(8) Flory, P. J. "Principles of Polymer Chemistry"; Cornell University Press: Ithaca, NY, 1953.
(9) Hocker, H.; Flory, P. J. *Trans. Faraday Soc.* **1971**, *67*, 2270.
(10) Palmen, K. J. Thesis, Technische Hochschule Aachen, West Germany, 1965.
(11) Ueberreiter, K.; Kanig, G. *J. Chem. Phys.* **1950**, *18*, 399.
(12) Posthuma de Boer, A.; Pennings, A. J. *Faraday Discuss. Chem. Soc.* **1979**, *68*, 345.
(13) Gibbs, J. H.; DiMarzio, E. A. *J. Chem. Phys.* **1958**, *28*, 373.
(14) Gibbs, J. H.; DiMarzio, E. A. *J. Chem. Phys.* **1958**, *28*, 807.
(15) Gibbs, J. H. "Modern Aspects of the Vitreous State", MacKenzie, J. D., Ed.; Butterworths: Washington, D.C., 1960; pp 152–187.
(16) DiMarzio, E. A.; Gibbs, J. H.; Fleming, P. D., III; Sanchez, I. C. *Macromolecules* **1976**, *9*, 763.
(17) O'Reilly, J. M. *J. Appl. Phys.* **1977**, *48*, 4043.
(18) Havlicek, I.; Vojta, V.; Ilavsky, M.; Hrouz, J. *Macromolecules* **1980**, *13*, 357.
(19) Gujrati, P. D. *J. Phys. A: Math. Gen.* **1980**, *13*, L437.
(20) Roe, R.-J.; Tonelli, A. E. *Macromolecules* **1978**, *11*, 114.
(21) Goldstein, M. *J. Chem. Phys.* **1976**, *64*, 4767.
(22) Roe, R.-J.; Tonelli, A. E. *Polym. Prepr., Am. Chem. Soc., Div. Polym. Chem.* **1981**, *21*, 419.
(23) DiMarzio, E. A.; Dowell, F. *J. Appl. Phys.* **1979**, *50*, 6061.
(24) DiMarzio, E. A. *J. Res. Natl. Bur. Stand., Sect. A* **1964**, *68A*, 611.
(25) Simha, R.; Boyer, R. F. *J. Chem. Phys.* **1962**, *37*, 1003.
(26) Boyer, R. F. *J. Macromol. Sci., Phys.* **1973**, *B7*, 487.
(27) Gordon, J. M.; Rouse, G. B.; Gibbs, J. M.; Risen, W. J., Jr. *J. Chem. Phys.* **1977**, *66*, 4971.

Method for Estimating the Entropy of Macromolecules with Computer Simulation. Chains with Excluded Volume

Hagai Meirovitch

Chemical Physics Department, Weizmann Institute of Science, Rehovot 76100, Israel.
Received March 18, 1982

ABSTRACT: An approximate method for estimating the entropy of macromolecules with computer simulation is developed and applied preliminarily to relatively short ($N \leq 49$) self-avoiding walks (SAWs) on a 3-choice square lattice and a 5-choice simple-cubic lattice. The accuracy of S_{EV}, the contribution of the excluded volume (EV) effect to the entropy, is estimated for both lattices to be better than 1%. However, when the SAWs are confined within a "box", additional long-range contacts are formed and the estimated accuracy of S_{EV} becomes not better than 2–7%. We discuss ways to improve the accuracy of the method and explain how it can be extended to polymer models with EV and finite interactions (attractive or repulsive) as well.

Introduction

Calculation of the entropy of systems with short-range interactions (e.g., simple liquids) by means of computer simulation is not trivial[1–6] and becomes very difficult for macromolecules, where long-range interaction prevails. Gō and Scheraga[7,8] developed a method (based on normal coordinate analysis) for calculating the conformational entropy of macromolecules undergoing small (i.e., harmonic) fluctuations around their stable state (e.g., the α-helical state of a polypeptide) and applied it to several short polypeptides.[9,10] They also calculated[7] the entropy of a polypeptide in its random coil state at the Θ point,[11,12] i.e., neglected the excluded volume effect (see also ref 13). Recently, Karplus and Kushick[14] suggested calculating the covariances of the internal coordinates directly from the molecular dynamics or Monte Carlo simulation rather than performing normal coordinate analysis and applied their method to the molecular dynamics simulation of decaglycine and butane. These approximate treatments cover only the two extreme cases of very small and very large conformational fluctuations and are not applicable to states with intermediate chain flexibility.

