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Mode-Coupling Smoluchowski Dynamics of Polymers in the Limit of Rigid Structures

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ABSTRACT: The time correlation functions of molecular configurational variables are calculated using a mode-coupling expansion of the Smoluchowski generalized diffusion equation with hydrodynamic interactions. For fluctuating three-dimensional structures the computation of the dynamics of the rigid limit represents a fundamental first step in the mode-coupling approach. For large rigid systems, using the three first-order vector modes of a noninfinite rate, higher order basis sets of the proper tensor rank are built to give the required mode-coupling dynamics. The results are found to be in very good agreement with the exact results obtained by an analytical solution of the rotational diffusion equation of rigid bodies. These rigid limits give simple accurate basis sets in the maximum correlation approximation (MCA) to the mode-coupling diffusion dynamics of fluctuating stiff synthetic polymers and biopolymers such as proteins and DNA double helices.

I. Introduction

Recently, a diffusive theory describing the local dynamics of polymer solutions was given which accurately evaluates memory function contributions by a maximum correlation approximation (MCA) to a mode-coupling expansion.[1] In this framework, the dynamics of stiff synthetic and biological macromolecules, such as proteins and DNA double helices, may be described as the diffusion of fluctuating three-dimensional (3-D) structures.[2] For these systems, the rotational dynamics of 3-D rigid structures represents a natural step and also a major contribution to the local dynamics of the fluctuating chain.[2,3] In this paper we develop simplified methods in the mode-coupling diffusion approach to obtain time correlation functions (TCFs) for local tensor variables of large rigid molecular systems.

It has already been shown that, for a linear rod, the second-order mode-coupling diffusion theory gives the exact hydrodynamic results for the bond time correlation functions (TCFs).[1] Now, we extend the mode-coupling approach to two- and three-dimensional structures. Given a rigid structure defined by a set of bond variables, the first-rank dynamics of a vector embedded in the structure are first obtained to first order in the mode-coupling expansion in terms only of the three vector modes of a noninfinite rate. Then higher order basis sets of the proper tensor rank are built by the combination of products of the reduced first-order vector modes to derive the required mode-coupling dynamics. In this way the number of elements in the higher order basis set is drastically reduced and the mode-coupling dynamics easily solved. In the case of simple one-, two-, and three-dimensional model rigid chains, the results obtained for first- and second-rank orientational local TCFs are compared to those obtained by the solution of the rotational diffusion equations[4,5] and found to be in very good agreement. Finally, these methods are applied to derive rotational diffusion properties of the rigid three-dimensional structure of a protein of 60 amino acids.

These rigid limits give accurate, simple basis sets in the MCA approximation to the mode-coupling diffusion dynamics of fluctuating stiff synthetic polymers and biopolymers such as proteins and DNA double helices.

Section II summarizes the mode-coupling expansion solution to the multidimensional Smoluchowski diffusion equation with hydrodynamic interaction, and the formal solutions for the TCFs and their correlation times are obtained. Section III defines TCFs of L-rank tensors and shows how to take advantage of the rotational invariance to compute them. Section IV discusses the problem of the basis sets in the mode-coupling expansion for rigid and fluctuating three-dimensional structures and for tensor variables of different ranks. Section V summarizes the exact results obtained by an analytical solution to the rotational diffusion equation of rigid bodies. Section VI compares exact correlation times for first- and second-order orientational TCFs for simple one-, two-, and three-dimensional chain structures to those obtained by the mode-coupling diffusion approach. Section VII considers application to the rigid three-dimensional structure of a small protein. Finally, in Section VIII a brief conclusion is given.

II. The Mode-Coupling Expansion Solution to Smoluchowski Dynamics

Here, we summarize the mode-coupling diffusion approach to dynamics in polymer solutions.[1] Given a polymer of N_a beads of friction coefficients ζ_i and coordinates $\mathbf{r}_i$, $i = 1, ..., N_a$, the dynamics of bond vectors connecting two beads, $\mathbf{l}_j$, $j = 1, ..., N_b$, is governed by the Smoluchowski operator L, the adjoint operator to the diffusion operator D, such that

$$\frac{\partial}{\partial t}\mathbf{l} = L\mathbf{l} \qquad (1)$$

where

$$L = \sum_{i,j=1}^{N_a} [\nabla_i \cdot \mathbf{D}_{ij} \cdot \nabla_j - (\nabla_i U/k_B T) \cdot \mathbf{D}_{ij} . \nabla_j] \qquad (2)$$

and $\mathbf{l}$ is the $3N_b$-dimensional array with the coordinates

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of the bond vectors. Here, the diffusion tensor is given by

$$\mathbf{D}_{ij} = D_i \mathbf{H}_{ij} \tag{3}$$

with

$$\mathbf{H}_{ij} = \mathbf{1}\delta_{ij} + \zeta_i \mathbf{T}_{ij}(1 - \delta_{ij}) \tag{4}$$

$$\mathbf{T}_{ij} = (8\pi\eta r_{ij})^{-1}[1 + \mathbf{r}_{ij}\mathbf{r}_{ij}/r_{ij}^2] \tag{5}$$

where **H** and **T** represent the hydrodynamic interaction matrix and Oseen tensor, respectively, with

$$D_i = k_{\mathrm{B}}T/\zeta_i \tag{6}$$

where D_i is the diffusion coefficient, U is the intramolecular potential, and η is the solvent viscosity.

