n \left[\frac{I_{n+1}}{I_n} - 1 \right]$$

and (4)

$$\gamma_2 \approx n \left[\frac{J_n}{J_{n+1}} - 1 \right]$$

Then γ_1 and γ_2 are plotted vs. $1/n$ in Figs. 1-3 for tetrahedral, cubic-four choice, and cubic-five choice lattice models, respectively. The lower series represent the γ_2 values and upper series γ_1 values. These alternating series can be extrapolated to $n = \infty$. The extrapolated values are

$$\left.\begin{array}{l} \lim_{n \to \infty} \gamma_1 \to 0.48 \\ \lim_{n \to \infty} \gamma_2 \to 0.52 \end{array}\right\} \quad \text{tetrahedral, cubic-4, and cubic-5 lattices, with no exclusion} \qquad (5)$$

and

$$\left.\begin{array}{l} \lim_{n \to \infty} \gamma_1 \to 0.455 \\ \lim_{n \to \infty} \gamma_2 \to 0.545 \end{array}\right\} \quad \text{tetrahedral, cubic-4 and cubic-5 lattices, with exclusion of first nearest neighbor interactions} \qquad (6)$$

Substituting these values in Eq. (3), we have calculated a_1 and a_2 for all the lattice models. The extrapolated values are shown in Table 7. Thus the asymptotic relations represented by Eq. (3) are not completely accurate in describing the behavior of long-chain macromolecules in solution. In order to obtain more accurate forms, we have first calculated the difference between the experimental I_n, J_n and the computed I_n, J_n, which are

$$\Delta I_n = a_1 n^{\gamma_1} - I_n$$

and

$$\Delta J_n = a_2 n^{-\gamma_2} - J_n \qquad (7)$$

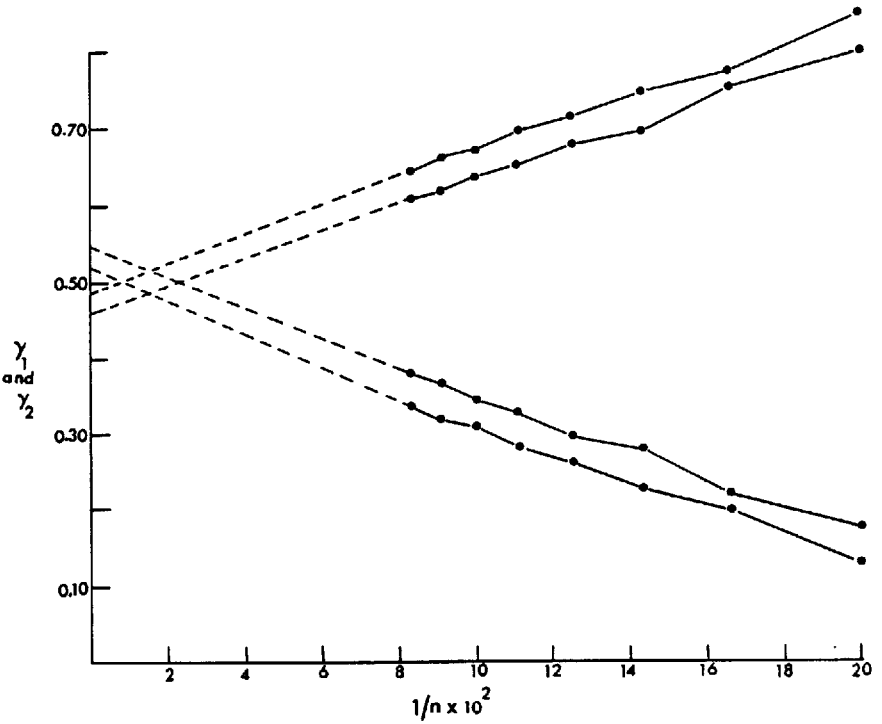

FIG. 1. The plot of γ_1 (upper two series) and γ_2 (lower two series) vs. 1/n for tetrahedral lattice model. The inner two series indicate the exclusion of first nearest neighbor interactions.

To examine the dependency of ΔI_n and ΔJ_n on n, we have plotted ΔI_n and ΔJ_n vs. 1/n in Figs. 4-7. From the graphs it appears that

