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## On the Use of Classical Statistical Mechanics in the Treatment of Polymer Chain Conformation<sup>1</sup>

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**ABSTRACT:** Two different treatments of the degrees of freedom of bond stretching and bond angle bending in chain polymers by classical statistical mechanics lead to different and nonequivalent expressions of the partition functions. If we fix the bond lengths and bond angles at the outset and treat them as constraints (the classical rigid model), the partition function is given by an integral of  $(\det \mathbf{G})^{-1/2} \exp[-\beta F(Q)]$  over the space of the dihedral angles  $Q$  in a polymer chain, where the elements of the matrix  $\mathbf{G}$  are the coefficients in the quadratic expression (in terms of generalized momenta conjugate to  $Q$ ) for the kinetic energy of the polymer chain, and  $F(Q)$  is the conformational energy of the polymer chain. If we conceptually allow bond lengths and bond angles to vary under an infinitely strong potential (the classical flexible model) and perform the integration of the Boltzmann factor over the momenta conjugate to the Cartesian coordinates, we obtain the partition function in the form of an integral of  $\exp[-\beta F(Q)]$  over the space of the dihedral angles  $Q$ . The origin of the difference in these two expressions lies in the different treatments of the vibrational motions involving bond lengths and bond angles. In order to decide which of the two expressions is to be used as the basis of a statistical mechanical study of the polymer chain in equilibrium, an expression for the partition function that is quantum mechanically correct for these vibrational motions is derived, and the approximations involved to obtain each of the two non-equivalent classical expressions from the quantum mechanical expression are examined. The classical rigid model can be derived from the quantum mechanical one (a) by applying the ground state approximation for all vibrations associated with bond stretching and bond angle bending (i.e., by neglecting contributions to the partition function from excited vibrational states), and (b) by neglecting the conformational dependence of the zero-point energy of these vibrations. The classical flexible model can be derived by treating all these vibrations classically, which would appear to be unwarranted because many of these vibrations are of sufficiently high frequency to require a quantum mechanical treatment. However, a quantitative analysis of the approximations involved in each of the two models reveals that, of the two nonequivalent classical treatments, the classical flexible model is better than the classical rigid model.

There has been considerable discussion of the basis for treating polymer chain conformation by classical statistical mechanics.<sup>2–8</sup> Various equilibrium conformational properties have been calculated from a classical statistical mechanical partition function  $Z$  of the form

$$Z = (\text{constant}) \int \exp[-\beta F(Q)] dQ \quad (1)$$

where  $\beta = 1/kT$  (with  $k$  being the Boltzmann constant and  $T$  the absolute temperature),  $Q$  stands for a set of dihedral angles which describes the conformation of the polymer chain, and  $F(Q)$  is the conformational (free) energy of the polymer in solution in a conformation specified by  $Q$ , or, in other words, the potential of the mean force operative on the polymer for various configurations of the solvent molecules. The quantity  $F(Q)$  is a free energy, for the polymer in solution, because it includes the free energy of solvation as a function of  $Q$ . The validity of the use of eq 1 was questioned in ref 2 and 4, and it was suggested in ref 4 (but no definite conclusion about the matter was reached) that it might be necessary to use the following form of the partition function:

$$Z = (\text{constant}) \int \left[ \frac{1}{\det \mathbf{G}} \right]^{1/2} \exp[-\beta F(Q)] dQ \quad (2)$$

Equation 2 was derived by fixing the bond lengths and bond angles (and regarding them as constraints), and then applying classical statistical mechanics to the constrained system. The elements of the matrix  $\mathbf{G}$  in eq 2 are the coefficients in the quadratic expression (in terms of generalized momenta) for the kinetic energy of the polymer chain. Such a model of a polymer chain, in which bond lengths and bond angles are fixed and are treated as constraints, and for which classical statistical mechanics is applied, may be defined as a "classical rigid model". In our earlier paper,<sup>6</sup> we provided a discussion which erroneously supported the necessity of using eq 2 to treat the equilibrium properties of polymer chains. In the present paper, we explore the origin of the differences between these two forms of the partition function, and show that, while both involve approximations, eq 1 is more accurate than eq 2 and, further, the use of eq 1 avoids the difficulty of not being able to treat the conformational dependence of  $\det \mathbf{G}$  in the integral of eq 2, as pointed out by Flory.<sup>7</sup>

We first demonstrate that eq 1 can be derived for a polymer chain in which the bond lengths and bond angles are conceptually allowed to vary, and for which classical statistical mechanics is applied. This is accomplished by allowing bond lengths and bond angles to vary, and by taking the limit of very small actual variations due to the strong potentials which govern them. This treatment of a polymer chain may be defined as that of a "classical flexible model". Thus, a partition function of the form of eq 1 is derived for the classical flexible model. This fact, that an equation of the form of eq 1 is obtained for the "classical flexible model" in which bond lengths and bond angles are conceptually allowed to vary, was already clearly recognized by Flory<sup>7</sup> and Volkenstein,<sup>9</sup> and we present a demonstration of it in the present paper. Once eq 1 is derived, we need consider only dihedral angles as the independent variables. In this sense, the fact that bond lengths and bond angles are allowed to vary is conceptual.

Second, we fix the bond lengths and bond angles at the outset (classical rigid model), and thus have the result of ref 6, viz., that eq 2 with the intractable factor  $\det \mathbf{G}$  is obtained in a classical statistical mechanical treatment. As in eq 1, the independent variables are the dihedral angles.

Thus, the two classical models lead to different and non-equivalent expressions for the partition function, in both of which only dihedral angles appear as the independent variables. In order to understand the origin of this difference, and to decide which of the two should be used to treat the equilibrium properties of polymer chains, we must investigate the apparently concealed freedom for bonds to stretch and for bond angles to bend. These constitute vibrational motions with frequencies, in general, in the infrared region between 400 and 3000  $\text{cm}^{-1}$ . Thus, such motions have to be treated quantum mechanically at room temperature. Therefore, a quantum mechanical expression for the partition function is derived by using a quantum mechanical partition function for such vibrational motions. (An argument is given in section III about the validity of the use of quantum mechanics for treating the high-frequency vibrational modes in a polymer embedded in solution.) It was argued in our previous paper<sup>6</sup> that the energies of such vibrations are larger than  $kT$  at room temperature, and therefore that their excitation can be neglected at room temperature (ground state approximation). (In reality, we are concerned only with the conformational dependence of the vibrational energy, and not with its absolute value.) With this assumption, approximation A (eq 30 of ref 6), in which the independent variables of integration in the partition function are the soft variables<sup>6</sup> (dihedral angles), was derived.<sup>6</sup> In this approximation, there is a small dependence of the average values of the hard variables<sup>6</sup> (bond lengths and bond angles), and of the zero-point vibrational energy of the hard variables, on the instantaneous values of the soft variables. Since the zero-point energy was retained, approximation A was not completely classical. In this sense, we might have created the wrong impression (in ref 6) that we were advocating the use of quantum mechanics to treat polymer chain conformation. However, as treated in ref 6, and as pointed out in ref 10, approximation A was introduced in ref 6 only for conceptual purposes, to delineate clearly several stages of approximations to reach the final classical treatment of approximation C,<sup>6</sup> and not for the purpose of advocating a quantum mechanical treatment. Incidentally, as pointed out by Hagler and Lifson,<sup>11</sup> if approximation A had actually been used, a significant error could have been introduced because some of the coupled motions of hard variables involving many atoms can have very low (softened) frequencies, thereby rendering the ground state approximation invalid for these motions. The situation can be even worse, since such softened modes are coupled to the motions of the soft variables and the solvent molecules (such an error would then carry through to

approximations B and C). After discussion of approximation A, approximation B (eq 31 of ref 6) was then introduced<sup>6</sup> by neglecting the dependence of the zero-point energy of the vibrations of the hard variables on the instantaneous values of the soft variables. Finally, approximation C (eq 32 of ref 6, which is the same as eq 2 of the present paper) was obtained by neglecting the dependence of the hard variables on the instantaneous values of the soft variables. Hence, aside from the neglect of the dependence of the average values of the hard variables on the soft variables, the main approximations involved in eq 2 are the ground state approximation of some possibly softened modes and the neglect of the zero-point energy.