By expanding the conditional probability (solution to the Smoluchowski equation) in a complete set of eigenfunctions of L, the time autocorrelation function (TCF) of any dynamic variable with zero average $f(\mathbf{l})$, may be expressed in the standard form

$$\langle f(t)\, f(0)\rangle = \sum_i \langle f|\psi_i\rangle\langle\psi_i|f\rangle \exp(-\lambda_i \mathrm{t}) \tag{7}$$

where λ_i and ψ_i are the eigenvalues and the normalized eigenfunctions of the operator L,

$$L\psi_i = -\lambda_i\psi_i \tag{8}$$

The matrix expansion method for the calculation of the TCF $\langle f(t)\, f(0)\rangle$ requires a solution of the eigenvalue problem of eq 8 by expanding ψ_i in a set of basis functions $\mathbf{\Phi} = \{\phi_m,\ m = 1, ..., M\}$,

$$\psi_i = \sum_{m=1}^{M} C_{m,i}\phi_m \tag{9}$$

thus converting eq 8 into the generalized matrix eigenvalue equation

$$\mathbf{FC} = \mathbf{SC\Lambda} \tag{10}$$

with $\mathbf{\Lambda}$ the diagonal matrix of the eigenvalues λ_m, **C** the eigenvector matrix of coefficients $C_{i,m}$, **S** the metric matrix,

$$S_{ij} = \langle\phi_i|\phi_j\rangle \tag{11}$$

and **F** the equilibrium force matrix:

$$F_{ij} = -\langle\phi_i|L\phi_j\rangle = \sum_{m,n=1}^{N_a} \langle(\nabla_m\phi_i)\cdot\mathbf{D}_{mn}\cdot(\nabla_n\phi_j)\rangle \tag{12}$$

The ensemble equilibrium averages, indicated within brackets in the above equations, are calculated as

$$\langle a|b\rangle = \int P_{\mathrm{eq}}(\mathbf{r})\, a(\mathbf{r})\, b(\mathbf{r})\, \mathrm{d}\mathbf{r} \tag{13}$$

with $P_{\mathrm{eq}}(\mathbf{r})$ the equilibrium distribution function. As the eigenfunctions ψ_i are orthonormalized, the coefficient matrix **C** should satisfy the normalization equation

$$\mathbf{C}^{\mathrm{T}}\mathbf{SC} = \mathbf{1} \tag{14}$$

Using transformation (9) the TCF in eq 7 becomes

$$\frac{\langle f(t)\, g(0)\rangle}{\langle fg\rangle_{\mathrm{eq}}} = \frac{1}{\langle fg\rangle_{\mathrm{eq}}}\sum_n\Big(\sum_i C_{i,n}\langle f|\phi_i\rangle\Big)\Big(\sum_j C_{j,n}\langle\phi_j|g\rangle\Big) \times \exp(-\lambda_n \mathrm{t}) \tag{15}$$

whose correlation time (CT) τ is, after application of eqs 10 and 14 to the integration of eq 15,

$$\tau = \frac{1}{\langle f^{\,2}\rangle}\int_0^\infty \langle f(t)\, f(0)\rangle\, \mathrm{d}t = \frac{1}{\langle f^{\,2}\rangle}\sum_{i,j=1}^{M}\langle f|\phi_i\rangle\, \langle f|\phi_j\rangle\, (\mathbf{F}^{-1})_{ij} \tag{16}$$

Given a basis set, the dynamics is derived by solving eq 10. Note that in the general case of a fluctuating molecule the matrix **S** is nonsingular and eq 10 is solved as

$$\mathbf{S}^{-1}\mathbf{FC} = \mathbf{C\Lambda} \tag{17}$$

while in the case of a rigid structure **S** is highly singular and the dynamic problem may still be solved by inverting eq 10 to

$$\mathbf{F}^{-1}\mathbf{SC} = \mathbf{C\Lambda}^{-1} \tag{18}$$

which has the same eigenvectors and inverse eigenvalues.

Increasing approximations to the evaluation of TCFs are obtained by considering increasing powers of the variables (bond vectors or their combinations) in the spirit of the mode-coupling theory.

The use of the hydrodynamic interactions in the Oseen form together with the introduction of dimensionless units require small modifications to the hydrodynamic interaction matrix:

$$\mathbf{D}_{ij} = D\mathbf{H}_{ij} \tag{3$'$}$$

$$\mathbf{H}_{ij} = (\zeta/\zeta_i)\mathbf{1}\delta_{ij} + \zeta_{\mathrm{r}}(6\pi\eta l)\mathbf{T}_{ij}(1 - \delta_{ij}) \tag{4$'$}$$

where ζ and D are the average friction coefficient and diffusion constant:

$$\zeta = \frac{1}{N_a}\sum_{i=1}^{M}\zeta_i;\ D = k_{\mathrm{B}}T/\zeta \tag{19}$$

while ζ_{r} and l are the averaged hydrodynamic strength

$$\zeta_{\mathrm{r}} = \zeta/6\pi\eta l \tag{20}$$

and the root-mean-square bond length, respectively, with

$$l^2 = \frac{1}{N_b}\sum_{i=1}^{N_b}\langle l_{\mathrm{i}}^{\,2}\rangle \tag{21}$$

Despite the precise definition given above, ζ_{r} is taken as a parameter whose values are restricted to the range $0 < \zeta_{\mathrm{r}} < 0.6$ to maintain a positive definite **H**. Here, we fix it at the standard value 0.25.[6]

