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Center of Diffusion of Flexible Macromolecules

William A. Wegener†

Center for Muscle Research, Baylor Medical Research Foundation, Dallas, Texas 75246.
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ABSTRACT: We analyze the translational diffusion of an isolated flexible macromolecule by starting on a microscopic level that includes all degrees of freedom and allows for coupling between translational, rotational, and internal motions. Every flexible macromolecule is found to have a unique center of diffusion, which is that point of the body undergoing the slowest average Brownian displacements. The configurationally dependent location of this point is determined from a second-order partial differential equation involving the internal degrees of freedom. A perturbation treatment reduces the diffusion equation governing all the body's degrees of freedom to the ordinary diffusion equation governing the translational motions of some equivalent point particle with diffusion coefficient D_t. By identification, the average microscopic motions of the center of diffusion are shown to characterize the diffusive motions of the body over large distances. We consider several bounds to the macroscopic translational diffusion coefficient D_t that might eliminate the need to explicitly determine the center of diffusion. As an example, a frictionless centrally hinged rod is considered by using bead model methods in order to provide a realistic treatment that includes hydrodynamic interactions between rod halves. For the 20-bead case considered, D_t increases less than 7% from a straight rigid rod and is estimated to at least 1% by bounds that include a simple rigid-body approximation.

Introduction

Brenner[1-4] first considered the effects of rotational–translational coupling on the diffusion coefficients that govern the random microscopic displacements of rigid bodies with irregular shapes. He showed that every rigid body has a unique center of diffusion where the 3×3 matrix describing the coupling is symmetric. Like the center of mass in inertial mechanics, this is the natural point to use when evaluating diffusive behavior. Even so, the description of diffusive behavior remains more complicated than inertial mechanics since rotations and translations generally cannot be uncoupled.

Brenner's work has been recently reexamined and extended by several groups interested in modeling complicated biological macromolecules at low Reynold's numbers.[5-15] In particular, it has now been rigorously established that the diffusional motions of a rigid body over macroscopic distances are the same as the average microscopic motions of its center of diffusion.[11] Since Brenner had derived a simple algebraic expression for the location of the center of diffusion, the needed macroscopic translational diffusion coefficient, denoted D_t, can be determined exactly within these models.

The situation is not as satisfactory regarding the proper determination of D_t for flexible macromolecules in which translational motions are coupled to additional internal modes.[8,15-17] Although methods exist for determining the instantaneous diffusion coefficients of a flexible body with some particular configuration (see, for example, ref 18–21), no relation has been established between the microscopic displacements that these coefficients directly govern and the body's translational diffusion over large distances.

In this paper, we show that an isolated flexible body does indeed have a unique center of diffusion whose average microscopic motions characterize its macroscopic motions. We first examine the positional dependence of the diffusion coefficients governing the translational displacements of a point in the body. From a minimization condition, an analytic expression is found for the location of a center of diffusion. In order to rigorously prove that the resulting point does characterize macroscopic motions, we turn to perturbation theory. In the limit of motion over distances large compared to body size, the diffusion equation governing all the body's degrees of freedom reduces to the usual diffusion equation governing the translational motions of a point particle with diffusion coefficient D_t. By identification, D_t is the translational diffusion coefficient governing the average displacements of the center of diffusion. As an example, we consider several cases of a centrally hinged rod that bends either freely within a variable limited range or under the influence of a restoring potential. In each case, the center of diffusion is determined and D_t is found to depend little on the type or degree of flexibility. Several approximations that eliminate the need to explicitly determine the location of the center of diffusion are shown to give excellent bounded estimates of D_t.

An assumption underlying the following analysis is that all configurations are dynamically interchangeable on an appropriate macroscopic time scale, so that a particle can indeed be described by one D_t. Generalizations to include noninterchanging configurations (untieable knots, etc.) will

†Present address: Ph.D. to M.D. Program (R-123), PO Box 016960, Miami, FL 33101.

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not be made, since the results should be merely the same as if multiple noninteracting species were present, each with their own D_t.