Third, in order to assess the relative merits of eq 1 and 2 for treating polymer conformation, we also examine, in the present paper, the nature of the approximations involved in eq 1. We demonstrate that eq 1 is obtained by taking the classical limit of the quantum mechanical expression for the vibrational partition function. The error in the statistical weight involved in taking this limit is not large for vibrational frequencies less than 400  $\text{cm}^{-1}$ .<sup>6</sup> However, most of the vibrational modes of the hard variables have frequencies higher than this. Hence, the approximation of taking the classical limit does not appear to be a good one, in principle, although, in practice, it *may not* introduce a large error (at room temperature). In any event, a detailed examination of the approximations involved reveals that eq 1 is better than eq 2, a conclusion that is now in accordance with that in ref 7.

It should be emphasized here that only the soft variables (dihedral angles) appear in eq 1 as independent variables, even though bond lengths and bond angles are allowed to vary conceptually to derive eq 1. Thus, in actual applications of eq 1, the bond lengths and bond angles can be kept fixed.

In section I, the mathematical definitions of the classical flexible model and the classical rigid model are given, and expressions for their partition functions are obtained and compared. In section II, an expression is derived for the partition function that is quantum mechanically correct for the vibrational motions involving bond lengths and bond angles, the approximations in the two classical models are delineated, and it is concluded that the classical flexible model is the better of the two. Section III is devoted to a summary and discussion of the results, including a discussion of the role of the solvent.

## I. Nonequivalence of the Two Classical Models

In this section, we define two different classical models, and deduce the Hamiltonians for each of these models. Then we discuss the expressions for their partition functions.

**A. Classical Flexible Model.** In the flexible model of a polymer chain, the independent variables are the bond lengths, bond angles, dihedral angles for rotation around bonds, and the external variables (for overall translation and rotation). The bond lengths and bond angles (hard variables) are designated by  $Q' = (q_1', q_2', \dots, q_l')$ . The dihedral angles and the external variables are designated *together* by  $Q = (q_1, q_2, \dots, q_m)$ , and referred to as soft variables; this terminology is different from that in our previous paper<sup>6</sup> in that we now include the external variables among the soft variables. The vibrational motions of the hard variables are assumed to be governed by a harmonic force field. Thus, in the expression for the conformational energy (i.e., potential energy, which becomes a free energy when solvent is introduced<sup>6</sup>),  $F(Q, Q')$ , given by eq 25 of ref 6, viz.,

$$F(Q, Q') = F_0(Q) + \frac{1}{2} \sum_{i,j=1}^l f_{ij}''(q_i' - q_{i0}') (q_j' - q_{j0}') \quad (3)$$

the time-average value  $Q_0' = (q_{10}', q_{20}', \dots, q_{l0}')$  of  $Q'$ , i.e., the value at which  $F(Q, Q')$  has the minimum value  $F_0(Q)$  for a

given set of values of the soft variables  $Q$ , is a function of the instantaneous value of the soft variables  $Q$ . However, we introduce an approximation by neglecting this dependence of  $Q_0'$  on  $Q$ , and replace  $Q_0'$  by the  $Q$ -independent strain-free value  $Q_1'$ . This is the same approximation as was introduced to obtain approximation C (classical rigid model) from approximation B in ref 6. The introduction of this approximation of replacing the  $Q$ -dependent  $Q_0'$  by the  $Q$ -independent  $Q_1'$  at this stage serves to convey the essential points of this paper more easily and concisely without too much loss of generality; however, for simplicity, we will retain the notation  $Q_0'$ . The force constants  $f_{ij}''$  [given by the second derivative of  $F(Q, Q')$  with respect to  $q_i'$  and  $q_j'$  at  $Q_0'$ ] are assumed to be independent of  $Q$ , as was also assumed in ref 6. This assumption is justified because the force constants  $f_{ij}''$  are determined mainly by the force field associated with covalent bonds, i.e., by the energy terms responsible for keeping bond lengths and bond angles constant. This force field is independent of the conformation of the polymer chain, or of the value of the soft variables  $Q$ .

The kinetic energy,  $K_f$ , of the flexible model is given in terms of the time derivatives of the Cartesian coordinates  $x_{k\alpha}$ , as

$$K_f = \frac{1}{2} \sum_{k=1}^n \sum_{\alpha=1}^3 m_k \dot{x}_{k\alpha}^2 \quad (4)$$

where  $n$  is the number of atoms in a polymer (therefore,  $3n = l + m$ ), and  $\alpha = 1, 2, 3$  designates the component of the Cartesian coordinates of the  $k$ th atom whose mass is  $m_k$ . If we take  $Q$  and  $Q'$  as independent variables (instead of  $x_{k\alpha}$ ), the kinetic energy,  $K_f$ , is given in the following form:

$$K_f = \frac{1}{2} \dot{Q}^+ \mathcal{H} \dot{Q} \equiv \frac{1}{2} (\dot{Q}^+, \dot{Q}'^+) \begin{pmatrix} \mathbf{H}^0 & \mathbf{H}' \\ \mathbf{H}'^+ & \mathbf{H}'' \end{pmatrix} \begin{pmatrix} \dot{Q} \\ \dot{Q}' \end{pmatrix} \quad (5)$$

where  $\dot{Q}$  and  $\dot{Q}'$  are  $m$ - and  $l$ -dimensional column vectors whose  $i$ th component is  $\dot{q}_i$  and  $\dot{q}_i'$ , respectively ( $\dot{Q}^+$  and  $\dot{Q}'^+$  are corresponding row vectors);  $\mathbf{H}^0$ ,  $\mathbf{H}'$ ,  $\mathbf{H}''$  are  $m \times m$ ,  $m \times l$ , and  $l \times l$  matrices; the superscript plus sign denotes a transpose. The elements of  $\mathbf{H}^0$ ,  $\mathbf{H}'$ , and  $\mathbf{H}''$  can be deduced from eq 4, and are given explicitly in Appendix A.

The Hamiltonian for the classical flexible model is then the sum of  $F(Q, Q')$  of eq 3 and  $K_f$  of eq 5.

**B. Classical Rigid Model.** In the rigid model of a polymer molecule, the hard variables (bond lengths and bond angles) are kept fixed. The kinetic energy,  $K_r$ , for this model is obtained by setting the time derivative of the hard variables equal to zero in eq 5; thus,

$$K_r = \frac{1}{2} \dot{Q}^+ \mathbf{H}^0 \dot{Q} \quad (6)$$

The conformational energy for this model is simply  $F_0(Q)$ .

**C. Partition Function for Classical Flexible Model.** The partition function for the classical flexible model,  $Z_f$ , can be obtained by expressing the kinetic energy of eq 4 in terms of momenta,  $p_{k\alpha} = \partial K_f / \partial \dot{x}_{k\alpha} = m_k \dot{x}_{k\alpha}$ , conjugate to the Cartesian coordinates,  $x_{k\alpha}$ , and then by performing the integration of the Boltzmann factor over the momentum space. The partition function  $Z_f$  is then given by

$$Z_f = \left[ \prod_{k=1}^n \left( \frac{m_k k T}{2\pi\hbar^2} \right)^{3/2} \right] \int \exp[-\beta F(Q, Q')] \prod_{k,\alpha} dx_{k\alpha} \quad (7)$$

The first factor, resulting from the integration over the momentum space, is independent of  $Q$  and  $Q'$ .