In this paper we report correlation times in dimensionless units; therefore, to recover real units all the times must be divided by σ:

$$\sigma = k_B T / l^2 \zeta \tag{22}$$

III. Time Correlation Functions for Tensor Variables

In this paper, the problem is addressed of constructing an efficient basis set for the eigenfunction in a highly correlated system such as an arbitrary shape rigid macromolecule. The eigenfunctions of the rotational diffusive operator for a rigid object are given in terms of the Euler angles of the rigid body orientation. The TCF of an L-rank irreducible spherical tensor can be computed exactly only when $2L + 1$ terms in the Green function for the rotational diffusion equation have been found.[4,5] These $2L + 1$ terms are related to the $2L + 1$ L-rank eigenvectors with noninfinite eigenvalues of the rotational diffusion operator. Autocorrelation functions accessed, for instance, by dielectric, fluorescence, Raman, and nuclear magnetic resonance experiments are of the following form:

$$P_L(t) = \langle P_L(\cos(\beta(t)))\rangle = \sum_{M=-L}^{L} \langle D_{M,0}^{(L)*}(\Omega(t)) D_{M,0}^{(L)}(\Omega(0))\rangle \tag{23}$$

where P_L is the Legendre polynomial of order L, β is the angle that a given vector spans in the time t, and the average is over all the possible choices of time origins (i.e., over the equilibrium distribution of orientations) and over the equivalent vectors in the sample. The functions $D_{M,N}^{(L)}$ are Wigner matrix elements and $D_{M,0}^{(L)}$ are irreducible spherical tensors.[7] As an example, P_1 of a given bond vector in the rigid molecule requires the three 1-rank terms of the Green function while P_2 requires the five 2-rank components.

Given a 3-D object, the correlation function P_L is then obtained from the $2L + 1$ modes of L-rank associated to finite rates of the diffusive equation written in terms of matrices (eq 10).

As f is an L-rank irreducible spherical function (of the type described in eq 23) of a molecular vector in a rigid molecule tumbling in an isotropic phase, the projections on the basis elements ϕ_m, required in eqs 7 and 15, $\langle f|\phi_m\rangle$, are nonzero if and only if ϕ_m is an L-rank function. Therefore, the ϕ_m basis functions must be constructed as L-rank functions. Within the mode-coupling approach, these functions are represented in terms of the N_b bond variables instead of the Euler angles of the rigid body orientation. But in any case, starting with N_b bond variables of the correct rank, the diffusive equation in terms of the matrices in eq 10 should give at the end $2L + 1$ modes of L-rank associated to noninfinite rates for the correlation function of rank L P_L.

One important feature is the requirement that the representation of the diffusive process is independent of the choice of the laboratory axis, the so-called “rotational invariance”. For a rigid molecule in isotropic phases, this requirement means the computation of the averages over the entire uniformly sampled orientational space. Evaluation of such integrals for the **S** and **F** matrix elements necessary in the mode-coupling approach is possible, but can be avoided simply by computing the scalar components (invariants) contained in the products of L-rank functions in the matrix elements. If an L-rank function is represented in terms of irreducible spherical tensors $T_M^{(L)}$ (with components $M = -L, -L + 1, ..., L-1, L$) the only scalar function, which is independent of the orientation of the laboratory axis, obtained as product of two such tensors is simply[7]

$$I_{1,2}^{(L)} = \frac{1}{2L+1} \sum_{M=-L}^{L} T_M^{(L)*}(1) T_M^{(L)}(2) = \frac{1}{2L+1} \sum_{M=-L}^{L} (-1)^M T_{-M}^{(L)}(1) T_M^{(L)}(2) \tag{24}$$

where with 1 and 2 we mean two generic basis function variables.

The $T_M^{(L)}$ functions as components of L-rank irreducible spherical tensors are proportional to the Wigner matrix $D_{M,0}{}^{(L)}(\Omega)$, where Ω describes the orientation, in terms of Euler angles, of a frame fixed with the geometrical variable with respect to the laboratory axis.

In isotropic phases the quantity $I^{(L)}$ is the only nonzero average since all the anisotropic terms disappear. This property can be applied to the calculation of **S** and **F** matrix elements since both matrices are averages of products of L-rank irreducible spherical tensors. While for the calculation of the **S** matrix, only invariants of the type in eq 24 are required, for the **F** generic 1,2-element we have

$$F_{1,2} = \langle a_{1,2}^{(M,N)}\rangle \tag{25}$$

$$a_{1,2}^{(M,N)} = \sum_{i,j=1}^{N_a} \nabla_i T_M^{(L)*}(1) \cdot \mathbf{D}_{ij} \cdot \nabla_j T_N^{(L)}(2) \tag{26}$$

and the corresponding invariant is

$$I_{1,2}^{(L)} = \frac{1}{2L+1} \sum_{M=-L}^{L} (-1)^M a_{1,2}^{(M,M)} \tag{27}$$

The **F** matrix elements are given as the ensemble average of tensor products of the form of the matrix $\boldsymbol{a}$; from the elements of matrix $\boldsymbol{a}$ the rotational invariants $I^{(L)}$ are calculated and for a rigid object this latter quantity ensures rotational invariance.