$$\lim_{n \to \infty} \Delta I_n = b_1$$

and

$$\lim_{n \to \infty} \Delta J_n = 0$$

where b_1 values are tabulated in Table 7. From this analysis it is

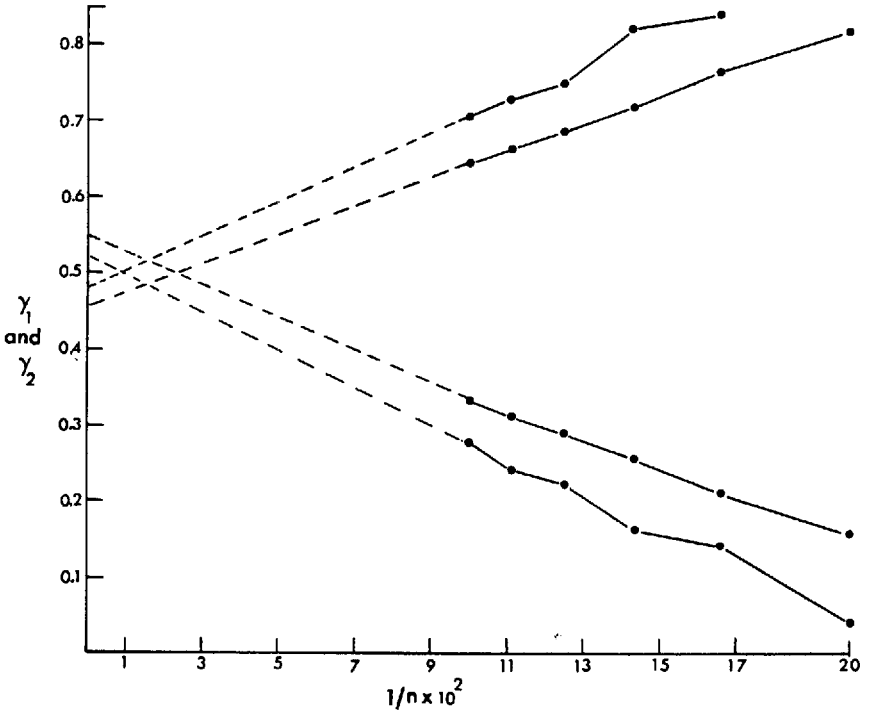

FIG. 2. The plot of γ_1 (upper two series) and γ_2 (lower two series) vs. 1/n for cubic-four choice lattice model. The inner two series indicate the exclusion of first nearest neighbor interactions.

clear that I_n and J_n can be represented by the following general types of relations.

For lattice model with no exclusion

$$\left.\begin{aligned} I_n &= a_1 n^{0.48} + b_1 \\ \text{and} \\ J_n &= a_2 n^{-0.52} \end{aligned}\right\} \quad \text{tetrahedral, cubic-4, and cubic-5} \qquad (8)$$

For lattice models with first nearest neighbor exclusion

$$\left.\begin{aligned} I_n &= a_1' n^{0.445} + b_1' \\ \text{and} \\ J_n &= a_2' n^{-0.545} \end{aligned}\right\} \text{tetrahedral, cubic-4, and cubic-5} \qquad (9)$$

All the parameters for Eqs. (8) and (9) can be found in Table 7. We have made no effort to examine the further dependence of I_n and J_n on n. Also, due to small amount of data available on ring molecules, we did not analyze the numerical results.

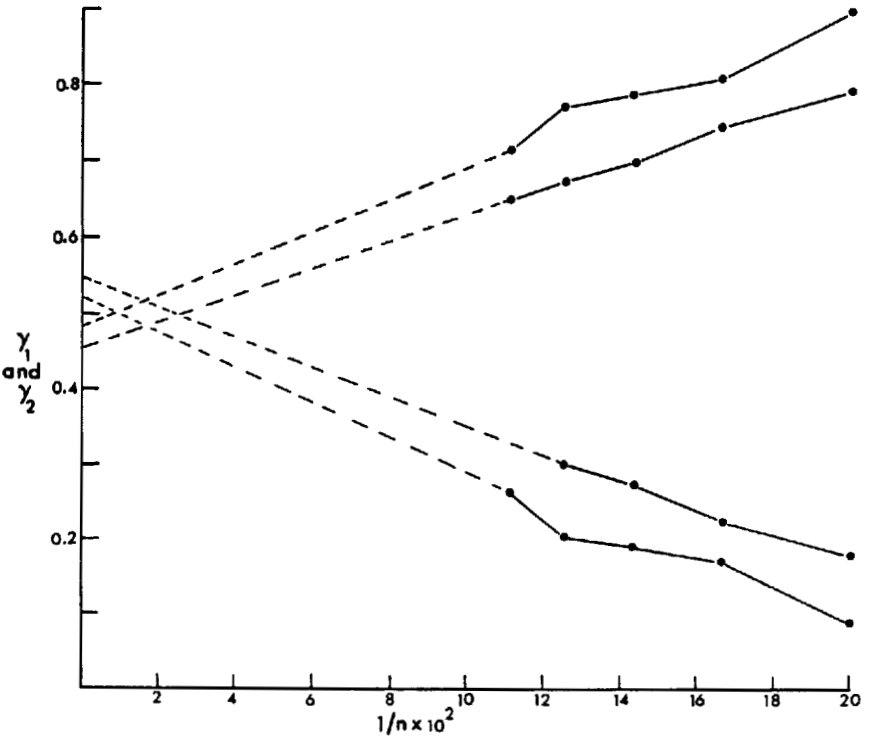

FIG. 3. The plot γ_1 (upper two series) and γ_2 (lower two series) vs. 1/n for cubic-five choice lattice model. The inner two series indicate the exclusion of first nearest neighbor interactions.

TABLE 7. The Values of the Parameters in Eqs. (8) and (9) for Various Models

Lattice models	No exclusion			With exclusion of first nearest neighbor interactions		
	a_1	b_1	a_2	a_1'	b_1'	a_2'
Tetrahedral	1.97	-0.14	4.03	2.04	-0.3	4.07
Cubic-4 choice	2.32	-0.19	4.7	2.17	-0.22	4.36
Cubic-5 choice	2.21	-0.17	4.42	2.07	-0.27	4.14