In the present work, we develop a different procedure for estimating entropy, which, in principle, can be applied to *any* macromolecular state simulated with *any* computer simulation technique.[15–18] In this preliminary study, however, we apply the method to a relatively simple model, the self-avoiding walks (SAWs) (or chains with excluded volume (EV)) simulated with the direct Monte Carlo (DMC) procedure[19] on a square and a simple-cubic (SC) lattice. To model the strong, long-range, attractive interactions in a protein molecule, for example, we also confine the chains within a small "box" of varying size. Because of "sample attrition",[15] we were able to study with DMC only short SAWs of $N \leq 49$ (where N is the number of links in a walk). However, the DMC procedure enables us to obtain accurate estimates for the entropy using an asymptotically exact formula and thereby to examine the accuracy of our results. Our results are also compared to estimates for the entropy obtained with series expansion, and we also discuss how to extend our method to self-interacting SAWs.

Theory

Direct Monte Carlo. Self-avoiding walks of N steps with equal probability can be generated on a lattice by successively selecting random steps until a walk of N steps has been constructed or until double occupancy occurs at some lattice site; in this case the process stops and a new walk is started. This procedure, known as direct Monte Carlo (DMC),[19] is very inefficient for generating samples of long walks. It is due to the law of sample attrition, saying that the ratio of walks of N steps that avoid self-intersection, W_N, to the total number of walks started, W_0, constitutes a fraction decreasing exponentially with N.[15] However, this ratio enables one to estimate the entropy. The following relation holds:

$$W_N/W_0 \cong C_N/q(q-1)^{N-1} \tag{1}$$

where q is the lattice coordination number (reverse steps are forbidden) and C_N is the total number of possible SAWs of N links starting from a given point. The entropy S is[20,21]

$$S = k_B \log C_N \cong k_B[\log q + (N-1)\log(q-1) + \log(W_N/W_0)] \tag{2}$$

where k_B is the Boltzmann constant. The first two terms in eq 2 define S_I, the entropy of an ideal chain without EV

0024-9297/83/2216-0249$01.50/0 © 1983 American Chemical Society

$$S_I = k_B[\log q + (N-1)\log(q-1)] \quad (3)$$

The last term in eq 2, which will be denoted $-S_{EV}$, is the negative contribution to the entropy due to EV

$$S_{EV} = S_I - S \cong -k_B \log (W_N/W_0) \quad (4)$$

Although the DMC is an inefficient procedure, we employ it in the present work since it enables us to compare our results with estimates for the entropy obtained with eq 2 and 4. These equations will also be used to estimate the entropy of chains with EV restricted within a box of size $(2L+1)^d$, where d is the dimensionality.

Exact Enumeration of SAWs. The exact number of SAWs of N steps, C_N, has been calculated up to $N = 24$ and $N = 19$ for the square and the simple-cubic (SC) lattices, respectively.[22] For large N, C_N is approximately expressed by[23]

$$C_N \cong C_0 N^{\gamma-1}\mu^N \quad (5)$$

where γ, μ, and C_0 are parameters calculated by series expansion (SE)[24] or renormalization group techniques.[25] For the square and SC lattice, we use the SE estimates $\gamma = {}^4/_3$ and ${}^7/_6$, respectively, and $\mu = 2.6385$ and 4.6838, respectively.[24] These values and the exact values of C_{24} and C_{19} enable us to solve eq 5 for the values of C_0, which are used to calculate C_N for $N = 39$ and $N = 49$.