Diffusion Matrices for Flexible Bodies

We consider an isolated flexible macromolecule undergoing random motions in a stationary viscous fluid of infinite extent. We assume the body has $m + 3$ degrees of freedom represented by generalized coordinates q^α. The stochastic properties of small displacements Δq^α occurring in time interval Δt obey a Brownian motion relation given by Fixman.[22] If $\langle\ \rangle$ denotes average value, then for all α, $\beta \leq m + 3$

$$\langle \Delta q^\alpha \Delta q^\beta \rangle = 2D^{\alpha\beta}\Delta t \tag{1}$$

where $D^{\alpha\beta}$ are the components of an $(m + 3)$-dimensional diffusion tensor $\mathbf{D}$ which is symmetric and positive-definite.

We now assign the first three coordinates to translational degrees of freedom and the last m coordinates to orientational degrees of freedom that include internal degrees of freedom as well as 3 degrees of freedom describing external orientations relative to laboratory axes. Let $\mathbf{r}_P$ be a position vector of some point P in the body relative to laboratory axes, and let φ be a compact notation denoting orientation. The $(m + 3)$-dimensional displacement vector $\Delta\mathbf{q}$ can then be represented as $(\Delta\mathbf{r}_P, \Delta\varphi)$, where $\Delta\mathbf{r}_P$ is a small displacement of point P and $\Delta\varphi$ is a small orientational displacement about P.

$\mathbf{D}$ partitions in this representation into a 3×3 matrix ${}^t\mathbf{D}_P$, governing motions of point P, an $m \times m$ matrix ${}^r\mathbf{D}$, governing orientational motions, and an $m \times 3$ matrix ${}^c\mathbf{D}_P$, governing coupling between orientational motions and motions of point P according to

$$\mathbf{D} = \begin{array}{c|c} {}^t\mathbf{D} & {}^c\mathbf{D}_P{}^\dagger \\ \hline {}^c\mathbf{D}_P & {}^r\mathbf{D} \end{array} \tag{2}$$

where $\dagger$ denotes matrix transpose. By the use of dyadic products of $\Delta\mathbf{r}_P$ and $\Delta\varphi$, eq 1 decomposes into three relations

$$\begin{aligned} \langle \Delta\mathbf{r}_P \Delta\mathbf{r}_P \rangle &= 2{}^t\mathbf{D}_P\Delta t \\ \langle \Delta\varphi \Delta\mathbf{r}_P \rangle &= 2{}^c\mathbf{D}_P\Delta t \\ \langle \Delta\varphi \Delta\varphi \rangle &= 2{}^r\mathbf{D}\Delta t \end{aligned} \tag{3}$$

To continue, let $\mathbf{r}_{PP'}$ denote the position vector directed from point P to any other point P' in the body. This vector is generally a function of the body's configuration and its configurational changes are given by a $3 \times m$ matrix $\mathbf{R}_{PP'}$, with components $(R_{PP'})^{i\alpha}$ for $i = 1, 3$ and $\alpha = 1, m$ given as the partial derivatives $\partial r_{PP'}{}^i/\partial\varphi^\alpha$. Since these changes reflect rigid rotations as well as internal motions, it is easy to show that $\mathbf{R}_{PP'}$ vanishes if $\mathbf{r}_{PP'}$ does, but otherwise some components always exist. Note that $\mathbf{R}_{PP'} = -\mathbf{R}_{P'P}$.

For a given orientational displacement $\Delta\varphi$, a displacement of P' is related to that of P according to

$$\Delta\mathbf{r}_{P'} = \Delta\mathbf{r}_P + \mathbf{R}_{PP'}\cdot\Delta\varphi \tag{4}$$

We can now establish the functional relation between the diffusion matrices evaluated, for a particular orientation, at two different points P and P'. The form of the Brownian motion expressions must be the same regardless of which point is used. Rewriting eq 3 at P' and replacing $\Delta\mathbf{r}_{P'}$ by eq 4, we find that ${}^r\mathbf{D}$ is independent of which point is used, while ${}^t\mathbf{D}_{P'}$ and ${}^c\mathbf{D}_{P'}$ are expressed as

$${}^t\mathbf{D}_{P'} = {}^t\mathbf{D}_P + \mathbf{R}_{PP'}\cdot{}^r\mathbf{D}\cdot\mathbf{R}_{PP'}{}^\dagger + {}^c\mathbf{D}_P{}^\dagger\cdot\mathbf{R}_{PP'}{}^\dagger + \mathbf{R}_{PP'}\cdot{}^c\mathbf{D}_P \tag{5a}$$

$${}^c\mathbf{D}_{P'} = {}^c\mathbf{D}_P + {}^r\mathbf{D}\cdot\mathbf{R}_{PP'}{}^\dagger \tag{5b}$$