In order to perform the integration in eq 7, we change the variables of integration from Cartesian coordinates,  $x_{k\alpha}$ , to internal coordinates (plus the six external variables),  $Q$  and  $Q'$ . In Appendix B, the Jacobian,  $D$ , for this transformation is obtained, and shown to be given by a product of two factors, depending only on the external and hard variables, respectively, and to be independent of the dihedral angles. By as-

suming that the potentials governing the hard variables are very strong, the minimum-energy values,  $Q_0'$ , may be assigned to the hard variables  $Q'$  in the  $Q'$ -dependent factor  $D(Q')$  of the Jacobian. Then the integration with respect to the external and hard variables can be performed (see Appendix B) to give

$$Z_f = \left[ \prod_k \left( \frac{m_k k T}{2\pi\hbar^2} \right)^{3/2} \right] \left[ \frac{(2\pi k T)^l}{\det \mathbf{F}''} \right]^{1/2} \left[ 8\pi^2 V \{D(Q_0')\} \right] \times \int \exp[-\beta F_0(Q)] dQ \quad (8)$$

where  $\mathbf{F}''$  is an  $l \times l$  matrix whose  $(i, j)$  element is  $f_{ij}''$ . Thus, for the classical flexible model, the problem of obtaining the partition function is reduced to an evaluation of the last integral in eq 8, involving only the *internal* soft variables as the variables of integration; the bond stretching and bond angle bending degrees of freedom do not appear explicitly. Thus, in actual applications of eq 8, which is the same as eq 1, the bond lengths and bond angles are kept fixed. However, in the process of deriving eq 8, these quantities are conceptually allowed to vary. It is in this sense that the use of eq 8 is based on the classical flexible model of a polymer chain.

**D. Partition Function for Classical Rigid Model.** We consider next the derivation of the partition function for the classical rigid model. For this purpose, we re-write the expression for  $K_r$  of eq 6 as

$$K_r = \frac{1}{2} P_r^+ \mathbf{G} P_r \quad (9)$$

where  $P_r$  is a generalized momentum conjugate to the soft variable  $Q$  in the rigid model ( $P_r = \partial K_r / \partial \dot{Q} = \mathbf{H}^0 \dot{Q}$ ), and  $\mathbf{G}$  is an  $m \times m$  matrix (equal to  $(\mathbf{H}^0)^{-1}$ ) given<sup>12</sup> by

$$\mathbf{G} [ \equiv (\mathbf{H}^0)^{-1} ] = \mathbf{G}^0 - \mathbf{G}' \mathbf{G}''^{-1} \mathbf{G}'^+ \quad (10)$$

where  $\mathbf{G}^0$ ,  $\mathbf{G}'$ ,  $\mathbf{G}''$  are  $m \times m$ ,  $m \times l$ , and  $l \times l$  submatrices of a  $3n \times 3n$  matrix  $\mathcal{G}$ ,

$$\mathcal{G} = \begin{pmatrix} \mathbf{G}^0 & \mathbf{G}' \\ \mathbf{G}'^+ & \mathbf{G}'' \end{pmatrix} \quad (11)$$

which is the inverse of the  $3n \times 3n$  matrix  $\mathcal{H}$  defined in eq 5. The elements of the matrices  $\mathbf{G}^0$ ,  $\mathbf{G}'$ , and  $\mathbf{G}''$  are given in Appendix A.

The partition function for the classical rigid model may be written as

$$Z_r = \left( \frac{1}{2\pi\hbar} \right)^m \int \exp[-\beta \{K_r + F_0(Q)\}] dP_r dQ \quad (12)$$

Introducing eq 9 for  $K_r$ , and integrating the Boltzmann factor over the momentum space and over the external variables, we obtain

$$Z_r = \left( \frac{k T}{2\pi\hbar^2} \right)^{m/2} (8\pi^2 V) \int \left[ \frac{1}{\det \mathbf{G}} \right]^{1/2} \exp[-\beta F_0(Q)] dQ \quad (13)$$

which is the same as eq 2. As in the case of eq 8, the integration in eq 13 is to be carried out only over the *internal* soft variables. However, in contrast to eq 8, the integrand includes the additional factor,  $[\det \mathbf{G}]^{-1/2}$ , which cannot be taken out of the integral sign because it is a function of the internal soft variables  $Q$ .

**E. Comparison of the Two Models.** We now have two classical models (eq 8 and 13) which appear to be nonequivalent. In order to obtain some understanding of the origin of the difference between these two expressions, we derive here another expression for  $Z_f$ . This derivation is based on the following expression for the Jacobian,  $D$ , which is derived in Appendix A.

$$D = \left[ \det \mathbf{G} \det \mathbf{G}'' \left( \prod_{k=1}^n m_k \right)^3 \right]^{-1/2} \quad (14)$$

Substituting this expression for  $D$  into eq 8, and using the relationship<sup>13</sup>

$$\det(\mathbf{F}''\mathbf{G}'') = \prod_{i=1}^l (2\pi\nu_i)^2 \quad (15)$$

where the  $\nu_i$ 's are the vibrational frequencies of the hard variables, we obtain the following expression for  $Z_f$ :

$$Z_f = \left(\frac{kT}{2\pi\hbar^2}\right)^{m/2} (8\pi^2V) \int \left[ \prod_{i=1}^l \frac{kT}{2\pi\hbar\nu_i} \right] \left[ \frac{1}{\det \mathbf{G}} \right]^{1/2} \times \exp[-\beta F_0(Q)] dQ \quad (16)$$

Since eq 8 and 16 are different expressions for the same quantity, the product of the first two factors in the integrand of eq 16 must be independent of the internal soft variables. However, the individual factors are not. The first factor in the integrand is a product of classical partition functions for harmonic oscillators having frequencies  $\nu_i$  ( $i = 1, 2, \dots, l$ ). Comparison of eq 16 with eq 13 reveals the make-up of the classical flexible model. It consists of the classical rigid model plus a set of  $l$  harmonic oscillators with conformation-dependent frequencies. If the conformation dependence of the frequencies of these oscillators were neglected, the two models would become equivalent.

It should be noted here that, even though the hard variables are allowed to vary conceptually in the classical flexible model, the potentials governing the hard variables were assumed to be very strong in deriving eq 8. Intuitively, the classical flexible model should become identical with the classical rigid model in the limit of infinitely strong potentials for variation of bond lengths and bond angles. However, application of classical statistical mechanics to the intuitively identical models led to nonequivalent expressions for the partition functions. By comparing eq 16 with eq 13, it appears that the partition function for the classical rigid model can be obtained by replacing  $\Pi(kT/2\pi\hbar\nu_i)$  in eq 16 by unity. In the limit of infinitely strong potentials,  $\Pi(kT/2\pi\hbar\nu_i)$  in the partition function for the classical flexible model becomes vanishingly small, while the corresponding quantity remains unity in the classical rigid model. In a sense, this appears as if the classical rigid model (with the larger value of the partition function in the limit of infinitely strong potentials) is more flexible than the classical flexible model. This superficially strange state of affairs arises from a fundamental deficiency of classical statistical mechanics when applied to high-frequency motions. Therefore, the underlying difference between the classical flexible and classical rigid models can be understood as procedural, arising because of the deficiency of classical statistical mechanics, rather than being intrinsic to the concept of flexibility vs. rigidity. However, the purpose of this paper is not to advocate a quantum mechanical treatment of polymers, but to assess the relative merits of the two nonequivalent classical models or procedures. For this purpose, and only for this purpose, we study the vibrational motions of the hard variables quantum mechanically in section II.

At this point, the reader is referred to Appendix C, where it is pointed out (parenthetically to the main development of the argument in this paper) that, whereas eq 1 (or eq 8) has been used almost universally in treating equilibrium properties of polymer chains, the situation is a bit different as far as the treatment of nonequilibrium problems is concerned.