Approximate Method for Estimating Entropy. We describe now a procedure, different from DMC, for generating SAWs with equal probability. Consider a lattice of any dimensionality with coordination number q, and let us construct a SAW that starts from the origin of the coordinate system. The first bond (step) is determined in one of q directions with equal probability $1/q$. In the next steps of the process ($k > 1$) the probability of selecting a direction ν ($\nu = 1, ..., q$) out of $q-1$ allowed ones is not constant $1/(q-1)$ as in the DMC but becomes a function of step k in the following way: Assume that we are at the kth step of the process; i.e., $k-1$ directions of the chain $\nu_1, ..., \nu_{k-1}$ have already been determined and we want to specify ν_k. The *exact* transition probability $p_k(\nu|\nu_1,...,\nu_{k-1})$ for selecting a direction ν should take into account all of the possible *partial* SAWs of $N-k+1$ bonds, which can be obtained in future steps of the process (steps $k, ..., N$). Those as-yet-undetermined partial SAWs should be distinguished from the $k-1$ bonds already fixed and therefore we call them the future SAWs (FSAWs). One can calculate $M_k{}^\nu(\nu_1,...,\nu_{k-1})$, the number of FSAWs starting with a direction ν at step k (for a given set of $\nu_1, ..., \nu_{k-1}$), and define the transition probability for ν

$$p_k(\nu|\nu_1,...,\nu_{k-1}) = M_k{}^\nu(\nu_1,...,\nu_{k-1})/\sum_\nu M_k{}^\nu(\nu_1,...,\nu_{k-1}) \quad (6)$$

ν_k is selected by a lottery according to the p_k's and the process continues. Once a SAW i of N bonds has been constructed, one knows its construction probability P_i, which is the product of the N sequential transition probabilities with which the directions $\nu_1, ..., \nu_N$ have been chosen

$$P_i = q^{-1}\prod_{k=2}^{N} p_k(\nu_k|\nu_1,...,\nu_{k-1}) \quad (7)$$

At each step of a particular construction *all* of the possible FSAWs are taken into account with equal probability. Furthermore, a construction cannot fail (ν_k that might lead to a failure is associated with $M_k{}^\nu = 0$, which means zero transition probability.) Hence, $P_i = C_N^{-1}$ for all i, which means that the entropy ($k_B \log C_N$) has zero fluctuation.[26] Obviously, this exact construction procedure is impractical for large N and we therefore suggest approximating it by defining (in the same manner as eq 6) transition probabilities $p_k(\nu|\nu_1,...,\nu_{k-1},b)$ based on FSAWs consisting only of b bonds, where b is a small number, rather than of $N-k+1$. Strictly speaking, the FSAW length is $b' = \min(b, N-k+1)$. In this case, a probability $P_i(b)$ can also be defined

$$P_i(b) = q^{-1}\prod_{k=2}^{N} p_k(\nu_k|\nu_1,...,\nu_{k-1},b) \quad (8)$$

However, it should be pointed out that, in contrast to P_i (eq 7), $P_i(b)$ depends on i since not all FSAWs are taken into account for their entire length. For that reason not every SAW attempted with the approximate procedure can successfully be completed, and therefore $P_i(b)$ constitutes only an approximate expression for the true probability of SAW i in the ensemble of all SAWs. Obviously, the larger b is, the better the approximation.[27]

Now suppose that a sample of n SAWs has been obtained with *any* computer simulation technique[15-17] and we want to estimate the entropy. For that, let us assume that this sample has been *hypothetically* generated with the approximate procedure described above rather than with the computer simulation method actually employed. Under this assumption one can reconstruct for each direction ν_k, $2 \le k \le N$, of SAW i the transition probability $p_k(\nu_k|\nu_1,...,\nu_{k-1},b)$ with which ν_k has been hypothetically determined and calculate $P_i(b)$ (eq 8). The entropy is estimated by $\bar{S}(b)$

$$\bar{S}(b) = -n^{-1}k_B\sum_{t=1}^{n}\log P_{i(t)}(b) \quad (9)$$

where $i(t)$ is SAW i sampled at time t. In this work, we are interested in $\bar{S}_{EV}(b)$, the entropy due to the EV effect