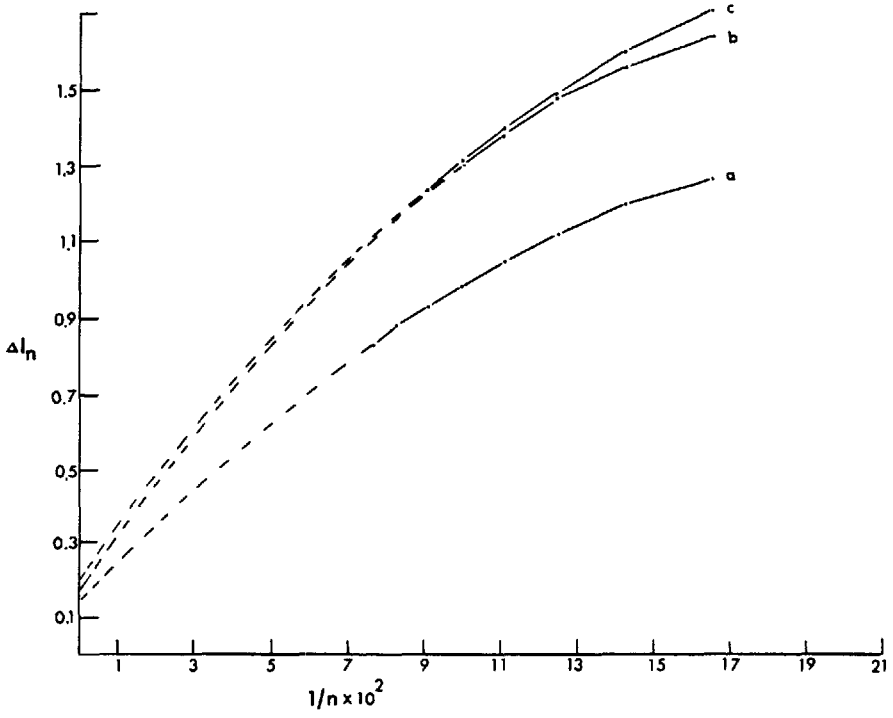

FIG. 4. The values of ΔI_n from Eq. (34) are plotted vs. 1/n for all three models: (a) diamond, (b) cubic-5, and (c) cubic-4.

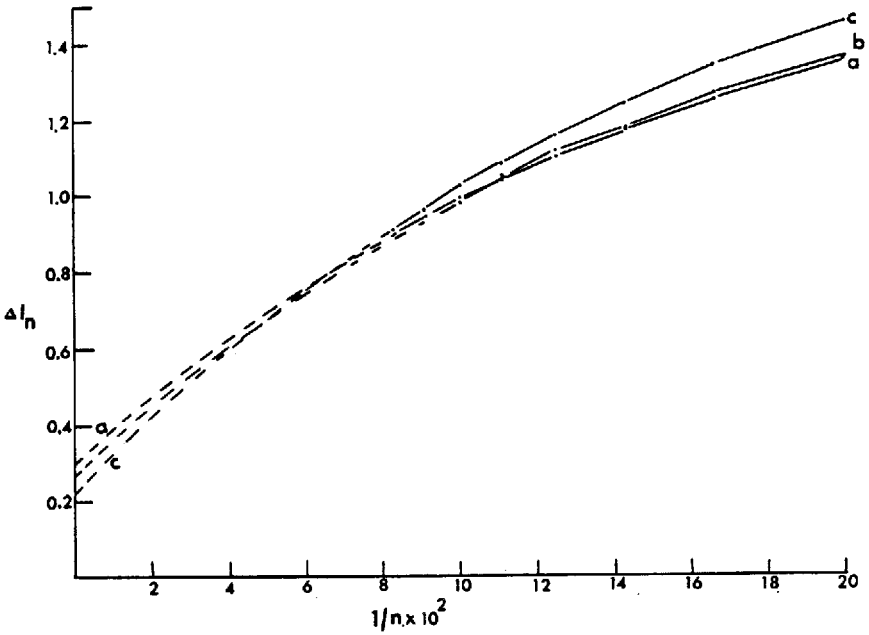

FIG. 5. The values of ΔI_n are plotted vs. 1/n for all three models with exclusion of first nearest neighbor interactions: (a) diamond, (b) cubic-5, and (c) cubic-4.

POLYSOMES

Polysomes are ribosomal aggregates and are thought to be the active units in protein synthesis in animals [12] as well as in bacterial systems [13]. Polysomes consist of ribonucleoprotein particles held together by a single stranded messenger RNA. Electron micrographs of thin cell portions have revealed such configurations as double rows, loops, spirals, circles, rosettes [14], and helices [15, 16].

Electron micrographs of cell-free preparations of polysomes indicate two types of configurations; the open configuration in which the ribosomes are visible as beads on a threadlike structure, and cluster configuration in which ribosomes are tightly packed together in a structure which resembles an ellipsoidal shape. Such clustering was thought to be caused by the drying procedure used to prepare

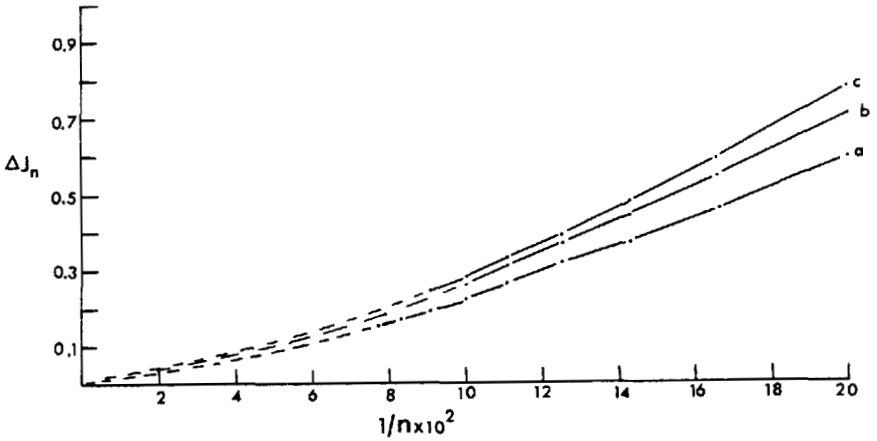

FIG. 6. The values of ΔJ_n from Eq. (34) are plotted vs. 1/n for all three models: (a) diamond, (b) cubic-5, and (c) cubic-4.