## II. Approximations Involved in the Two Classical Models

Since the vibrational frequencies of the hard variables are generally high compared to  $kT/h$ , their behavior must be treated quantum mechanically. Therefore, if a classical model is used, it must be justified as a valid approximation to the quantum mechanical one. We can obtain the quantum me-

chanical partition function,  $Z_{QM}$ , from eq 16 by replacing the classical partition function for a harmonic oscillator of frequency  $\nu_i$ , viz.,  $(2\pi\hbar\nu_i/kT)^{-1}$ , by the quantum mechanical expression,  $[2 \sinh(\pi\hbar\nu_i/kT)]^{-1}$ . Thus,

$$Z_{QM} = \left(\frac{kT}{2\pi\hbar^2}\right)^{m/2} (8\pi^2V) \int \left[ \prod_{i=1}^l \left(2 \sinh \frac{\pi\hbar\nu_i}{kT}\right)^{-1} \right] \times \left[ \frac{1}{\det \mathbf{G}} \right]^{1/2} \exp[-\beta F_0(Q)] dQ \quad (17)$$

It is a very good approximation to treat the external and internal soft variables classically, as is done in eq 17.

At this point, the reader is referred to Appendix D, where the above derivation of eq 17, or, more generally, the procedure for separating the motions of the hard and soft variables, is re-examined.

We shall first discuss the physical nature of the approximations involved in both the classical rigid and flexible models by comparing  $Z_r$  (of eq 13) and  $Z_f$  (of eq 16) with  $Z_{QM}$  (of eq 17). The partition function  $Z_f$  can be derived from  $Z_{QM}$  by reversing the procedure whereby  $Z_{QM}$  was obtained from  $Z_f$ , viz., by taking the classical limit in the quantum mechanical partition functions of harmonic oscillators, i.e., by replacing  $[2 \sinh(\pi\hbar\nu_i/kT)]^{-1}$  by  $(2\pi\hbar\nu_i/kT)^{-1}$ . Of course, this procedure is valid for small  $\nu_i$ 's, satisfying  $2\pi\hbar\nu_i/kT \ll 1$ . However, the error incurred by this replacement, as was shown in Figure 1 of ref 6, is less than 20% of the statistical weight for  $2\pi\hbar\nu_i$  up to  $2.1kT$ . At room temperature, this corresponds to frequencies up to  $440 \text{ cm}^{-1}$  (see, also, the discussion of eq 20 and 21, below). However, many of the vibrational modes associated with the hard variables have frequencies higher than this, for which the above replacement is not as good. In the high-frequency limit, the quantum mechanical partition function can be replaced by  $\exp(-\pi\hbar\nu_i/kT)$ . This is a partition function of a system totally in the ground state, with energy  $\pi\hbar\nu_i$ , i.e., the contributions from all of the excited states of the harmonic oscillator are neglected. The error incurred by this replacement is<sup>6</sup> less than 20% of the statistical weight for  $2\pi\hbar\nu_i$  down to  $1.6kT$ . At room temperature, this corresponds to frequencies down to  $330 \text{ cm}^{-1}$ . Most of the vibrational frequencies of the hard variables lie in the range  $\geq 330 \text{ cm}^{-1}$ , except that some coupled motions involving many atoms in a polymer molecule can have very low (softened) frequencies, as was pointed out by Hagler and Lifson.<sup>11</sup> If (a) the ground state approximation is employed for all hard vibrational modes in a polymer molecule, including the possibly softened modes, for which the approximation is apparently invalid, and (b) the conformational dependence of the zero-point energy of these vibrations is neglected, then the partition function  $Z_r$  for the classical rigid model is obtained from  $Z_{QM}$ . Errors are introduced in both approximations (a) and (b). The classical flexible model involves an apparently unwarranted approximation in which the high-frequency vibrations are treated classically. In order to judge which of the two classical models is the better, we carry out here a somewhat more quantitative analysis of the approximations involved in each of the two models.

The classical partition functions,  $Z_r$  (of eq 13) or  $Z_f$  (of eq 16), could be derived from eq 17 if the quantities  $\Gamma_r$  and  $\Gamma_f$ , defined in eq 18 and 19, respectively, were independent of the conformation of the polymer;  $\Gamma_r$  and  $\Gamma_f$  are the ratios of the quantum mechanical vibrational partition function to the corresponding quantities in  $Z_r$  and  $Z_f$ .

$$\Gamma_r = \prod_{i=1}^l \left( \frac{1}{2} \sinh \frac{x_i}{2} \right) \quad (18)$$

and

$$\Gamma_f = \prod_{i=1}^l \left( x_i / 2 \sinh \frac{x_i}{2} \right) \quad (19)$$

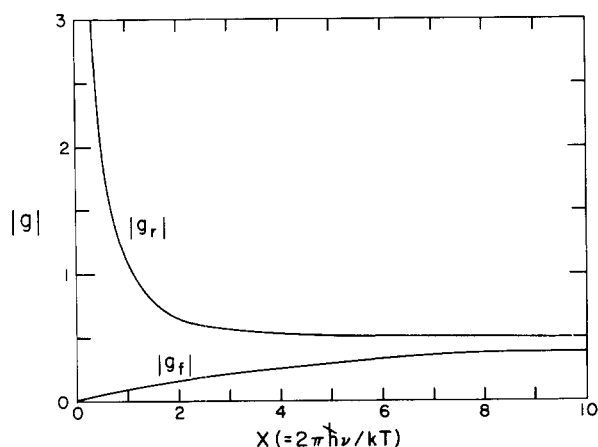


Figure 1. Plot of absolute values of  $|g_r|$  and  $|g_f|$ , defined by eq 22 and 23, respectively, as functions of  $x = 2\pi\hbar\nu/kT$ .

where  $x_i = 2\pi\hbar\nu_i/kT$ . However, neither of these quantities is independent of conformation. Therefore, both the classical rigid and classical flexible models involve an approximation to the extent that  $\Gamma_r$  and  $\Gamma_f$ , respectively, depend on conformation. The smaller the dependence of the  $\Gamma$  factor on conformation, the better are the classical models.  $\Gamma_f$  is the same as  $\Gamma$  of eq 8 of ref 7.

In order to examine the conformational dependence of  $\Gamma_r$  and  $\Gamma_f$ , we may consider the quantities  $\Gamma_r/\Gamma_{r0}$  and  $\Gamma_f/\Gamma_{f0}$ , where  $\Gamma_{r0}$  and  $\Gamma_{f0}$  are the values of  $\Gamma_r$  and  $\Gamma_f$ , respectively, for a particular conformation taken as a reference. If this ratio is always close to unity for all conformations of the polymer, then the corresponding classical model is a good approximation. Taking the logarithm of these quantities, we have

$$\ln(\Gamma_r/\Gamma_{r0}) = \sum_{i=1}^l g_r(x_{i0})\Delta x_i \quad (20)$$

and

$$\ln(\Gamma_f/\Gamma_{f0}) = \sum_{i=1}^l g_f(x_{i0})\Delta x_i \quad (21)$$

where  $\Delta x_i \equiv x_i - x_{i0}$  is the shift of the value of  $x$  of the  $i$ th mode from that of the reference conformation, and

$$g_r(x_{i0}) = \frac{d}{dx} \ln \left( 1/2 \sinh \frac{x}{2} \right) \Big|_{x=x_{i0}} = -\frac{1}{2} \coth \frac{x_{i0}}{2} \quad (22)$$

$$g_f(x_{i0}) = \frac{d}{dx} \ln \left( x/2 \sinh \frac{x}{2} \right) \Big|_{x=x_{i0}} = \frac{1}{x_{i0}} - \frac{1}{2} \coth \frac{x_{i0}}{2} \quad (23)$$

In Figure 1, the values of  $|g_r|$  and  $|g_f|$  (both  $g_r$  and  $g_f$  being negative) are plotted as functions of  $x$ . Both  $|g_r|$  and  $|g_f|$  converge to  $1/2$  for  $x \rightarrow \infty$ , i.e., in the limit of high vibrational frequencies. For finite values of  $x$ ,  $|g_f|$  is always smaller than  $|g_r|$ . The quantity  $\Delta x_i$  assumes various values for various conformations of the polymer. The distribution of the values of  $\ln(\Gamma_r/\Gamma_{r0})$  and  $\ln(\Gamma_f/\Gamma_{f0})$  can be discussed in terms of the distributions of the  $\Delta x_i$ 's. Because  $|g_r| > |g_f|$ , the distribution of the values of  $\ln(\Gamma_r/\Gamma_{r0})$  is larger than that of  $\ln(\Gamma_f/\Gamma_{f0})$ . This indicates that the classical flexible model is better than the classical rigid model. In the limit of very low vibrational frequencies, i.e., for  $x \rightarrow 0$ , it is seen that  $|g_f| \rightarrow 0$  and  $|g_r| \rightarrow \infty$ ; i.e., the approximations involved in the classical flexible and classical rigid models tend to be negligible and infinitely large, respectively. Since most of the frequencies are high ( $x \gtrsim 2.0$ ), the classical rigid model is not totally unrealistic, although the classical flexible model is the better of the two.