$$\bar{S}_{EV}(b) = S_I - \bar{S}(b) \quad (10)$$

Note that the values of $P_i(b)$ are not equal and therefore the fluctuation of $S(b)$, $\Delta S(b)$, is larger than zero; however, $\Delta S(b)$ is expected to decrease with the improvement of the approximation, i.e., increasing b; we shall estimate it by $\Delta\bar{S}(b)$

$$\Delta\bar{S}(b) = \{n^{-1}\sum_{t=1}^{n}[-k_B \log P_{i(t)}(b) - \bar{S}(b)]^2\}^{1/2} \quad (11)$$

It should be remarked that the main contribution to S_{EV} comes from the small loops, which are more frequent than the large ones. Therefore, one would expect that small values of b would already lead to relatively accurate results for S_{EV}. However, when the chain is confined within a "box", more *long-range* contacts are formed and b should therefore be increased. It should also be pointed out that the approximate construction procedure for SAWs described above takes into account at each step k *all* of the $k-1$ directions previously determined as well as the FSAWs of length b. Therefore, our approximation is better than approximations based on higher order Markov chains previously studied.[21,29-31]

Our method is also expected to be useful for estimating the entropy of chains with EV as well as finite attractive or repulsive interactions where eq 2 and 4 cannot be employed. In this case, however, for each step k of the process, one has to calculate the energy $E_{l(\nu)}$ of every FSAW l starting in direction ν. $E_{l(\nu)}$ takes into account the interaction energy between future steps of l among themselves and the interaction energy between future steps of l and the $k-1$ past steps. $M_k{}^\nu(b)$ is then defined by Boltzmann factors

$$M_k{}^\nu(b) = \sum_{l(\nu)}\exp(-E_{l(\nu)}/k_BT) \quad (12)$$

where T is the absolute temperature. The transition

Table I
Entropy of Self-Avoiding Walks on a 3-Choice Square Lattice[a,b]

$N = 19$					$N = 39$				$N = 49$			
L	b	S/Nk_B	S_{EV}/Nk_B	$\Delta S/Nk_B$	L	b	S/Nk_B	S_{EV}/Nk_B	L	b	S/Nk_B	S_{EV}/Nk_B
∞	1		0.0559 (4)[e]	0.0409 (3)	∞	1		0.0624 (2)	∞	1		0.0640 (3)
	4		0.0800 (1)	0.0074 (1)		4		0.0960 (3)		4		0.0993 (1)
	7	1.03315 (1)	0.08060 (1)	0.00152 (2)		7	1.0073 (2)	0.0987 (2)		7	1.0019 (2)	0.1026 (2)
	DMC[c]	1.0324 (3)	0.0813 (3)			DMC	1.0067 (4)	0.0993 (4)		DMC	1.0005 (1)	0.1040 (1)
	series[d]	1.03316	0.08059			series	1.0069	0.0991		series	1.0009	0.1035
6	1		0.125 (1)	0.062 (1)	13	1		0.080 (1)	18	1		0.0715 (4)
	4		0.163 (3)	0.036 (1)		4		0.1137 (4)		4		0.1063 (3)
	8	0.9389 (1)	0.1747 (1)	0.0086 (1)		8	0.9900 (3)	0.1160 (3)		7	0.9949 (3)	0.1096 (3)
	DMC	0.938 (1)	0.176 (1)			DMC	0.986 (1)	0.119 (1)		DMC	0.9922 (3)	0.1122 (3)
5	1		0.162 (2)	0.0679 (5)	10	1		0.091 (2)	14	1		0.081 (2)
	4		0.2166 (4)	0.0345 (5)		4		0.132 (1)		4		0.1170 (3)
	8	0.8860 (4)	0.2277 (4)	0.0101 (3)		8	0.967 (1)	0.138 (1)		7	0.9830 (3)	0.1214 (3)
	DMC	0.885 (1)	0.229 (1)			DMC	0.961 (1)	0.145 (1)		DMC	0.979 (1)	0.126 (1)