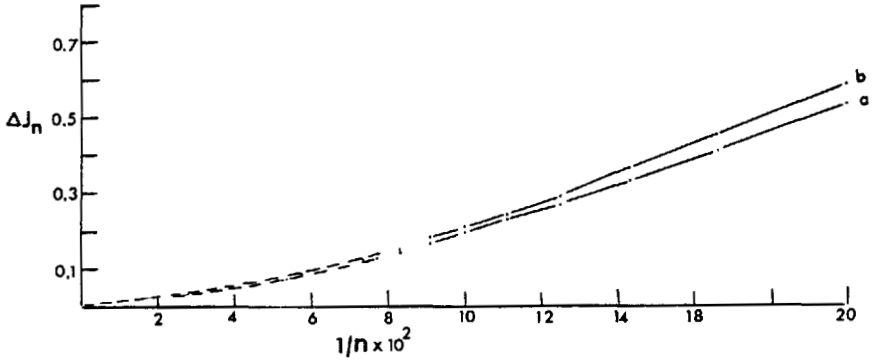

FIG. 7. The values of ΔJ_n are plotted vs. 1/n for two models with exclusion of first nearest neighbor interactions: (a) diamond, and (b) cubic-4.

samples for the electron micrographs since the percentage of clustering was reduced when more carefully prepared samples were used [17]. Besides these structures, other structures like circles with a handle or turned inward as if to start a spiral [18], irregular clumping and

extended arrays [19], and flattened helices [18, 20] have also been observed.

These experimental observations under the electron microscope suggest that ordered configurations may exist in solution. In the past few years several attempts have been made to interpret sedimentation data on polysomes in terms of the model configurations. Gierber [21] approximated the polysomes as a linear chain of spherical particles approximated by the equivalent ellipsoid to account for the experimental sedimentation coefficients, and he concluded that the linear chain model accounts for the smaller aggregates (n = 2 to 3) and is too open to fit the data for polysomes containing more than three ribosomes. Eiserling et al. [22] obtained good agreement with the experimental values of sedimentation coefficients of polyribosomes in a DNA-dependent amino acid incorporating system from Escherichia coli extracts using polygonal models containing up to five ribosomes. Pfuderer et al. [23] used the helical models having three or four ribosomes per turn and a pitch of 18 or 20° to fit their experimental sedimentation data of rat liver polysomes. Filson and Bloomfield [11] analyzed the sedimentation data of polysomes from rat liver in terms of random coil and helical models and concluded that helical configurations are too compact and random coil configurations are too extended to account for the actual configuration. They also conjectured that the true configuration is a mixture of two.

Let us consider that polysomes are made up of n identical ribosomes evenly spaced along the messenger RNA, so that the Kirkwood-Reiseman equations for sedimentation and diffusion coefficients can be applied in this case also. We define two functions, one for the sedimentation coefficient following Filson and Bloomfield [11] and another for the diffusion coefficient:

$$I_n = (S_n - S_1)/S_2 - S_1) \tag{10}$$

$$J_n = [D_n - (D_1/n)]/D_2 - (D_1/2)] \tag{11}$$

where $S_1(D_1)$, $S_2(D_2)$, and $S_n(D_n)$ are the sedimentation (diffusion) coefficients of the first, second, and nth ribosomes. Substituting the values of $S_1(D_1)$, $S_2(D_2)$, and $S_n(D_n)$ from Eq. (2) into Eqs. (10) and (11), we have

$$I_n = \frac{1}{n} \sum_{\substack{i=1 \\ i \neq j}}^{n} \sum_{j=1}^{n} \langle r_{ij}^{-1} \rangle \tag{12}$$

and

$$J_n = \frac{2}{n^2} \sum_{i \neq j} \sum \langle r_{ij}^{-1} \rangle$$

$$= \frac{2}{n} I_n \qquad (13)$$

where r_{ij}^{-1} is the reciprocal distance between the ith and jth ribosomes measured in units of the nearest neighbor spacing. The numerical values of I_n and J_n for chain and ring molecules can be found in Tables 1, 2, and 3 for tetrahedral, cubic-four choice, and cubic-five choice lattices, respectively, and for chains and ring molecules with exclusion of first nearest neighbor interactions in Tables 4, 5, and 6, respectively, for tetrahedral, cubic-four choice, and cubic-five choice lattices.

Polygonal Configurations

In Fig. 8 we have plotted the numerical values of I_n vs the number of ribosomes up to n = 12 for all three lattice models with and without exclusion of first nearest neighbor interactions. Experimental values of I_n shown in the figure by circles are calculated from the data of Pfuderer et al. [23] using their "best values" and taking into account their estimated probable error. The S_{11} (= 335) and probable errors for I_8, I_{10}, I_{11}, and I_{12} have been estimated. The calculated I_n values for the tetrahedral lattice fall below the experimental values and for the other two lattices fall above the experimental values except that I_{10} for the cubic-four choice with exclusion of first nearest neighbor interactions falls below the experimental value. It appears that the polygonal configurations for tetrahedral lattice are too open and for the other two lattice models are too compact to compare with experimental results. However, the calculated values fall in the range of probable errors which shows that lattice models can be used, at least for polysomes containing a small number of ribosomes.