### III. Discussion

From the apparently correct reasoning that a classical treatment of vibrational modes with frequencies higher than

$400 \text{ cm}^{-1}$  is not warranted, and that most of the vibrational motions of the hard variables have frequencies in this range, we were led in the previous paper<sup>6</sup> to the erroneous conclusion that eq 2 should be used. The analysis in this paper, however, shows that one should use eq 1 instead of eq 2, where eq 1 is obtained by treating all vibrational motions of the hard variables classically. The erroneous conclusion in ref 6 was reached because of an inadequacy in the analysis of the approximations involved. As was already discussed in the introductory section and in section II, the approximations involved in the classical rigid model (eq 2) are introduced in two steps; one is associated with the ground state approximation, which certainly does not appear warranted for softened modes, and the other is the neglect of the conformation dependence of the zero-point energy of the vibrations of the hard variables. Taken together, these two approximations (eq 2) turn out to involve an error larger than that entailed in the classical treatment of high-frequency vibrations (eq 1); i.e., eq 1 is a better approximation than eq 2.

The classical flexible treatment, used in order to obtain eq 1, is certainly good for the softened coupled motions of the hard variables, the treatment of which is the weakest point<sup>11</sup> in the classical rigid model. While it is shown in this paper that eq 1 is a better approximation than eq 2, the question remains as to how good eq 1 is in an absolute sense. Even though an apparently invalid classical treatment is used for the high-frequency vibrations of the hard variables in obtaining eq 1, these vibrations are localized (in the sense that they involve only a few atoms or one residue; i.e., any local group mode such as the N–H stretching frequency is not affected very much by the rest of the molecule except, of course, when hydrogen bonding is involved) and tend to be rather insensitive to changes in conformation. For vibrations involving more than one residue (and, therefore, somewhat sensitive to changes in conformation), and also having high enough frequencies to render the classical treatment invalid, some error may be involved. This can be expressed in another way as follows. Because the high-frequency vibrations are insensitive to conformational changes,  $\Delta x_i \rightarrow 0$  as  $x_{i0} \rightarrow \infty$ . Also, as shown in Figure 1,  $g_f(x_{i0}) \rightarrow 0$  as  $x_{i0} \rightarrow 0$ . Therefore, the contribution to the summation of eq 21 becomes appreciable, if at all, only in the intermediate range of values of  $x_{i0}$ . If this contribution is appreciable, it expresses quantitatively the inadequacy of the classical flexible model. At present, however, there are no indications that such problems exist, and, therefore, eq 1 can be regarded as acceptable, as proposed by Flory.<sup>7</sup>

Even though the practical applicability of the classical flexible model is not questioned, the approximations involved implicitly in the model should be recognized clearly. One of the main approximations was discussed in the preceding paragraph. Another important approximation introduced in deriving the classical flexible model is the neglect of the dependence of  $Q_0'$  and  $f_{ij}''$  on  $Q$  in eq 3. In general,  $Q_0'$  in eq 3 is a function of  $Q$ . One source of this dependence comes from the procedure used to obtain eq 3, in which the linear term in eq D-4 was eliminated, in Appendix D. As shown in Appendix D, the quantity  $Q_0'$  in eq 3 should be interpreted as meaning  $Q_0' - \mathbf{F}''^{-1}\mathbf{F}'$  in eq D-5; the second term of the latter expression depends on  $Q$  because  $\mathbf{F}'$  is  $Q$  dependent. If we did not introduce the approximation of neglecting the dependence of  $Q_0'$  on  $Q$ , the practicability of the model would be impaired seriously. Even without this approximation, we would obtain eq 1 for the partition function, with only the soft variables being independent ones. However, we would then have to regard the hard variables as functions of the soft variables; i.e., we would have to change the values of the bond lengths and bond angles as the conformation changes. Although this is not impossible for a small molecule,<sup>14</sup> or for a small number of conformations in a large molecule, such a treatment would be intractable for

### Appendix A Derivation of Equation 14

The cartesian coordinates  $x_{k3}$  are functions of  $Q$  and  $Q'$ , and vice versa. Hence, substitution of

$$x_{k3} = \sum_{i=1}^3 \frac{\partial x_{k3}}{\partial q_i} q_i + \sum_{i=1}^3 \frac{\partial x_{k3}}{\partial q'_i} q'_i \quad (A-1)$$

into eq. 4 leads to eq. 5. The elements of the matrices  $H'$ ,  $H''$ , and  $H'''$ , that appear in eq. 5, are given by

$$h'_{ij} = \frac{\partial}{\partial q_i} \sum_{k=1}^3 \frac{\partial x_{k3}}{\partial q_j} \quad (A-2)$$

$$h''_{ij} = \frac{\partial}{\partial q_i} \sum_{k=1}^3 \frac{\partial x_{k3}}{\partial q'_j} \quad (A-3)$$

$$h'''_{ij} = \frac{\partial}{\partial q'_i} \sum_{k=1}^3 \frac{\partial x_{k3}}{\partial q'_j} \quad (A-4)$$

The matrix  $H'$  of eq. 5 can also be expressed as

$$H' = \mathbf{g}^{-1} \mathbf{M} \mathbf{g} \quad (A-5)$$

where  $\mathbf{M}$  is a  $3n \times 3n$  diagonal matrix whose elements are  $(m_1, m_1, m_1, m_2, m_2, m_2, \dots, m_n, m_n, m_n)$ , and  $\mathbf{g}$  is a  $3n \times 3n$  matrix,  $\mathbf{g} = (\mathbf{g}, \mathbf{g}')$ , where  $\mathbf{g}$  and  $\mathbf{g}'$  are  $3n \times m$  and  $3n \times n'$  matrices whose  $(k,i)$ -elements are given by  $\partial x_{k3}/\partial q_i$  and  $\partial x_{k3}/\partial q'_i$ , respectively.