[a] N is the number of bonds in a walk, $2L + 1$ is the box's size, and b defines our approximation (see text). [b] S is the total entropy, S_{EV} the entropy due to excluded volume, and ΔS the fluctuation of S (for definition, see text). [c] DMC denotes results obtained with eq 2 and 4. [d] Series denotes the series expansion results obtained from C_N (eq 8 using parameters from ref 23). For $N = 19$, the exact value of C_{19} is used. [e] The statistical error of the last digit appears in parentheses; e.g., 0.0559 (4) = 0.0559 ± 0.0004. These errors have been calculated from three different DMC runs with different random number sequences.

Table II
Entropy of Self-Avoiding Walks on a 5-Choice Simple-Cubic Lattice[a]

	$N = 19$				$N = 39$			$N = 49$		
b	L	S/Nk_B	S_{EV}/Nk_B	$\Delta S/Nk_B$	L	S/Nk_B	S_{EV}/Nk_B	L	S/Nk_B	S_{EV}/Nk_B
1	∞		0.0344 (3)	0.249 (1)	∞		0.0407 (3)	∞		0.0421 (7)
4			0.0408 (3)	0.00325 (4)			0.0501 (1)			0.0524 (1)
5		1.5781 (3)	0.0409 (3)	0.00187 (7)		1.5639 (1)	0.0503 (1)		1.5605 (4)	0.0527 (4)
DMC		1.5784 (3)	0.0406 (3)			1.5639 (2)	0.0503 (2)		1.5601 (6)	0.0530 (6)
series		1.5784	0.0406			1.5639	0.0502		1.5606	0.0525
1	5		0.078 (1)	0.0396 (3)	8		0.0567 (5)	8		0.0598 (2)
4			0.0911 (1)	0.0223 (1)			0.0683 (2)			0.0741 (2)
5		1.52632 (3)	0.09272 (3)	0.0185 (2)		1.5451 (2)	0.0691 (2)		1.5382 (2)	0.0751 (2)
DMC		1.5230 (7)	0.0960 (7)			1.5416 (4)	0.0725 (4)		1.5321 (3)	0.0811 (3)
1	4		0.122 (1)	0.0517 (5)	6		0.077 (1)	7		0.0679 (1)
4			0.1478 (4)	0.0239 (1)			0.0975 (2)			0.0854 (2)
5		1.4681 (2)	0.1511 (2)	0.0161 (1)		1.5144 (3)	0.0988 (3)		1.5260 (2)	0.0874 (2)
DMC		1.465 (2)	0.155 (2)			1.507 (1)	0.107 (1)		1.5185 (5)	0.0945 (5)

[a] See explanations for Table I.

probabilities are defined with the help of eq 6. We intend in the future to apply our method to such systems (e.g., see ref 32 and 33).

Finally, we point out that the present method for estimating the entropy is based on the concepts of a stochastic process described recently for the square Ising lattice.[34]

Results and Discussion

The results for the entropy of SAWs on square and SC lattices are summarized in Tables I and II, respectively. Samples of SAWs of length $N = 19$, $N = 39$, and $N = 49$ have been obtained with the DMC procedure. This enables one to estimate the entropy with eq 2 and 4 and these results are labeled DMC in the tables. For both lattices the sample size W_N ($W_N = n$) ranges from ~500 to ~5000, where the number of walks started, W_0, ranges from 30 000 to 180 000 for the square lattice and from 10 000 to 30 000 for the SC lattice. The chains are studied in unbounded space ($L = \infty$) and alternatively they are restricted to "boxes" of size $(2L + 1)^d$, where d is the dimensionality (i.e., the walls of the "box" are excluded). Our results for S_{EV} (eq 10) have been calculated for three values of b, and for the best approximation (the largest value of b) we also provide the values of S (eq 9). For comparison we have calculated for the unbounded ($L = \infty$) SAWs the SE estimates for the entropy using eq 5. The fluctuations $\Delta S(b)$ have been obtained with eq 11 and are presented only for $N = 19$. It should be pointed out that for both lattices and for all values of L our results for S_{EV} must decrease monotonically with the improvement of the approximation, i.e., with increasing b. Our best approximation therefore constitutes a higher bound for the true values of S_{EV} (see ref 21). As expected, $\Delta S(b)$ decrease with increasing b; this holds for all chain lengths studied.