Finally, the equations for the rotational invariants in eqs 24 and 27 are slightly modified using the property $T_{-M}{}^{(L)} = (-1)^M T_M{}^{(L)}*$:

$$I_{1,2}^{(L)} = \frac{1}{2L+1} [T_0^{(L)}(1) T_0^{(L)}(2) + 2 \sum_{M>0} Re(T_M^{(L)*}(1)) Re(T_M^{(L)}(2)) + 2 \sum_{M>0} Im(T_M^{(L)*}(1)) Im(T_M^{(L)}(2))] \tag{28}$$

to get

$$I_{1,2}^{(L)} = \frac{1}{2L+1} [\phi_0^{(L)}(1) \phi_0^{(L)}(2) + 2 \sum_{M\neq 0} \phi_M^{(L)}(1) \phi_M^{(L)}(2)] \tag{29}$$

where $\phi_M{}^{(L)}$ is the real part of $T_{|M|}{}^{(L)}$ when $M < 0$ and the imaginary part of $T_{|M|}{}^{(L)}$ when $M > 0$. These $\phi_M{}^{(L)}$ functions are the same basis functions introduced by eq 9, with the two indexes L, M replacing the running m index in order to deal with tensorial functions. The same modification holds in the expression for the **F** matrix elements.

IV. Reduced Basis Sets for Rigid Structures

We outline below an efficient procedure for finding a reduced basis set to compute accurate tensor time correlation functions. The first step amounts to solving the diffusion equation with a basis linear in the bonds in order to get the first order P_1 dynamics:

$$\{l_{i,x}\} \qquad i = 1, ..., N_{\mathrm{b}} \tag{30}$$

The first-order solution is obtained by diagonalization of eq 18, which gives the first-order P_1 eigenfunctions $m_{i,x}$:

$$m_{i,x} = \sum_{j=1}^{N_b} C_{j,i} l_{j,x} \tag{31}$$

These eigenfunctions may be considered as a new basis set equivalent to the bond basis set in eq 30, giving identical results for the eigenvalues, which are the mode relaxation rates, and for TCFs.

For a rigid structure in d dimensions, only d eigenvalues are not infinite, and the TCF has only d exponential contributions. Therefore, the full mode basis set of N_b elements in eq 31 can be substituted with a reduced first-order P_1 basis set of only d elements, the modes corresponding to noninfinite relaxation rates:

$$\Phi_{\mathrm{I}}^{(1)} = \{m_{i\alpha}, \quad i = 1, ..., d\} \qquad \text{(RM1 I)} \tag{32}$$

with the upper index (1) referring to the rank of P_1 and the bottom index “I” to the first order in the mode-coupling expansion. Hereafter, we use Greek letters to indicate the $2L + 1$ components of every L-rank function.

Because of the phase isotropy, the dynamics are insensitive to the x, y, and z components of the modes. The x, y, and z space dependence of the modes emerges from the use of Cartesian representation of irreducible spherical 1-rank tensors.

To refine the P_1 dynamics, a reduced second-order basis set is obtained by adding to the first-order one a set of elements that is constructed by multiplying 1-rank functions in the modes of eq 32 and scalar functions in the modes. This yields getting elements of third powers in the modes (and therefore in the bond variables) displaying the desired 1-rank tensorial behavior:

$$\Phi_{\mathrm{II}}^{(1)} = \Phi_{\mathrm{I}}^{(1)} \cup \{\phi_{i,M}^{(1)}\} \qquad \text{(RM1 II)} \tag{33}$$

with

$$\begin{aligned}
\phi_{i,0}^{(1)} &= m_{i1,z}(\mathbf{m}_{i2}\cdot\mathbf{m}_{i3}) \\
\phi_{i,-1}^{(1)} &= \sqrt{\frac{1}{2}}\, m_{i1,x}(\mathbf{m}_{i2}\cdot\mathbf{m}_{i3}) \\
\phi_{i,1}^{(1)} &= \sqrt{\frac{1}{2}}\, m_{i1,y}(\mathbf{m}_{i2}\cdot\mathbf{m}_{i3}) \qquad i1 = 1, ..., d; \\
& \qquad i2 = 1, ..., d; \quad i2 \le i3
\end{aligned} \tag{34}$$

Hereafter, the tensorial notation for the base elements $\phi_M^{(L)}$ of eq 29 will be used. For a rigid 3-D molecule, therefore, the reduced basis set to compute 1-rank TCFs has $3 + 3(3 \times 2) = 21$ elements.

For 2-rank functions in the form of d-like atomic orbitals (i.e., real and imaginary parts of 2-rank irreducible spherical functions), a reduced first-order basis set can be taken in the following form:

$$\Phi_{\mathrm{I}}^{(2)} = \{\phi_{i,M}^{(2)}\} \qquad \text{(RM2 I)} \tag{35}$$

where

$$\begin{aligned}
\phi_{i,0}^{(2)} &= \frac{1}{2}(3m_{i1,z}m_{i2,z} - \mathbf{m}_{i1}\cdot\mathbf{m}_{i2}) \\
\phi_{i,-2}^{(2)} &= \sqrt{\frac{3}{8}}(m_{i1,x}m_{i2,x} - m_{i1,y}m_{i2,y}) \\
\phi_{i,2}^{(2)} &= \sqrt{\frac{3}{8}}(m_{i1,x}m_{i2,y} + m_{i1,y}m_{i2,x}) \\
\phi_{i,-1}^{(2)} &= \sqrt{\frac{3}{8}}(m_{i1,x}m_{i2,z} + m_{i1,z}m_{i2,x}) \\
\phi_{i,1}^{(2)} &= \sqrt{\frac{3}{8}}(m_{i1,y}m_{i2,z} + m_{i1,z}m_{i2,y}) \\
& \qquad i1 = 1, ..., d; \quad i1 \le i2
\end{aligned} \tag{36}$$