Eiserling et al. [22] used polygonal models to explain the experimental sedimentation data on polysomes in the DNA-dependent amino acid incorporating system from E. coli extracts. They assigned a pentagon for a cluster of five, a square for a cluster of four, a triangle for a cluster of three, and two straight chains for a cluster of two. We have calculated I_n from their experimental sedimentation values taking S_1 = 70S, and the values are tabulated in Table 8. The experimental values of I_3, I_4, and I_5 are compared with the computed values. These polygonal structures seem to fit the coiled configurations

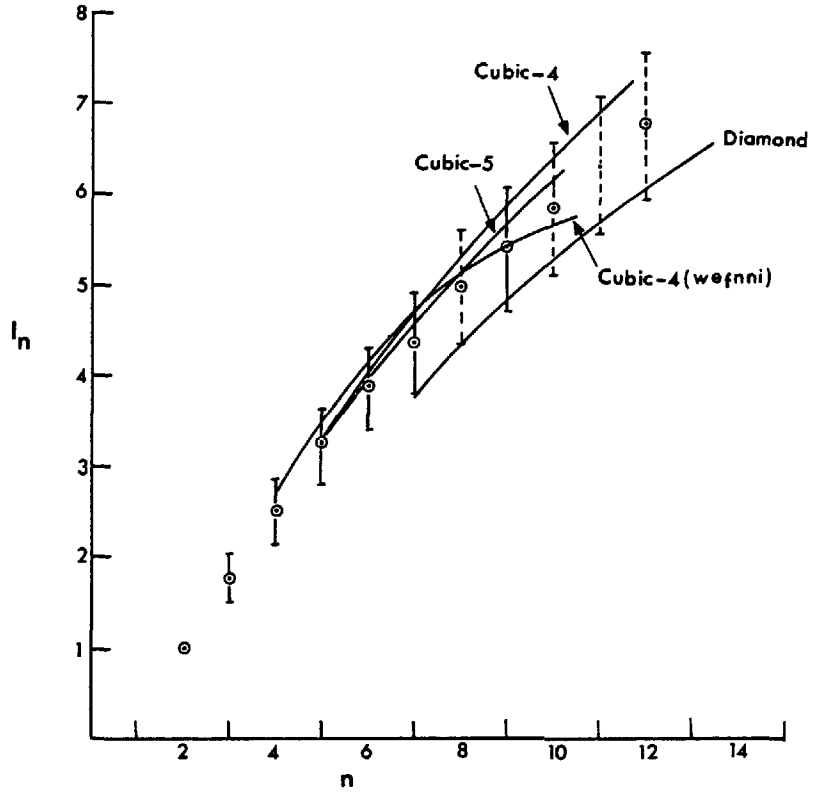

FIG. 8. The plot of I_n(ring) vs. n for diamond, cubic-4, cubic-4 with excluded first nearest neighbor interactions (wefnni), and cubic-5 lattice models. Experimental values taken from Ref. 23.

also, at least in the cases of I_3 and I_4. The computed values of I_3 and I_4 for the tetrahedral lattice model fit very closely to the experimental values. However, the computed I_5 values for all the models are far less than the experimental value, which suggests that the configurations are too extended. Moreover, the polygons of odd size do not exist on these models. The square configuration can be obtained on cubic-four and cubic-five choice lattice models. Comparing the I_4 value for these models with the experimental value indicates that the computed square structures are too compact. Thus it appears that the polygonal structures for smaller aggregates (n = 3, 4) can also be fitted to open coil configurations.

TABLE 8. The Experimental and Computed I_n Values for Polysomes in DNA-Dependent Amino Acid Incorporating System from E. coli Extracts

n	I_n (experimental)	I_n (calculated)
3	1.75	1.74158 (tetrahedral, chain)
4	2.375	2.35268 (tetrahedral, chain)
5	3.25	

Coiled Configurations

The numerical values of I_n for all three lattice models with and without exclusion of first nearest neighbor interactions are plotted in Fig. 9. Experimental values for rat liver [23] are shown by circles and are included for the sake of comparison. The I_n values for all the systems fall below the experimental values and, furthermore, I_n values for exclusion of first nearest neighbor interactions even fall below the I_n values with no exclusion. Smaller aggregates, for example, n = 2, 3, and 4 cubic-four and cubic-five choice models, give better estimates of experimental values, and the tetrahedral model underestimates the experimental values. For higher aggregates, as the number of ribosomes increase, the I_n values for all the models start to deviate from the experimental values. The largest deviation occurs in the case of the tetrahedral model which even falls outside the range of probable error, and the smallest deviation occurs for the cubic-four choice model with no exclusion. The behavior of all these lattice models can be explained in terms of their lattice structure. The tetrahedral model yields smaller I_n values due to its more open structure, while the cubic-four choice yields larger values due to its more compact nature compared to the other two lattice models. From the overall picture it can be concluded that the cubic-four choice model with no exclusion is the better choice for the study polysomes, at least for smaller aggregates.

DEOXYRIBONUCLEIC ACID

The sedimentation coefficient of double-stranded DNA has been investigated experimentally [24-28] and theoretically [3] using the