The Square Lattice. Let us discuss first the results for the unbounded chains ($L = \infty$). For $N = 19$ our best result ($b = 7$) for S_{EV} is equal to the SE value within the statistical error 0.012%; for $N = 39$ and $N = 49$ the results for S_{EV} obtained by these two methods differ by 0.4% and 0.9%, respectively. The difference from the DMC estimates is 0.9%, 0.6%, and 1.4% for $N = 19$, $N = 39$, and $N = 49$, respectively (the DMC and the SE results agree within 1%). It should be noted that the results for S obtained by the three methods are in much better agreement than those for S_{EV}; this follows trivially from the fact that S_{EV} constitutes only ~10% of S_I (eq 3).

Confining the chain within the walls of a $(2L + 1) \times (2L + 1)$ "box" imposes additional long-range restrictions and

we therefore expect that the accuracy of our best results for S_{EV} decrease with decreasing L. Indeed, the deviations of these results from the corresponding DMC estimates for $N = 49$ are about 2.3% and 4% for $L = 18$ and $L = 16$, respectively; for $N = 39$, the deviations are 2.5% and 4.8% for $L = 13$ and $L = 10$, respectively (only for $N = 19$ a slight trend in the opposite direction is observed). It should be pointed out that the convergence of our approximations to the "correct" DMC values (as a function of b) is rapid for both the bounded and unbounded SAWs: the results for S_{EV} for our crudest approximation ($b = 1$) deviate from the DMC values by 30–40%. The results for $b = 4$ are already much more accurate and deviate from the DMC results only by 0.7–7%. This behavior occurs because most of the contribution to the entropy comes from the short loops.

The SC Lattice. The results for the SC lattice (Table II) show behavior similar to that which has been detected for the square lattice. For $L = \infty$ the results for S_{EV} for our best approximation $b = 5$ deviate from the SE and DMC estimates by less than 0.8%. For $L \neq \infty$ the deviation is larger and ranges from 3% ($N = 19, L = 4$) to 7.5% ($N = 49, L = 7$), which is comparable to the deviation observed for the square lattice. Since the ratio S_{EV}/S_I is smaller for the SC lattice than for the square lattice, the results for S obtained by the three methods are in a better agreement for the SC lattice than for the square lattice. It should be pointed out that the results for S_{EV} for the crudest approximation ($b = 1$) deviate only by 15–28% from the DMC values as compared to 30–40% for the square lattice. This stems from the fact that the excluded volume effect is stronger in the square lattice than in the SC lattice.

Better approximations for the entropy can be obtained by increasing the length b of the FSAWs. However, this will also increase the required computer time since most of it is spent on calculating the hypothetical transition probabilities.

Conclusions

We have developed a general method for estimating the entropy of macromolecules with computer simulation and applied it to relatively short SAWs ($N \leq 49$) on square and SC lattices. Our results are compared to the results obtained from series expansion and from the DMC data using eq 2 and 4. For the unbounded chains ($L = \infty$), the accuracy is estimated to be better than 1%. When the chain is confined in a box, the accuracy worsens and ranges between ~2% and 7%. As the next step, we intend to apply the method to lattice models of macromolecules with EV as well as with attractive interactions.[32,33]

Acknowledgment. This work has been supported by the Sir Charles Clore–Weizmann Fund Postdoctoral Fellowship. I thank Professor Z. Alexandrowicz for helpful discussions.