This is the reduced first-order basis set for the P_2 dynamics, and the functions are second powers of the reduced first-order P_1 modes. The reduced second-order basis set for 2-rank TCFs is built by adding to the first-order basis set in eq 35 products of the first-order basis functions and scalar functions of the vector modes:

$$\Phi_{\mathrm{II}}^{(2)} = \Phi_{\mathrm{I}}^{(2)} \cup \{\phi_{i,M}^{(2)}\} \qquad \text{(RM 2 II)} \tag{37}$$

where

$$\begin{aligned}
\phi_{i,0}^{(2)} &= \frac{1}{2}(3m_{i1,z}m_{i2,z} - \mathbf{m}_{i1}\cdot\mathbf{m}_{i2})(\mathbf{m}_{i3}\cdot\mathbf{m}_{i4}) \\
\phi_{i,1}^{(2)} &= \sqrt{\frac{3}{8}}(m_{i1,x}m_{i2,x} - m_{i1,y}m_{i2,y})(\mathbf{m}_{i3}\cdot\mathbf{m}_{i4}) \\
\phi_{i,2}^{(2)} &= \sqrt{\frac{3}{8}}(m_{i1,x}m_{i2,y} + m_{i1,y}m_{i2,x})(\mathbf{m}_{i3}\cdot\mathbf{m}_{i4}) \\
\phi_{i,3}^{(2)} &= \sqrt{\frac{3}{8}}(m_{i1,x}m_{i2,z} + m_{i1,z}m_{i2,x})(\mathbf{m}_{i3}\cdot\mathbf{m}_{i4}) \\
\phi_{i,4}^{(2)} &= \sqrt{\frac{3}{8}}(m_{i1,y}m_{i2,z} + m_{i1,z}m_{i2,y})(\mathbf{m}_{i3}\cdot\mathbf{m}_{i4}) \\
& i1 = 1, ..., d; \quad i1 \le i2; \quad i3 = 1, ..., d; \quad i3 \le i4
\end{aligned} \tag{38}$$

Note that, for simplicity's sake, the same notation has been used for first- and second-order mode-coupling functions.

These fourth-power (in the P_1 modes, and in turn in the bonds) basis functions display the same 2-rank properties as those in eq 36. The resulting basis set for a 3-D molecule has $3 \times 2 + (3 \times 2) \times (3 \times 2) = 42$ elements.

A final remark concerns the calculation of the **F** matrix. The calculation of the gradient of each basis function with respect to the bead position can be performed using the derivative of composite functions to get

$$F_{p,q}^{(\alpha,\omega)} = \sum_{j,\beta}\frac{\partial\phi_{p,\alpha}}{\partial m_{j,\beta}}\sum_{k,\mu}\frac{\partial m_{k,\beta}}{\partial l_{k,\mu}}\sum_{m,\gamma}\frac{\partial l_{k,\mu}}{\partial x_{m,\gamma}}\sum_{n,\delta}D_{m,n}^{(\gamma,\delta)} \times \left(\sum_{o,\epsilon}\frac{\partial\phi_{q,\omega}}{\partial m_{o,\epsilon}}\sum_{l,\nu}\frac{\partial m_{o,\epsilon}}{\partial l_{l,\nu}}\frac{\partial l_{l,\nu}}{\partial x_{n,\delta}}\right) = \sum_{j,\beta}\frac{\partial\phi_{p,\alpha}}{\partial m_{j,\beta}}\sum_{o,\epsilon}\frac{\partial\phi_{q,\omega}}{\partial m_{o,\epsilon}}\sum_{k}\sum_{l}C_{k,j}^{(1)}C_{l,o}^{(1)}B_{k,l}^{(\beta,\epsilon)} \tag{39}$$

with

$$B_{k,l}^{(\beta,\epsilon)} = \sum_{m,n}\sum_{\gamma,\delta}\frac{\partial l_{k,\beta}}{\partial x_{m,\gamma}}D_{m,n}^{(\gamma,\delta)}\frac{\partial l_{l,\epsilon}}{\partial x_{n,\delta}} \tag{40}$$

a matrix of the type in eq 26. Using this property, the kernel of the calculation is the computation of the matrix **B**, which is built with 1-rank functions of the bond vectors.

In addition, for the model calculations in Section VI, we also performed the P_1 calculations with a second-order basis that includes all the possible first and third powers of the bonds (trilinear basis hereafter)[1]:

$$\{l_{ix},\quad i = 1, ..., N_{\mathrm{b}}\} \cup \{l_{\mathrm{mx}}(\mathbf{l}_p\cdot\mathbf{l}_q),\quad m,p = 1, ..., N_{\mathrm{b}};\ q = p, ..., N_{\mathrm{b}}\}\quad \text{(trilinear)} \tag{41}$$

Calculations using this full second-order basis set for P_1 are useful for checking the results obtained by reduced mode basis sets.

V. The Exact Solution to the Rotational Dynamics of Bead Structures

The analytical solution of the rotational diffusion equation and the way to compute, within a bead model of the hydrodynamics of the polymer, the correlation functions P_L of every bond in the molecule, have been reported in the literature. Favro[4] and Berne and Pecora[5] gave the analytical expressions for the eigenfunctions of the rotational operator for a general rigid body as an expansion of Wigner matrix elements $D_{M,N}^{(L)}(\alpha,\beta,\gamma)$, where α, β, and γ are the Euler angles of the frame where the diffusive tensor is diagonal with respect to the laboratory axis. Szabo[8] reported applications of such equations for the calculation of $P_2(t)$ in cylindrically symmetric molecules. Finally, Bernal et al.[9] and Pastor[10] reported the derivation of the diffusion tensor **D** in terms of the bead structure and friction coefficients in the model.