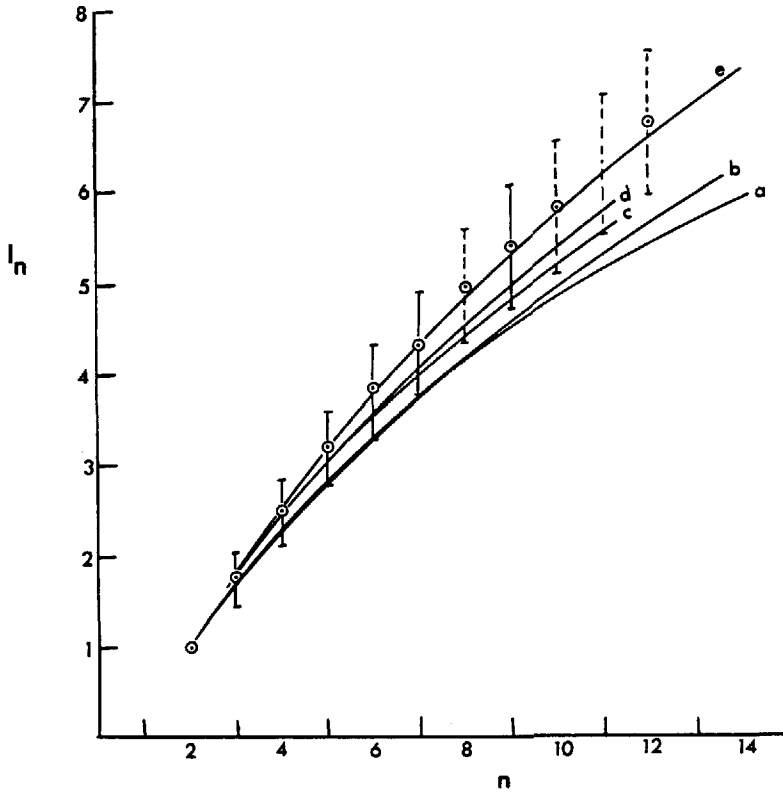

FIG. 9. The plot of I_n(chain) vs. n for various lattice models: (a) diamond lattice with excluded first nearest neighbor interactions, (b) diamond, (c) cubic-4 with excluded first nearest neighbor interactions, (d) cubic-5, and (e) cubic-4.

Kratky-Porod wormcoil model. Furthermore, the effect of excluded volume has also been examined [9]. In addition to double-stranded DNA, the data on the sedimentation coefficient of single-stranded DNA is also available. An excellent review on this subject has been published [29]. All these experimental and theoretical efforts have concentrated on determining the flexibility of single- and double-stranded DNA. The flexibility is usually expressed through the parameter known as persistence length or the Kuhn statistical length. The determination of flexibility of DNA might be more vital to understand the genetic

property of DNA, which is considered to be the sole carrier of genetic information in living organisms. Surprisingly, the flexibility of DNA is known only with large uncertainty [32].

The flexibility of DNA or any macromolecule can also be measured in terms of the δ-type parameter which is defined in Eq. (1). This parameter represents the excluded volume effect as well as flexibility and tells us how much the macromolecule deviates from its most random coiled configuration. Since DNA configurations are known to have flexibility intermediate between that of a rigid rod and a random coil, it is possible to use lattice models having this character to study DNA molecules. Such a study is initiated in the present investigation.

We have obtained the numerical solution for the sedimentation coefficient using tetrahedral, cubic-four choice, and cubic-five choice lattice models with and without exclusion of first nearest neighbor interactions. For no exclusion models the S° was represented as

$$S^\circ = \frac{M_0(1 - \bar{v}\rho)}{f} \left[1 + \left(\frac{a}{b}\right)(a_1 n^{0.48} + b_1)\right] \tag{14}$$

and for exclusion of first nearest neighbor interactions S° was

$$S^\circ = \frac{M_0(1 - \bar{v}\rho)}{f} \left[1 + \left(\frac{a}{b}\right)(a_1' n^{0.455} + b_1')\right] \tag{15}$$

where all the terms are defined in Eq. (2). One way to obtain information about the flexibility of DNA (single or double stranded) is to compare the exponent of the molecular weight in Eqs. (14) and (15) with that of the experimental equation. We have made the comparison with the two experimental equations on double-stranded DNA. Doty et al. [26] fitted their experimental data on sedimentation coefficients to

$$S^\circ_{20,w} = 0.063 M_w^{0.37} \tag{16}$$

Comparing the exponents of the molecular weight in Eqs. (14), (15), and (16), the exponent in Eq. (16) is much smaller than the calculated exponents for both systems. This means that the DNA molecule, in this case, is more rigid than the lattice models. Hence, both systems with and without exclusion of first nearest neighbor interactions for all the lattice models cannot be used to study this type of DNA due to their more coiled nature. In order to apply lattice models to this type of

DNA, more rigidity has to be introduced into the system. Such a characteristic can easily be brought about by exclusion of second and possibly higher order nearest neighbor interactions. Another experimental equation is due to Sponar et al. [30] who fitted their sedimentation data on calf thymus DNA to

$$S^{\circ}_{20,w} = 0.0135 M^{0.463} \tag{17}$$

This equation has a larger exponent than Eq. (16). This large value was attributed to the more flexible nature of DNA prepared by a different method. The experimental exponent falls within the limit of the lattice model study. In other words, the experimental exponent lies in between the two systems studied using lattice models. It is clear from this comparison that the lattice models may be used to investigate DNA molecules with this nature.

In addition to double-stranded DNA, we have also examined the flexibility of single-stranded DNA. Eigner and Doty [31] reported on the investigation of denaturated (presumably single-stranded) DNA in 0.15 M Na^{+}. They obtained the following relation between the sedimentation coefficient and molecular weight:

$$S^{\circ}_{20,w} = 0.022 M_w^{0.48} \tag{18}$$

By comparing the exponent of the molecular weight in Eq. (18) with that of Eqs. (14) and (15), it is obvious that the single-stranded DNA has the flexibility of the lattice models with no exclusion of first nearest neighbor interactions. The rigidity of double-stranded DNA comes from base pairing. When the double-stranded DNA denaturates or transforms into two single-stranded DNAs, the base pairing no longer exist, and the net result is an increase in configurational entropy. The increase in configurational entropy appears in the form of flexibility. Therefore, the flexibility of a configuration may be considered as a manifestation of configurational entropy as well as of other effects.