Microscopic Translational Diffusion

The configurations of an isolated particle are assumed to be distributed according to standard Boltzmann statistics. As such, the average translational motions of a point can be obtained by averaging over all orientational coordinates with the internal configurations weighted by an equilibrium Boltzmann distribution while all external orientations are taken as equally probable. This average will be denoted by an overbar, such that, if $f = f(\varphi)$ is some function of orientations, then $\bar{f}$ is defined as

$$\bar{f} = N\int f(\varphi)\, \exp(-\beta V) g^{1/2}\, \mathrm{d}^m\varphi \tag{6a}$$

with normalization coefficient N given as

$$N^{-1} = \int \exp(-\beta V) g^{1/2}\, \mathrm{d}^m\varphi \tag{6b}$$

and where $\beta \equiv (kT)^{-1}$, k is the Boltzmann constant, T is the absolute temperature, $V = V(\varphi)$ is an internal potential, $\mathrm{d}^m\varphi$ is the m-dimensional volume element for orientational coordinates, and $g^{1/2}$ is an effective Jacobian. g is the determinant of some appropriate metric tensor for the orientational degrees of freedom and has been the subject of considerable debate.[23-28] When explicitly needed in later application to a freely hinged rod, $g^{1/2}$ will simply be chosen to agree with conventional statistical mechanical weighting factors.

Because the distribution is isotropic with respect to external orientations, the average of any body-fixed 3×3 matrix is equal to the average of one-third its trace times the unit matrix $\mathbf{I}$. As such, we define coefficient ${}^t\bar{D}_P$ according to

$${}^t\bar{D}_P = (1/3)\,\overline{\mathrm{Tr}\ {}^t\mathbf{D}_P} \tag{7}$$

where Tr denotes trace. From eq 3, ${}^t\bar{D}_P$ characterizes the average Brownian motion displacements of point P according to

$$(1/3)\overline{\langle \Delta\mathbf{r}_{P'}\cdot\Delta\mathbf{r}_P \rangle} = 2{}^t\bar{D}_P\Delta t \tag{8}$$

From eq 5a and 7, the positional dependence of this coefficient can be expressed

$${}^t\bar{D}_{P'} = {}^t\bar{D}_P + (1/3)\,\overline{\mathrm{Tr}\,(\mathbf{R}_{PP'}\cdot{}^r\mathbf{D}\cdot\mathbf{R}_{PP'}{}^\dagger)} + (2/3)\,\overline{\mathrm{Tr}\,(\mathbf{R}_{PP'}\cdot{}^c\mathbf{D}_P)} \tag{9}$$

Since ${}^r\mathbf{D}$ is positive-definite, the right-hand side term that is quadratic in $\mathbf{R}_{PP'}$ is never negative. From the nonvanishing properties of $\mathbf{R}_{PP'}$ mentioned above, this term vanishes only if points P and P' coincide for all configurations. The remaining linear term in $\mathbf{R}_{PP'}$ is indefinite in sign. If it is, say, positive for some P', then a point P'' exists as defined by $\mathbf{r}_{PP''} = -\mathbf{r}_{PP'}$ for which the term would be negative because $\mathbf{R}_{PP''} = -\mathbf{R}_{PP'}$.

If the linear term vanishes, then ${}^t\bar{D}_{P'} > {}^t\bar{D}_P$. Thus, there can be at most one point P in the body where the linear term vanishes for all other points P', and, by construction, this must be the unique local minimum of ${}^t\bar{D}_P$, rather than some other extremum. To show existence, let P'' be defined by $\mathbf{r}_{PP''} = \epsilon\mathbf{r}_{PP'}$ for some small constant ϵ. Since $\mathbf{R}_{PP''} = \epsilon\mathbf{R}_{PP'}$, the linear and quadratic terms vary as ϵ and ϵ^2 from their values determined for P'. As long as the linear term exists for P', ϵ can always be chosen small enough and with the right sign to ensure that ${}^t\bar{D}_{P''} < {}^t\bar{D}_P$. Thus, if ${}^t\bar{D}_P$ has a local minimum at some point P, the linear term must vanish there for all other points P'. On the other hand, if the linear term does not vanish at P for all other points, then ${}^t\bar{D}_{P'} < {}^t\bar{D}_P$ holds for some other point P''. Since ${}^t\bar{D}_P$

is positive and has some lower bound D_- the linear term must therefore vanish in the limit that ${}^t\bar{D}_P \to D_-$.