As a summary of these results, we give the final equations for $P_L(t)$:

$$P_L(t) = \sum_{k=1}^{2L+1}\exp(-\lambda_k t)A_k{}^*A_k \qquad A_k = \sum_{a=-L}^{L}D_{a,0}^{(L)*}(M\rightarrow E)C_a^{(k)} \tag{42}$$

where E is a frame with z pointing along the relaxing vector and M is a frame rigidly attached to the principal axis of the diffusion tensor. Notice that eq 42 is identical to eq 7 where the projections of the bond variables onto the modes are written as orientations of such variables with respect to the principal diffusion axis. For readers' convenience, the matrix $C_a^{(k)}$ and the λ_k are reported in Table 1 for $L = 1$ and 2. The limiting step in the above calculations is the inversion of a $3N_a \times 3N_a$ friction matrix in order to get the diffusion tensor of the molecule. Note that, for the sake of comparison with the mode-coupling approach, we neglect the side blocks in the friction matrix coupling translational and rotational motions.

Table 1. Rotational Diffusion of a Rigid Body of Arbitrary Shape in Isotropic Phase: Rates and Coefficients of Equation 42

		P_1
k	λ	C_a $a = -1,0,1$
1	$D_{yy} + D_{zz}$	$(-1/2^{1/2}, 0, 1/2^{1/2})$
2	$D_{xx} + D_{zz}$	$(-1/2^{1/2}, 0, 1/2^{1/2})$
3	$D_{xx} + D_{yy}$	$(0, 1, 0)$
		P_2
k	λ	$\mathrm{C_a}$ $a = -2,-1,0,1,2$
1	$3(D + D_{zz})$	$(1/2^{1/2}, 0, 0, 0, 1/2^{1/2})$
2	$6D + 2\Delta$	$(\mathrm{b/N}2^{1/2}, 0, \mathrm{a/N}, 0, \mathrm{b/N}2^{1/2})$
3	$6D - 2\Delta$	$(-\mathrm{a/N}2^{1/2}, 0, \mathrm{b/N}, 0, -\mathrm{a/N}2^{1/2})$
4	$3(D + D_{yy})$	$(0, -1/2^{1/2}, 0, 1/2^{1/2}, 0)$
5	$3(D + D_{xx})$	$(0, 1/2^{1/2}, 0, 1/2^{1/2}, 0)$

where

$D = 1/3(D_{xx} + D_{yy} + D_{zz})$
$a = 3^{1/2}(D_{xx} - D_{yy})$
$b = 2D_{zz} - D_{xx} - D_{yy} + 2\Delta$
$N = 2(\Delta b)^{1/2}$
$\Delta = [(D_{xx} - D_{yy})^2 + (D_{zz} - D_{yy})(D_{zz} - D_{xx})]^{1/2}$

Table 2. Dimensionless Correlation Times ($\sigma\tau$) for Rods of Different Length[a]

(a)P_1

N_b	exact	RM1 I	RM1 II	Trilinear
9	33.106	20.794	33.067	33.106
10	43.095	26.912	43.045	43.095
20	258.24	155.84	257.93	
100	42925	28617	42925	
200	338350	225567	338350	

(b)P_2

N_b	exact	RM2 I	RM2 II
9	11.035	6.168	11.022
10	14.365	7.975	14.348
20	86.080	45.89	85.977
100	14309	8585.0	14308
200	112978	67670	112783

[a] Key: The column headings are as follows: N_b, the number of bonds; exact, dimensionless correlation times calculated by solving exactly the rotational diffusion equation for the rod; RM1 I, RM1 II, RM2 I, RM2 II, mode-coupling diffusion results obtained by using first- and second-order reduced basis sets related to P_1 and P_2 TCFs; trilinear, dimensionless correlation times for the full second-order basis set computation of P_1.

VI. Model Comparisons

We first show the application of the reduced mode-coupling approach to simple molecular models with identical beads which span different molecular geometries.

In Table 2 we report the P_1 and P_2 bond correlation times in rods of different length, constructed as a linear array of equally spaced identical beads. Trilinear mode-coupling computations are exact. The first-order computations using the reduced basis sets are coincident with the full first-order basis set computations but both are much lower than the exact results. On the contrary,

Table 3. Dimensionless Correlation Times ($\sigma\tau$) for a Rectangular Prism of Sides 1 × 1.5 × 2 [a]

(a)P_1

bond	exact	RM1 I	RM1 II	trilinear
1	1.635	0.4731	1.634	1.635
2	1.776	0.7760	1.775	1.778
3	2.144	1.154	2.142	2.144

(b)P_2

bond	exact	RM2 I	RM2 II
1	0.5507	0.2948	0.5504
2	0.6062	0.3640	0.6060
3	0.7167	0.4519	0.7160

[a] Key: The three bonds (1, 2, and 3) are along the three sides of the prism. Column headings are the same as those in Table 2.

Table 4. Dimensionless Correlation Times ($\sigma\tau$) for the *ttttttt* Model[a]

(a)P_1

bond	exact	RM1 I	RM1 II	trilinear
1	16.124	10.302	16.105	16.124
2	15.123	9.598	15.103	15.123

(b)P_2

bond	exact	RM2 I	RM2 II
1	2.9380	1.5758	2.9354
2	2.4348	1.2503	2.4317

[a] Key: The bonds (1 and 2) connect the beads in the sequence order and equivalent bonds are not repeated. Column headings are the same as those in Table 2.