References and Notes

(1) Hansen, J. P.; Verlet, L. *Phys. Rev.* **1969**, *184*, 151.
(2) Salsburg, Z. W.; Jacobson, J. D.; Fickett, W.; Wood, W. W. *J. Chem. Phys.* **1959**, *30*, 65.
(3) Valeau, J. P.; Card, D. N. *J. Chem. Phys.* **1972**, *57*, 5457.
(4) Alexandrowicz, Z. *J. Stat. Phys.* **1976**, *14*, 1.
(5) Meirovitch, H. *Chem. Phys. Lett.* **1977**, *45*, 389.
(6) Binder, K., Ed. "Monte Carlo Methods in Statistical Physics"; Springer-Verlag: Berlin, Heidelberg, New York, 1979; p 7.
(7) Gō, N.; Scheraga, H. A. *J. Chem. Phys.* **1969**, *51*, 4751.
(8) Gō, N.; Scheraga, H. A. *Macromolecules* **1976**, *9*, 535.
(9) Gō, N.; Lewis, P. N.; Scheraga, H. A. *Macromolecules* **1970**, *3*, 628.
(10) Gō, N.; Gō, M.; Scheraga, H. A. *Macromolecules* **1974**, *7*, 137.
(11) Flory, P. J. "Principles of Polymer Chemistry"; Cornell University Press: Ithaca, NY, 1953; Chapter 14.
(12) Flory, P. J. "Statistical Mechanics of Chain Molecules"; Wiley: New York, 1969; p 32.
(13) DeVoe, H. In "Structure and Stability of Macromolecules"; Timosheff, S. N., Fasman, G. D., Eds.; Marcel Dekker: New York, 1969; Chapter 1.
(14) Karplus, M.; Kushick, J. N. *Macromolecules* **1981**, *14*, 325.
(15) Wall, F. T.; Windwer, S.; Gans, P. J. In "Methods of Computational Physics"; Academic Press: New York, 1963; Vol. I.
(16) Verdier, P. H.; Stockmayer, W. H. *J. Chem. Phys.* **1962**, *36*, 227.
(17) Alexandrowicz, Z. *J. Chem. Phys.* **1969**, *51*, 561.
(18) McCammon, J. A.; Gelin, B. R.; Karplus, M. *Nature (London)* **1977**, *267*, 585.
(19) Wall, F. T.; Hiller, L. A., Jr.; Wheeler, D. J. *J. Chem. Phys.* **1954**, *22*, 1036.
(20) Temperley, H. N. V. *J. Res. Natl. Bur. Stand.* **1956**, *56*, 55.
(21) Fisher, M. E.; Sykes, M. F. *Phys. Rev.* **1959**, *114*, 45.
(22) Sykes, M. F.; Guttman, A. J.; Watts, M. G.; Roberts, P. D. *J. Phys. A* **1972**, *5*, 653.
(23) McKenzie, D. S. *Phys. Rep.* **1976**, *27C*, 35.
(24) Watts, M. G. *J. Phys. A* **1975**, *8*, 61.
(25) Le Guillou, J. C.; Zinn-Justin, J. *Phys. Rev. B* **1980**, *21*, 3976.
(26) Meirovitch, H.; Alexandrowicz, Z. *J. Stat. Phys.* **1976**, *15*, 123.
(27) A similar procedure with $b = 1$ has been examined by Rosenbluth and Rosenbluth;[28] however, they correct the bias defined by $P_i(b)$ (eq 8) whereas we do not.
(28) Rosenbluth, A. W.; Rosenbluth, J. *J. Chem. Phys.* **1955**, *23*, 356.
(29) Montroll, E. W. *J. Chem. Phys.* **1954**, *22*, 1036.
(30) Mazur, J. *J. Chem. Phys.* **1964**, *41*, 2256.
(31) Mazur, J. In "Markov Chains and Monte Carlo Calculations in Polymer Science"; Lowry, G. G., Ed.; Marcel Dekker: New York, 1970; Chapter 6.
(32) Taketomi, H.; Ueda, Y.; Gō, N. *Int. J. Pept. Protein Res.* **1975**, *7*, 445.
(33) Gō, N.; Taketomi, H. *Int. J. Pept. Protein Res.* **1979**, *13*, 235.
(34) Meirovitch, H. *J. Phys. A: Math. Gen.* **1982**, *15*, 2063.