A further verification of the applicability of lattice models to the study of DNA can also be made by considering the sedimentation ratio of linear and ring configurations. It is known that circular DNA sediments about 10-20% faster than linear DNA of the same molecular weight. This ratio remains fairly constant or only varies slightly over the entire range of excluded volume effect [29]. Since the ratio I_n (linear)/I_n (ring) is directly proportional to the sedimentation ratio, we have calculated this ratio for all the lattice models which are listed in Table 9. Due to the small number of data available,

TABLE 9. The Values of the Ratios for Tetrahedral, Cubic-Four Choice, and Cubic-Five Choice Lattice Models with and without Exclusion of First Nearest Neighbor Interactions

No. of structural elements	I_n(chain)/I_n(ring) no exclusion			I_n(chain)/I_n(ring) with exclusion		
	Tetrahedral	Cubic-4 choice	Cubic-5 choice	Tetrahedral	Cubic-4 choice	Cubic-5 choice
4		0.93544	0.93544		0.91392	0.88783
5						
6	0.90214	0.91958	0.88174	0.89431	0.87748	0.85305
7						
8	0.88168	0.90447	0.87925	0.86501	0.85970	0.87814
9						
10	0.88532			0.87602	0.83653	0.87531
11						
12	0.87917			0.88456	0.86002	

these ratios cannot be extrapolated accurately to n = ∞ in order to examine the validity of the lattice model studies.

POLYPEPTIDE CHAINS

The polypeptide chains are the most commonly encountered units in native and synthetic proteins. Therefore, it is worthwhile to examine their flexibility. Tanford et al. [33] studied the hydrodynamic properties of 12 different proteins and obtained the general relationship between the sedimentation coefficient and the number of residues per chain. Their relation is

$$S^{\circ} = (1 - \bar{v}\rho)\,(0.286)M^{0.473} \tag{19}$$

where $\bar{v}$ and ρ are the apparent specific volume and density of the solvent, respectively. These authors concluded that the polypeptide chains in proteins have random coil behavior. We have made a comparison between the experimental exponent and the calculated exponents. The experimental value in Eq. (19) lies in between the calculated values shown in Eqs. (14) and (15). Hence, we conclude that the lattice models can be used in studying the polypeptide chains.

POLYSTYRENES

The lattice model studies can also be used to obtain information about the flexibilities of polystyrenes. McCormick [34, 35] investigated the sedimentation coefficients of polystyrene and α-methylstyrene and proposed the following equations:

$$S = 0.0169M^{0.48} \text{ (polystyrene)}$$

and

$$S = 0.0172M^{0.49} \text{ (}\alpha\text{-methylstyrene)} \tag{20}$$

where both polystyrene and α-methylstyrene appears to have the same molecular weight exponent. Comparing Eq. (20) with our calculated equations, it is clear that polystyrene and α-methylstyrene have the flexibilities of the random coil with no exclusion of first nearest neighbor interactions.

DISCUSSION

In the present investigation we have demonstrated that lattice model studies can be applied to a variety of macromolecular systems, mainly to understand their flexibility and hence their spatial distribution. The term "flexibility," which has been used extensively here, is not to be confused with "local chain stiffness." We have used the term "flexibility" to describe the deviation of the "configurational status" from Gaussian behavior. The deviation from Gaussian behavior may be understood from two points of view: 1) solvent and 2) solute. According to the first point of view, as we pass from the excluded volume problem to the excluded first nearest neighbor interaction problem, we increase the solvent-solute interactions. Thus the decrease in the exponent may be due to such interactions. These solvent-solute interactions also seem to influence the configurational properties, for example, the exponent in the mean square end-to-end distance equation has been found to increase when these interactions are included. According to the second point of view, the excluded first nearest neighbor interaction chain is more extended than one with excluded volume, which is in turn more extended than the Gaussian chain. If we keep on excluding the second and higher neighbor interactions, we ultimately reach rodlike behavior. Thus the degree of extension varies from the most flexible (Gaussian) state to the rodlike state. Since the degree of extension varies, we assume that the flexibility also varies. Therefore, the excluded first nearest neighbor interaction chain might possess less flexibility than that of the excluded volume chain. In other words, the decrease in the exponent may be attributed to the "configurational status" in their respective conditions. Thus from our study it appears that the lattice model studies are certainly promising to an understanding of the true nature of macromolecules. The lattice model studies can also be applied with confidence to other macromolecular phenomena. Such studies have already been successful in the theory of helix-to-random coil transition [36, 37].

We have tried to fit I_n data to experimental values of polysomes from two different sources. The experimental data on rat liver polysomes is compared with calculated ring and linear configurations in Figs. (8) and (9). The I_n values for tetrahedral-ring configurations fall below the experimental values while for the other two lattice rings the configurations fall above the experimental values. Moreover, the calculated values for the higher aggregates deviate considerably from the experimental values. This can be explained in terms of their lattice structure. The tetrahedral-ring configurations are too extended and the other two lattice rings are too compact. The true configurations of polysomes are intermediate between these two cases. It can be seen

from Fig. 9 that the coiled configurations for all the lattice models are too extended to compare with the experimental values. However, for lower aggregates (n = 2, 3, 4, 5) the values are very close to the experimental values. For higher aggregates, the linear configurations of the cubic-four choice lattice seem to approximate the true polysome configurations. The agreement between the experimental and calculated values may be achieved by introducing a little more compactness in cubic-four choice configurations. In other words, the true polysome configurations closely resemble those of the cubic-four choice configurations but have a little more compactness. The polysomes in DNA-dependent amino acid incorporating systems from E. coli extracts, which were previously fitted to the triangle and square type, are fitted to open configurations. In view of this study, it can be said that the lower aggregates can be understood easily in terms of ring or chain configurations, but the higher aggregates cannot be understood due to their more complicated nature.

The flexibilities of double- and single-stranded DNA have been examined by comparing the experimental and calculated δ parameters. The single-stranded DNA possesses the flexibility of the excluded volume configuration while the double-stranded DNA possesses the flexibility of the excluded volume configuration with exclusion of second order or possibly higher order nearest neighbor interaction. To arrive at this conclusion, we have compared two equations, one experimental and another calculated, in which the experimental equation lacks an intercept and is based on heterogeneous samples, which can be criticized. In any case, the comparison gives us some idea about the flexibilities of macromolecules. We have also shown that besides these applications, the lattice model studies can also be applied to other systems such as protein polypeptide chains and polystyrenes whose behavior is similar to that of the random coil with no exclusion of first nearest neighbor interactions.