Table 5. Dimensionless Correlation Times ($\sigma\tau$) for the $g^+g^+g^+g^+g^+g^+g^+$ Model[a]

(a)P_1

bond	exact	RM1 I	RM1 II	trilinear
1	6.169	3.194	6.133	6.161
2	6.034	3.115	5.997	6.022
3	5.913	3.077	5.875	5.897
4	6.052	3.125	6.016	6.041
5	6.157	3.185	6.121	6.150
6	6.050	3.123	6.014	6.039
7	5.910	3.075	5.873	5.895
8	6.031	3.113	5.995	6.020
9	6.167	3.193	6.131	6.160

(b)P_2

bond	exact	RM2 I	RM2 II
1	1.584	0.4738	1.573
2	1.572	0.4591	1.562
3	1.546	0.4657	1.535
4	1.575	0.4595	1.565
5	1.582	0.4734	1.571
6	1.575	0.4594	1.564
7	1.545	0.4655	1.535
8	1.572	0.4590	1.561
9	1.584	0.4736	1.573

[a] Key: The bonds connect the beads in the sequence order. Column headings are the same as those in Table 2.

Table 6. Dimensionless Correlation Times ($\sigma\tau$) for the $g^-g^-g^+tg^-g^-g^+$ Model[a]

(a)P_1

bond	exact	RM1 I	RM1 II	trilinear
1	4.277	1.277	4.257	4.272
2	4.308	1.095	4.284	4.302
3	6.215	3.222	6.182	6.205
4	6.607	3.570	6.561	6.596
5	4.433	1.221	4.407	4.427
6	6.604	3.566	6.558	6.593
7	6.211	3.218	6.178	6.202
8	4.309	1.305	4.289	4.304
9	6.285	3.223	6.241	6.274

(b)P_2

bond	exact	RM2 I	RM2 II
1	1.555	0.7798	1.547
2	1.566	0.7330	1.556
3	1.982	0.8522	1.972
4	2.118	1.000	2.104
5	1.581	0.7098	1.572
6	2.117	0.9988	2.103
7	1.981	0.8509	1.971
8	1.557	0.7694	1.549
9	2.003	0.8751	1.991

[a] Key: The bonds connect the beads in the sequence order. Column headings are the same as those in Table 2.

reduced second-order computations for both P_1 and P_2 are very close to the exact results. Errors in computations with the reduced basis sets are expected to arise from two sources. The first is due to error propagation in the derivation of eigenvectors C_{ij} during the first step of the basis construction. The second (and main) source is related to the use of bond variables in fixed combinations, where the combination is approximated by the first-order P_1 modes. This latter constraint is not important for the rod, but becomes more important for structures in two and three dimensions.

Roughly. the same accuracy is obtained in the description of the reduced bond dynamics in a rectangular prism (Table 3) of edges 1 × 1.5 × 2. Slightly larger errors appear in the description of chains composed of 10 beads in three different conformations, *ttttttt* (all trans-planar zigzag geometry), $g^+g^+g^+g^+g^+g^+g^+g^+$ (a right-hand helix) and $g^-g^-g^+tg^-g^-g^+$ (a sort of disordered rigid structure) (Tables 4−6). The bending angles are all 112°; the symbol t means a dihedral of 180°, g^+ means 300°, and g^- means 60°. The largest error is about 3% and there is an evident increase in the error with the increase in globularity of the model. These errors in correlation times are almost uniformly spread along the chain.

VII. Results for the Rigid 3-D Structure of a Protein

We have applied the same devices to a 60 residue protein in a known structure, a rigid representation of a segment of *vnd*/NK-2, the *Drosophila melanogaster* ventral nervous defective homeodomain protein.[11,2] We have approximated the protein as a chain of 60 beads centered on the Cα atoms, each with a hydrodynamic radius computed as the sum of the radii of multiple elementary units, (i.e., CH_2, C═O, etc.) that in turn are computed within the van der Waals volume increment method.[12] The NK-2 structure has been reported by Tsao et al.[13] and the data have been recovered by the Protein Data Bank (the first structure within the 30 proposed). First-order calculations of nuclear magnetic resonance spin−lattice relaxation times for this protein modeled both as a rigid and fluctuating structure are reported in ref 2. In Figure 1 we have plotted the P_2 correlation times obtained for the NH backbone bond vectors in the virtual bond model (the structure is represented by 59 virtual bonds joining consecutive Cα atoms) of the rigid structure. As in the model calculations in section VI, the first-order pattern is only a rough approximation to the exact result (in a factor of about