The elements of the matrices  $\mathbf{g}$ ,  $\mathbf{g}'$  and  $\mathbf{g}''$  appearing in eq. 11 are given by

$$g_{ij} = R(\theta) \begin{pmatrix} d_{ij} \\ 0 \\ 0 \end{pmatrix} \quad (B-4)$$

$$g'_{ij} = R(\theta) \begin{pmatrix} 0 \\ d_{ij} \\ 0 \end{pmatrix} \quad (B-5)$$

$$g''_{ij} = R(\theta) \begin{pmatrix} 0 \\ 0 \\ d_{ij} \end{pmatrix} \quad (B-6)$$

where  $R(\theta)$  and  $I(\theta)$  are the following matrices for rotation of coordinates:

$$R(\theta) = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos \theta & -\sin \theta \\ 0 & \sin \theta & \cos \theta \end{pmatrix} \quad (B-7)$$

$$I(\theta) = \begin{pmatrix} \cos \theta & -\sin \theta & 0 \\ \sin \theta & \cos \theta & 0 \\ 0 & 0 & 1 \end{pmatrix} \quad (B-8)$$

Now, in order to calculate the Jacobian  $D$  for the change of variables from  $x_k$  ( $k = 2, \dots, n$ ) to those in expression B-3, we perform the change in a series of steps. In the first step, the following change is made:

$$(y_2, y_3, \dots, y_n) \rightarrow (y_2, y_3, \dots, y_{n-1}, d_n, y'_n, y''_n) \quad (B-9)$$

The Jacobian for this change of  $y'_n = d_n, y''_n = y_n$  is calculated as the determinant of the derivative matrix

### Appendix C Historical Treatment of Non-Equilibrium Properties of Polymers

In this Appendix, it is pointed out (from the point of view of historical interest) that the classical rigid model has been used sometimes in the treatment of non-equilibrium properties of polymers. In fact, Kirkwood<sup>24</sup> once treated a diffusion equation in a constrained space, i.e., he used the classical rigid model in his discussion of non-equilibrium problems. (See reference 8 for a further analysis of Kirkwood's treatment.)

In order to see clearly how Kirkwood used the classical rigid model, let us assume for simplicity that all atoms of the polymer chain have the same mass  $m_0$ , and then write

$$Q^{-1} = H^{-1} = \frac{1}{m_0} \mathbf{g}^{-1} \mathbf{g} = \frac{1}{m_0} \mathbf{g} \quad (C-1)$$

Here, the  $m \times m$  matrix  $\mathbf{g}$  is the metric tensor for the constrained space corresponding to fixed bond lengths and bond angles. Its  $(i,j)$ -element,  $g_{ij}$ , is given by

$$g_{ij} = \sum_{k=1}^3 \frac{\partial x_{k3}}{\partial q_i} \frac{\partial x_{k3}}{\partial q_j} \quad (C-2)$$

When eq. C-1 is used for eq. 13, the latter becomes

$$Z_T = \left( \frac{m_0 k T}{2\pi} \right)^{3n/2} \int \exp \left( -\frac{1}{2} \mathbf{g}^{-1} \mathbf{g} \right) \exp(-\beta F_0(Q)) dQ \quad (C-3)$$

This is essentially the same equation that Kirkwood used (eq. 5

$$h'_{ij} = \frac{\partial}{\partial q_i} \sum_{k=1}^3 \frac{\partial x_{k3}}{\partial q_j} \quad (A-6)$$

$$h''_{ij} = \frac{\partial}{\partial q_i} \sum_{k=1}^3 \frac{\partial x_{k3}}{\partial q'_j} \quad (A-7)$$

$$h'''_{ij} = \frac{\partial}{\partial q'_i} \sum_{k=1}^3 \frac{\partial x_{k3}}{\partial q'_j} \quad (A-8)$$

Direct matrix multiplication will demonstrate that the matrix  $H'$  of eq. 11 is the inverse of the matrix  $H'$  of eq. 5.

Now, the derivation of eq. 14 is based on eq. A-9, which is proved in reference 8

$$\det H' = \det G \det G'' \quad (A-9)$$

Using eqs. A-1 and A-9, and the fact that  $H'$  is the inverse of  $H'$ , the Jacobian  $D = \det \mathbf{g}$  can be expressed as in eq. 14.

### Appendix B Proof that the Jacobian is Independent of Conformation of a Polymer Molecule; Derivation of Equation 2

In order to demonstrate that the Jacobian, for changing variables from cartesian coordinates to internal coordinates (hard and soft variables) plus 6 external variables, is independent of conformation, let the polymer consist of  $n$  atoms whose positions are given by  $x_k$  ( $k = 1, 2, \dots, n$ ), and let us first change the variables from  $x_k$  to  $y_k$ , defined below.

$$\begin{pmatrix} y_2 \\ y_3 \\ \vdots \\ y_n \end{pmatrix} = R(\theta) \begin{pmatrix} x_2 \\ x_3 \\ \vdots \\ x_n \end{pmatrix} \quad (B-10)$$

$$\begin{pmatrix} \cos \theta & -\sin \theta & 0 \\ \sin \theta \cos \theta & d_n \cos \theta \cos \theta & -d_n \sin \theta \cos \theta \\ \sin \theta \sin \theta & d_n \cos \theta \sin \theta & d_n \sin \theta \cos \theta \end{pmatrix} \quad (B-10)$$

and is  $d_n^2 \sin \theta$ . In the second step, the following change is made:

$$(y_2, y_3, \dots, y_{n-1}, d_n, y'_n, y''_n) \rightarrow (y_2, y_3, \dots, y_{n-2}, d_{n-1}, y'_{n-1}, y''_{n-1}, d_n, y'_n, y''_n) \quad (B-11)$$

The Jacobian for this change is calculated similarly to be  $d_{n-1}^2 \sin \theta_{n-1}$ . By repeating these steps until all variables are changed, we obtain the following result for the total Jacobian  $D$ :

$$D = \sin \theta \prod_{k=2}^n d_k^2 \sin \theta_k \quad (B-12)$$

which shows that  $D$  is independent of dihedral angles, and is given as a product of two factors, one depending only on the hard variables and the other only on the external variables. This result was stated without derivation on p. 303, eq. 6-12, of reference 3.

We now derive eq. 8 from eq. 7. First,  $\frac{\partial}{\partial q_i} dx_{k3}$  of eq. 7 is replaced by  $D \partial Q / \partial q_i$ , where  $D$  is given by eq. B-12, and

$$y_1 = x_1 \quad (B-1)$$

$$y_k = x_k - x_{k-1} \quad (k = 2, 3, \dots, n) \quad (B-2)$$

The Jacobian for this change can easily be shown to be unity.

The variables  $y_1$  serve to define the overall translational degrees of freedom of the molecule. Instead of using  $3(n-1)$  variables in  $y_k$  ( $k = 2, 3, \dots, n$ ), we define the following variables:

- (i)  $(n-1)$  bond lengths  $d_k$  ( $k = 2, 3, \dots, n$ )
- (ii)  $(n-2)$  bond angles  $\theta_k$  ( $k = 3, 4, \dots, n$ )
- (iii)  $(n-3)$  dihedral angles  $\phi_k$  ( $k = 4, 5, \dots, n$ )
- (iv) 3 external variables,  $\theta, \phi$  and  $\psi$ , to describe the overall rotation of the molecule.

The definitions of  $d_k$ ,  $\theta_k$  and  $\phi_k$  are given in Fig. 2. In order to define the external variables for overall rotation, we introduce two imaginary atoms, the  $(-1)^{th}$  and  $0^{th}$ , whose positions are given by  $x_{-1}$  and  $x_0$ , respectively. We define  $y_0$  and  $y_1$  formally by eq. B-2, and define the positions of the two imaginary atoms so that  $y_0$  and  $y_1$  have only  $y$ - and  $x$ - (non-vanishing) components, respectively. With these imaginary atoms, we can formally define "bond angle"  $\theta_2$  and "dihedral angles"  $\phi_2$  and  $\phi_3$ . These three angles, identified as  $\theta, \phi$  and  $\psi$ , respectively, below, serve as the variables for the overall rotational degrees of freedom. It is easy to show that  $y_k$  is given by

$$dQ = dx_1 dy_1 dz_1 dd_2 dd_3 \dots \prod_{k=2}^n d\theta_k \quad (B-13)$$

and

$$dQ' = \prod_{k=2}^n \frac{dd_k}{d_k} \frac{d\theta_k}{\sin \theta_k} d\phi_k \quad (B-14)$$

Since the integrand in eq. 7 is independent of the external variables,  $dx_1 dy_1 dz_1 dd_2 dd_3 \dots$  integration over these variables gives  $5^{-2} V$ , where  $V$  is the volume of the system. It may then be assumed that the dependence of the remaining integrand on the hard variables  $Q'$  is dominated by that in  $\exp(-\beta F(Q, Q'))$ ; i.e., the potentials governing the hard variables are assumed to be very strong. Thus, the minimum-energy values  $d_{k0}$  and  $\theta_{k0}$  may be assumed for the hard variables  $d_k$  and  $\theta_k$  in eq. B-12 for the Jacobian, which becomes

$$D(Q_0') = \prod_{k=2}^n d_{k0}^2 \frac{d\theta_k}{\sin \theta_{k0}} \quad (B-15)$$

This reduces eq. 7 to

$$Z_T = \left( \frac{m_0 k T}{2\pi} \right)^{3n/2} \int \exp(-\beta F_0(Q)) \exp(-\beta F(Q, Q_0')) \prod_{k=2}^n \frac{dd_k}{d_k} \frac{d\theta_k}{\sin \theta_k} d\phi_k \quad (B-16)$$

Then the integration with respect to  $Q'$  (i.e.,  $d_k$  and  $\theta_k$ ) can be performed to give eq. 8.

of reference 24); i.e., in reference 24, Kirkwood used the classical rigid model for a treatment of the non-equilibrium properties of polymers.