We conclude that if one wants to extract accurate information about the macromolecular systems using the direct enumeration study of lattice models as it is done here, it is necessary either to obtain information about higher step walks or to devise a method to reduce the uncertainty involved in the extrapolation of short step walks. The first case appears, at least for the time being, impossible due to the computer time required.

NOTE ADDED

Recently, K. E. Reinert, J. Strassburger, and H. Triebel (Biopolymers, 10, 285 (1971)) studied homogeneous samples of DNA and obtained

$$S^0 - 2.5 = 0.0190 M^{0.435}$$

Comparing the exponent of the molecular weight with the exponents in Eqs. (14) and (15), it is obvious that this exponent also falls well below the lattice model exponents. Hence, the conclusion reached using the exponents of the heterogeneous samples remain valid even if the homogeneous sample is considered.

REFERENCES

[1] C. Tanford, Physical Chemistry of Macromolecules, Wiley, New York, 1961, Chap. 6.
[2] J. Reisman and J. G. Kirkwood, Rheology, Academic, New York, 1956, Vol. 1, p. 495.
[3] J. E. Hearst and W. H. Stockmayer, J. Chem. Phys., 37, 1425 (1962).
[4] J. E. Hearst, J. Chem. Phys., 38, 1062 (1963).
[5] J. E. Hearst, J. Chem. Phys., 40, 1506 (1964).
[6] J. E. Hearst, J. Chem. Phys., 42, 1449 (1965).
[7] J. G. Kirkwood, Rec. Trav. Chim. Pays-Bas, 68, 649 (1949).
[8] J. G. Kirkwood, J. Polym. Sci., 12, 1 (1954).
[9] H. B. Gray, Jr., V. A. Bloomfield, and J. E. Hearst, J. Chem. Phys., 46, 1493 (1967).
[10] J. Reisman and J. G. Kirkwood, Rheology, Academic, New York, 1956, Vol. 1.
[11] D. P. Filson and V. A. Bloomfield, Biochem. Biophys. Acta, 155, 169 (1968).
[12] F. O. Wettstein, F. Staehelein and H. Noll, Nature, 197, 430 (1963); J. R. Warner, A. Rich, and C. E. Hall, Science, 138, 1399 (1962); A. Geirber, J. Mol. Biol., 6, 148 (1963).
[13] W. Gilbert, J. Mol. Biol. 6, 374 (1963); Y. Kiho and A. Rich, Proc. Nat. Acad. Sci., U.S., 51, III (1964).
[14] G. E. Palade, J. Biophys. Biochem. Cytol., 1, 59 (1955).
[15] O. Behnke, Exp. Cell Res., 30, 597 (1963).
[16] C. H. Waddington and M. M. Perry, Exp. Cell Res., 30, 599 (1963).
[17] J. R. Warner, A. Rich, and C. E. Hall, Science, 1388, 1399 (1962).
[18] E. Shelton and E. L. Kuff, J. Mol. Biol., 22, 23 (1966).
[19] A. Rich, S. Penman, Y. Becker, J. E. Darnall, and C. Hall, Science, 142, 1658 (1963).
[20] E. L. Benedetti, W. S. Bont, and H. Bloemendal, Lab. Invest., 15, 196 (1966).
[21] A. Gierber, J. Mol. Biol., 6, 148 (1963).
[22] F. Eiserling, J. G. Levin, R. Byrne, U. Karlsson, M. W. Nirenberg, and F. S. Sjötrand, J. Mol. Biol., 10, 536 (1964).

[23] P. Pfuderer, P. Cammarano, D. R. Holladay, and G. D. Novelli, Biochem. Biophys. Acta, 109, 595 (1965).
[24] G. Cohen and H. Eisenberg, Biopolymers, 4, 429 (1966).
[25] G. Cohen and H. Eisenberg, Biopolymers, 6, 1077 (1968).
[26] P. Doty, B. B. McGill, and S. A. Rice, Proc. Nat. Acad. Sci., U.S., 44, 432 (1958).
[27] Y. Kawade and I. Watanabe, Biochim. Biophys. Acta, 19, 5.3 (1958).
[28] E. Burgi and A. Hersey, J. Mol. Biol., 3, 458 (1961).
[29] V. A. Bloomfield, "Hydrodynamic Properties of DNA," in Macromolecular Reviews, Vol. 3, Wiley (Interscience), New York, 1968.
[30] J. Sponar, M. Boublik, and H. Votavova, Collect. Czech. Chem. Commun., 30, 2920 (1965).
[31] J. Eigner and P. Doty, J. Mol. Biol., 12, 549 (1965).
[32] J. B. Hays, M. E. Magar, and B. H. Zimm, Biopolymers, 8, 531 (1969).
[33] C. Tanford, K. Kawahara, and S. Lapanje, J. Amer. Chem. Soc., 89, 729 (1967).
[34] H. W. McCormick, J. Polym. Sci., 36, 341 (1959).
[35] H. W. McCormick, J. Polym. Sci., 41, 329 (1959).
[36] M. E. Fisher, J. Chem. Phys., 45, 1469 (1066).
[37] M. Kumbar and S. Windwer, J. Chem. Phys., 50, 5257 (1969).
[38] M. Kumbar, Ph.D. Thesis, Adelphi University, 1969.
[39] M. Kumbar and S. Windwer, J. Chem. Phys., 49, 4057 (1968).