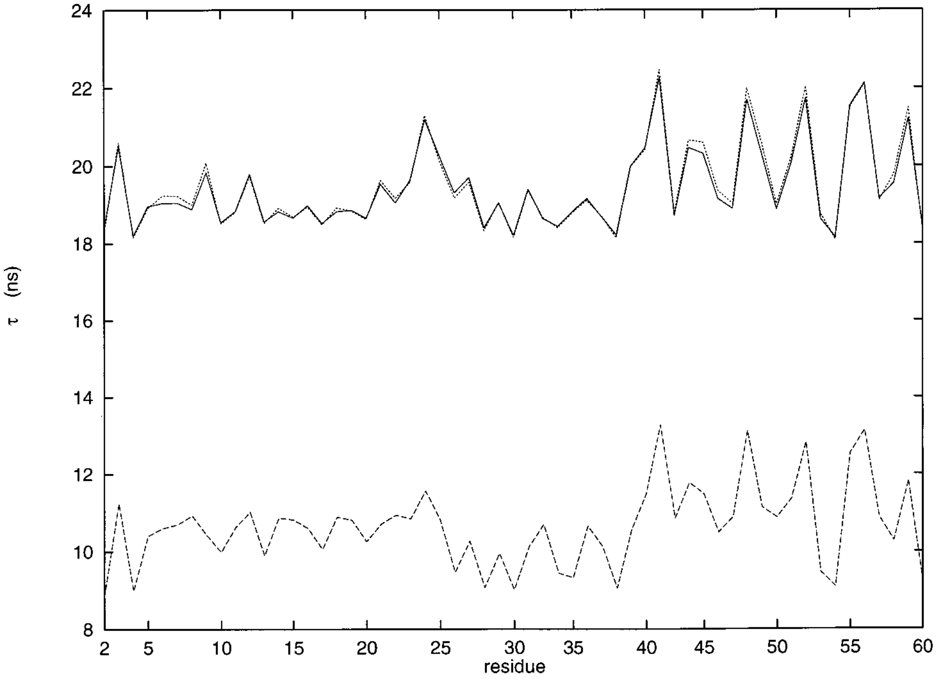

Figure 1. P_2 correlation times for the 57 main-chain peptide NH bonds in the virtual bond model of rigid NK-2: exact results (solid line), RM2 I model (dashed line), and RM2 II model (dotted line).

2). The second-order reduced mode-coupling correlation times (obtained using the basis set RM2 II for P_2) are almost coincident with the exact results. This shows that for a large globular system the error is almost the same as that found in the case of the simple models in section VI. First-order and reduced second-order mode-coupling correlation times display fairly similar patterns since, as summarized in section V, the rotational dynamics of a vector depends just on the orientation of the vector within the rigid particle. This fingerprint of the three-dimensional structure is fairly well-reflected on both levels of the expansion. The accurate description of the protein dynamics obtained in the rigid limit by the mode-coupling method is promising for a further application of theory to the interpretation of experimental data like NMR relaxivities in fluctuating protein structures.

VIII. Conclusions

The Smoluchowski equation with hydrodynamic interactions is solved by the mode-coupling approach to describe the dynamics of polymer solutions. This method expands the eigenfunctions of the adjoint of the diffusion operator in basis sets of increasing number of elements chosen as increasing powers of the bond vector components or in general of the slow variables. While the first order in the mode-coupling expansion represents the optimized Rouse Zimm theory, higher order powers are in general required to get reliable solutions to polymer dynamics. The exploding number of elements occurring with increasing powers are reduced by the method of maximum correlation approximation (MCA), which amounts to including in the basis set powers of only those variables which present the maximum correlation to the relaxing physical variable. It should be noted that the MCA picture is consistent with the concept of localized cooperative motions as found in MD simulations or in the wide experimental experience on the local dynamics of polymer solutions.

Different methods for constructing the proper MCA basis sets should be used to treat flexible polymers as alkanes[14] or polyisoprene,[15] or polymers with more definite structures as proteins[2,3] and DNA. For stiff proteins or B-structured DNA, the dynamics can be described as the rotational diffusion of a fluctuating 3-D structure. As a consequence, the rotational diffusion of the rigid limit for the fluctuating structure represents a useful first step in the calculations. We have developed a method to treat efficiently, in the mode-coupling diffusion approach, the rotational dynamics of rigid molecular structures. This method selects as basic functions the d (with d the dimensionality of the structure) first-order P_1 modes of noninfinite rate, obtained by solving the first-order mode-coupling equation for a certain choice of fundamental bond vectors. These d modes are the new collective variables describing the high correlation of the rigid structure and are used to construct basis sets of the proper tensorial rank and order in the mode-coupling expansion. In addition, we have formalized the mode-coupling diffusion approach to compute TCFs of different rank, such as P_1 and P_2 , in such a way as to take advantage of the symmetry of the problem by full use of tensor variables and of rotational invariants. It is shown, for several simple model structures and for a protein structure, that reduced second-order calculations are sufficient to give very good approximations to the exact P_1 and P_2 functions, obtained by solving the rotational diffusion equation for rigid bodies. In conclusion, the rotational diffusion of a rigid structure is obtained in the mode-coupling diffusion approach by drastically reducing the number of functions in the basis sets by a choice of a few new collective variables describing the high correlation between the bonds in the rigid structure. More importantly, this method selects the main functions in the basis set to be used even in the case of macromolecules fluctuating around a 3-D structure, to construct an efficient MCA basis set. This MCA basis set is obtained, at a first stage, by using the same basis set (see eqs 33 and 37 for P_1 and P_2, respectively) selected in the rigid computation for the fluctuating structure, while fluctuation effects enter via the ensemble averages, evaluated by MD simulations starting from the same rigid 3-D structure. Note that in the derivation of these dynamics the slowest step computationally is the computation of first-order modes for P_1. This step may be speeded up, if necessary, by reducing the number of bonds chosen as fundamental variables. To improve this first stage of calculation, in the case of a protein or a DNA double helix containing a particular active site, local functions (with the proper symmetry and mode-coupling order) of those bonds describing in details the active site should be added to the collective variables chosen in the first stage to represent the high correlations of the rigid structure. This procedure should reduce drastically the mode-coupling computations in proteins and biological macromolecules, giving at the same time reliable local dynamics to be compared to NMR relaxations and fluorescence anisotropy experiments. Calculations of these kind on proteins and DNA double helices are currently being carried out in our laboratory.

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