### Appendix D On the Separation of the Motions of the Hard and Soft Variables

In this Appendix we re-examine first, the procedure for obtaining the quantum mechanical partition function,  $Z_{QM}$ , from eq. 16 (by replacing the classical partition function for a harmonic oscillator by the quantum mechanical one) and, then, the assumptions made<sup>8</sup> in separating the conformational energy  $F(Q, Q')$  into two terms, one depending only on  $Q$  and the other depending only on  $Q'$ .

The Hamiltonian for a system in which the vibrations in the hard variables are treated quantum mechanically has the same form as that for the classical flexible model, but  $P$  and  $Q'$  are now quantum mechanical operators. If  $\hat{Q}$  represents the generalized momenta

$$\hat{Q} = \begin{pmatrix} P \\ P' \end{pmatrix} \quad (D-1)$$

defined by  $K_2/\hat{Q} = \hat{Q}^2/2$ , where  $\hat{Q} = \begin{pmatrix} Q \\ Q' \end{pmatrix}$ , then the kinetic energy  $K_2$  of eq. 5 can be written as

$$K_2 = \frac{1}{2} \hat{Q}^T \hat{G} \hat{Q} \quad (D-2)$$

Hence, the Hamiltonian  $H_2 + F(Q, Q')$  can then be written as

$$\begin{aligned} \frac{1}{2} (\hat{Q}^T \hat{P}^T) \begin{pmatrix} \hat{Q}^T & \hat{Q}^T \hat{P}^T \\ \hat{Q}^T & \hat{Q}^T \hat{P}^T \end{pmatrix} \begin{pmatrix} \hat{Q} \\ \hat{Q}' \end{pmatrix} + F_0(Q) + \frac{1}{2} (\hat{Q}^T - \hat{Q}_0^T) \hat{P}^T (Q' - Q_0') \\ = \frac{1}{2} (\hat{P}^T + \hat{P}^T \hat{Q}^T \hat{Q}^{-1}) \hat{Q}^T (\hat{P} + \hat{Q}^{-1} \hat{Q}_0^T \hat{P}) \\ + \frac{1}{2} (\hat{Q}^T - \hat{Q}_0^T) \hat{P}^T (Q' - Q_0') + \frac{1}{2} \hat{P}^T \hat{Q} \hat{P} - F_0(Q) \end{aligned} \quad (D-3)$$

Here, the matrix  $\hat{G}$  is given by eq. 10. Since  $\hat{Q}^T \hat{Q}^{-1} \hat{P}$  and  $\hat{Q}_0^T$  are numbers (i.e., not quantum mechanical operators), the operators  $(\hat{P}^T + \hat{P}^T \hat{Q}^T \hat{Q}^{-1} \hat{P})$  and  $(\hat{Q}^T - \hat{Q}_0^T)$  satisfy the same commutation relations as do  $\hat{P}$  and  $\hat{Q}$ . Therefore, the sum of the first two terms on the right-hand side of eq. D-3 is equivalent to the Hamiltonian of harmonic oscillators with frequencies  $\omega_i$  ( $i = 1, 2, \dots, i$ ) determined from the eigenvalues of the matrix  $\hat{G} \hat{P}^T \hat{P}$ . Hence, we can obtain the quantum mechanical partition function,  $Z_{QM}$ , of eq. 17 from eq. 16 by replacing the classical partition function for a harmonic oscillator by the quantum mechanical one.

It should be noted that the first and third terms on the right-hand side of eq. D-3 can be regarded as the kinetic energies of the motions of the hard and soft variables, respectively. Thus, it appears as if there is no coupling between these two energy terms. However, in the process of this separation, the matrix of coefficients for the kinetic energies of the soft variables has been changed from  $\hat{G}'$  in eq. D-2 to  $\hat{G}$  (defined by eq. 10) in eq. D-3. In a sense, the kinetic energy of the soft

variables has been renormalized in the separation process. A similar renormalization of the potential energy of the soft variables  $F_0(Q)$  of eq. 3 was, in fact, assumed implicitly when the second term on the right-hand side of eq. 3 was separated from the first term. Equation 3 was derived<sup>6</sup> by assuming a harmonic force field for the vibrational motions of the hard variables. By expanding  $F(Q, Q')$  in terms of  $Q'$  for a given value of  $Q$ , we obtain the following expression:

$$F(Q, Q') = F_0(Q) + \sum_{i=1}^N f_{i1}''(q_{i1}' - q_{i1}^0) + \frac{1}{2} \sum_{i,j=1}^N f_{ij}''(q_{i1}' - q_{i1}^0)(q_{j1}' - q_{j1}^0) \quad (D-4)$$

At this stage, the coefficients  $f_{i1}''$  and  $f_{ij}''$ , as well as  $F_0(Q)$ ,

are functions of the soft variables. The derivation of eq. 3 from eq. D-4 is shown below.

Equation D-4 can be rewritten as follows:

$$F(Q, Q') = F_0(Q) + \frac{1}{2} f''^T P^{-1} f' + \frac{1}{2} (Q' - Q_0' - f''^T P^{-1} f')^T P (Q' - Q_0' - f''^T P^{-1} f') \quad (D-5)$$

where  $f''^T = (f_{11}'', f_{21}'', \dots, f_{N1}'')$  and  $f' = (f_{11}', f_{21}', \dots, f_{N1}')$ . A term-by-term multiplication in the third term on the right-hand side of eq. D-5 leads to eq. D-4. The second term on the right-hand side of this equation is a function of  $Q$  because  $f''$  is  $Q$ -dependent. Therefore, the function  $F_0(Q)$  in eq. 3 should be understood to mean the sum of the first two terms on the

right-hand side of eq. D-5. Further, the second term on the right-hand side of eq. D-3 should be interpreted as the third term on the right-hand side of eq. D-5. However, the operators  $(P' + Q'^{-1} Q_0'^T P)$  and  $(Q' - Q_0' + f''^T P^{-1} f')$  satisfy the same commutation relations as do  $P'$  and  $Q'$ , because  $Q_0'^{-1} Q_0'^T P$  and  $Q_0' - f''^T P^{-1} f'$  are numbers (i.e., not quantum mechanical operators). Therefore, eq. D-5 is equivalent to eq. 3, provided that  $F_0(Q)$  in eq. 3 is interpreted to include the second term on the right-hand side of eq. D-5, and that  $Q_0'$  in eq. 3 is interpreted to mean  $Q_0' - f''^T P^{-1} f'$  in eq. D-5. This is the reason why we assumed eq. 3 at the outset. By taking the coefficients  $f_{ij}''$  or the matrix  $P''$  to be independent of  $Q$ , as was assumed in the text, the separation of the hard and soft variables is achieved.

the usual conformational analysis of a large molecule. The introduction of the approximation of neglecting the dependence of  $f_{ij}''$  on  $Q$  in eq. 3 was also crucial to making the model practicable. Without this approximation,  $[\det F'']^{-1/2}$  in eq. 8 would have to be retained in the integrand, and the calculation of this factor as a function of  $Q$  would not be practical in the usual conformational analyses. It should be noted that the assumption that  $f_{ij}''$  is independent of  $Q$  is not equivalent to the assumption that the vibrational frequencies of the hard variables are independent of  $Q$ . The dependence of the vibrational frequencies of the hard variables on  $Q$  arises from the  $Q$  dependence of the matrix  $G''$ , defined in eq. A-8, since  $f_{ij}''$  is assumed to be independent of  $Q$ . Thus, the assumptions that  $Q_0'$  and  $f_{ij}''$  are independent of  $Q$  were introduced mainly for practical reasons. The validity of these assumptions was not examined to any great extent in this paper, but was taken for granted for most practical problems. However, these assumptions limit, to some extent, the applicability of the classical flexible model.