By the preceding arguments, a unique point always exists in every flexible body where ${}^t\bar{D}_P$ has its minimum value. This point is referred to as the center of diffusion and is that particular point D satisfying

$$0 = \overline{\mathrm{Tr}\ (\mathbf{R}_{DP}\cdot{}^c\mathbf{D}_D)} \tag{10}$$

for any point P. From eq 5, 9, and 10, ${}^t\bar{D}_P$ can be written as

$${}^t\bar{D}_P = {}^t\bar{D}_D + (1/3)\,\overline{\mathrm{Tr}\ (\mathbf{R}_{PD}\cdot{}^r\mathbf{D}\cdot\mathbf{R}_{PD}{}^\dagger)} = {}^t\bar{D}_D - (1/3)\,\overline{\mathrm{Tr}\ (\mathbf{R}_{PD}\cdot{}^c\mathbf{D}_P)} \tag{11}$$

Equations 10 and 11 hold for an arbitrary flexible body. In order to obtain somewhat simpler expressions, we make use of the fact that the internal potential $V(\varphi)$ is completely general and can maintain any desired internal distribution via the Boltzmann weighting factor. In particular, we now assume for the remainder of this section that the internal coordinates are themselves unrestricted or cyclic. This allows us to carry out orientational integration by parts without generating surface terms along internal boundaries.

Explicitly writing out eq 10, integrating by parts with regard to the partials $\partial/\partial\varphi^\alpha$ involved in $\mathbf{R}_{DP}$, and ignoring any surface terms yields

$$0 = \sum_{i=1}^{3}\sum_{\alpha=1}^{m}\int (r_{DP})^i \partial[\exp(-\beta V) g^{1/2} ({}^cD_D)^{\alpha i}]/\partial\varphi^\alpha\ \mathrm{d}^m\varphi$$

Since this holds for any point P, $\mathbf{r}_{DP}$ is a completely arbitrary vector function of φ. In order for the expression to always vanish, the remaining integrand terms must vanish identically for each component i and orientation φ. Thus the center of diffusion is defined according to

$$0 = \sum_{\alpha=1}^{m} \partial[\exp(-\beta V) g^{1/2} ({}^cD_D)^{\alpha i}]/\partial\varphi^\alpha \tag{12a}$$

for $i = 1, 2, 3$. This expression may be written in noncomponent form as

$$0 = \nabla_\varphi\cdot[\exp(-\beta V)\,{}^c\mathbf{D}_D] \tag{12b}$$

where ∇_φ is the orientational del operator whose covariant components $(\nabla_\varphi)_\alpha$ are given as $\partial/\partial\varphi^\alpha$ if the operator acts on a function and $g^{-1/2}\partial(g^{1/2}\ldots)/\partial\varphi^\alpha$ in eq 12 and elsewhere if the operator is contracted with contravariant components of a vector to give its divergence. (Note from eq 3 that the $3 \times m$ matrix ${}^c\mathbf{D}_P$ is a set of 3 m-dimensional vectors when derivatives with respect to orientational coordinates are concerned; i.e., its components transform this way if we change orientational coordinates but not positional coordinates.)

Orientational gradients of V give rise to an internal m-dimensional generalized force $\mathbf{f} = -\nabla_\varphi V$. Equation 12 can then be stated as the condition that a 3-dimensional vector $\mathbf{d}_P$ vanish, where $\mathbf{d}_P$ is defined as

$$\mathbf{d}_P = (\nabla_\varphi + \beta\mathbf{f})\cdot{}^c\mathbf{D}_P \tag{13}$$

In the absence of surface terms, the identity

$$\overline{\mathrm{Tr}\ (\mathbf{R}_{PD}\cdot{}^c\mathbf{D}_P)} = -\mathbf{d}_P\cdot\mathbf{r}_{PD} \tag{14}$$

can be shown to hold, so that eq 11 reduces to the simpler form

$${}^t\bar{\mathbf{D}}_P = {}^t\bar{\mathbf{D}}_D + (1/3)\overline{\mathbf{d}_P\cdot\mathbf{r}_{PD}} \tag{15}$$

Thus, in the absence of orientational boundaries, the average microscopic displacements of an arbitrary point P differ from those of the center of diffusion by a factor involving the average projection of $\mathbf{d}_P$ along $\mathbf{r}_{PD}$.