Once the classical treatment is regarded as acceptable, the effect of the solvent can be included simply, from a conceptual point of view, as already discussed in ref. 6 and 15. The conformational energy  $F(Q)$  of a polymer in solution conceptually consists of two terms,  $U(Q)$ , the intramolecular interaction energy of the polymer in the absence of the solvent, and  $V(Q)$ , the free energy of solvation defined by eq. 37 of ref. 6. The sum of these two, i.e.,  $F(Q) = U(Q) + V(Q)$ , is the potential of mean force in the polymer molecule for various configurations of the solvent molecules. Once the effect of the solvent is included properly in  $F(Q)$ , then one can treat the polymer as if it is present in vacuum, but governed by the potential of mean force. Equation 37 of ref. 6 is formal and, in practice, a phenomenological treatment must be employed; for this purpose, solvation parameters are introduced to represent the potential of mean force.<sup>16</sup>

Because the conformational energy  $F(Q, Q')$  in eq. 3 is the quantity which includes the effect of the solvent, we have to reexamine at this point the validity of the application of quantum mechanics (made in section II) to the vibrational motions of the hard variables. As already discussed in the introductory section, the coefficients  $f_{ij}''$  in eq. 3 are determined mainly by the force field associated with covalent bonds and, therefore, are not affected by the solvent. Most of the high-frequency vibrational modes (which depend not only on  $f_{ij}''$  but also on the kinetic energy) are not affected by the solvent.<sup>17</sup> Therefore, these high-frequency modes can be treated quantum mechanically by treating the polymer as if it were in vacuum. Since the softened low-frequency vibrational modes of the hard variables couple to the motions of the soft variables<sup>11</sup> and the solvent molecules, such normal mode frequencies obtained for an isolated molecule may not have much meaning for a polymer in solution. Even though the statistical weights of classical harmonic oscillators are given by exact expressions for these softened low-frequency modes, a value of unity has been assigned to these statistical weights in the classical rigid model; this is one of the main sources of

error in the classical rigid model. In the classical flexible model, these modes are treated classically, anyway, and present no problem because, in the classical treatment, the polymer-solvent interactions can be included conceptually in the free energy of solvation  $V(Q)$ , as discussed in the previous paragraph.

In our molecular theory<sup>18-21</sup> of the helix-coil transition, we first<sup>18</sup> encountered the problem of choosing between eq. 1 and 2 as our starting point. In ref. 6, we erroneously concluded that eq. 2 should be the basic equation. However, the intractability of the factor  $\det G$  in eq. 2 for the random coil state was recognized clearly in ref. 6. Therefore, in the molecular theory of the helix-coil transition, eq. 1 instead of eq. 2 was employed both for helix and coil as an interim approximation. Now, according to the analysis of the present paper, our treatment in the molecular theory of conformational transitions<sup>18-21</sup> turns out to be legitimate rather than an interim assumption.<sup>22</sup> It should be stressed here that the partition functions for the helix and the coil were calculated on the basis of the same equation (eq. 1) with the same value of the constant, viz., 1. In the actual calculations, we used the harmonic approximation for the helix, and the near-neighbor approximation for the coil. The validity of these approximations has been discussed elsewhere;<sup>18-21</sup> however, they are of such a nature that they do not compromise the essential point that they are in principle calculated on the same basis (i.e., with the constant taken as unity in eq. 1). In these calculations, the effect of solvent was

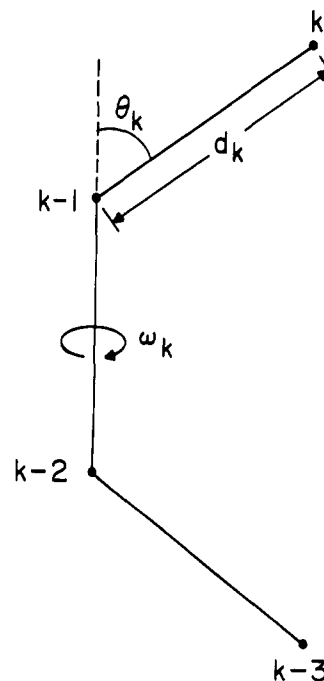


Figure 2. Definition of variables required to define geometry and conformation of polymer chain.

incorporated into the conformational energy function in three ways: (1) specific interactions of one or more solvent molecules with backbone NH and CO groups of the residues in coil sequences, (2) effect of the solvent molecules in which they are regarded as a bulk medium with a dielectric constant other than unity, and (3) additional interaction energies between atoms, or groups of atoms, in a polymer, arising from the presence, nearby, of solvent molecules (hydrophobic bond, in the case where the solvent is water). This treatment of the solvent effect is still rough and can be refined further, but it does represent a first attempt to incorporate the effect of solvation. However, the helix-coil transition occurs primarily as a consequence of a balance between the enthalpy gain and entropy loss associated with the coil-to-helix transition; the entropy loss comes primarily from the fact that the conformational fluctuations become very limited in a helix compared to a random coil. Since we are concerned only with extracting the primary factors responsible for the transition, our rather rough treatment of the solvent is regarded as adequate.

The fact that eq 1 is derived for the classical flexible model does not imply that we actually have to vary bond lengths and bond angles. The independent variables in eq 1 are dihedral angles. (Bond lengths and bond angles are varied only conceptually in the process of deriving eq 1.) Therefore, in actual calculations of the conformational properties of a polymer chain, we may fix the bond lengths and bond angles. If one is concerned with a stable conformation of a polymer chain with small conformational fluctuations, the stable conformation may be calculated by first minimizing the conformational energy; then the conformational entropy can be calculated from the second derivative matrix  $\mathbf{F}$  of the conformational energy at the minimum point, as  $-\frac{1}{2}R \ln \det \mathbf{F}$ .

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**Miniprint Material Available:** Full-sized photocopies of Appendixes A–D (12 pages). Ordering information is given on any current masthead page.

## References and Notes

- (1) This work was supported at Kyushu University by grants-in-aid from the Ministry of Education, Japan, and at Cornell University by research grants from the National Institute of General Medical Sciences of the National Institutes of Health, U.S. Public Health Service (GM-14312), from the National Science Foundation (BMS75-08691), and from Walter and George Todd.
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- (17) If a part of the polymer molecule becomes hydrogen bonded to a solvent molecule, depending on the conformation of the polymer, the high-frequency vibrational modes may be affected. In such a case,  $\det \mathbf{F}''$  in eq 8 becomes  $Q$  dependent, and cannot be taken out of the integrand. Such a situation can still be treated by the classical flexible model as follows. We assume a  $Q$ -independent value for  $f_{ij}''$  (i.e., the value for the non-hydrogen-bonded state), even though the real value may be different when the group is hydrogen bonded. This difference can be taken into account by a  $Q$ -dependent correction factor which can be included in the free energy of solvation  $V(Q)$ .
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