Using eq 5b to replace ${}^c\mathbf{D}_P$ in eq 13 determines the position of the center of diffusion relative to any other point P. The relative position vector $\mathbf{r}_{PD}$ is the solution of the equation

$$(\nabla_\varphi + \beta\mathbf{f})\cdot{}^r\mathbf{D}\cdot\nabla_\varphi\mathbf{r}_{PD} = -\mathbf{d}_P \tag{16}$$

where we have rewritten the matrix $\mathbf{R}_{PD}{}^\dagger$ in the dyadic form $\nabla_\varphi\mathbf{r}_{PD}$. (Note that $\mathbf{r}_{PD}$ is a set of 3 functions when derivatives with respect to orientational coordinates are concerned; i.e., the component values of $\mathbf{r}_{PD}$ are independent of the coordinates used to represent an orientation φ).

When there are no internal degrees of freedom, our results agree with those previously obtained for rigid bodies. In this case, the diffusion matrices ${}^t\mathbf{D}_P$, ${}^c\mathbf{D}_P$, and ${}^r\mathbf{D}$ are all 3×3 matrices, and the $\mathbf{d}_P$ vector reduces to $\nabla_\varphi\cdot{}^c\mathbf{D}_P$, which involves only changes of ${}^c\mathbf{D}_P$ under rigid rotational displacements. From rigid-body kinematics, the Cartesian components of $\mathbf{d}_P$ can be explicitly expressed as[11]

$$d_P{}^i = \sum_{j,k=1}^{3} \epsilon_{ijk}\,{}^cD_P{}^{jk} \tag{17}$$

where $\epsilon_{123} = \epsilon_{312} = \epsilon_{231} = 1$, $\epsilon_{132} = \epsilon_{321} = \epsilon_{213} = -1$, otherwise $\epsilon_{ijk} = 0$.

As seen, $\mathbf{d}_P$ vanishes if and only if ${}^c\mathbf{D}_P$ is symmetric. From simple kinematics, the operator relations $\mathbf{R}_{PP'} = -\mathbf{r}_{PP'}\,\mathbf{x}$ and $\mathbf{R}_{PP'}{}^\dagger = \mathbf{x}\,\mathbf{r}_{PP'}$ hold for a rigid body, where $\mathbf{x}$ denotes vector cross-product. With these replacements, the transformation relations given in eq 5 agree with previous expressions for rigid bodies.[4,11] Let $\nabla_{\varphi'}$ then act on eq 5b, and use methods given in Appendix B of ref 29 to evaluate orientational divergences according to

$$\nabla_{\varphi'}\cdot{}^r\mathbf{D}\cdot\nabla_\varphi\mathbf{r}_{PP'} = -\nabla_{\varphi'}\cdot({}^r\mathbf{D}\ \mathbf{x}\ \mathbf{r}_{PP'}) = -[(\mathrm{Tr}\ {}^r\mathbf{D})\mathbf{I} - {}^r\mathbf{D}]\cdot\mathbf{r}_{PP'} \tag{18}$$

where $\mathbf{I}$ is the unit matrix. We obtain previous expressions for the location of the center of diffusion relative to any other point P in the body[4,11]

$$\mathbf{r}_{PD} = [(\mathrm{Tr}\ {}^r\mathbf{D})\mathbf{I} - {}^r\mathbf{D}]^{-1}\cdot\mathbf{d}_P \tag{19}$$

where the exponent -1 denotes matrix inverse.

Explicit results like these for rigid bodies generally cannot be obtained for flexible bodies, primarily because hydrodynamic interactions between different portions of the body act to produce diffusion matrices with complicated dependence on internal configurations. To locate point D from some other point P, then, we must generally solve a second-order partial differential equation in m dimensions for each of the 3 components of the relative position vector $\mathbf{r}_{PD}$. As shown later by the example of a bent rod, orientational motions of highly symmetric bodies can sometimes be decoupled into internal motions and overall rigid motions. In these special cases, rigid-body kinematics can then be used to reduce eq 16 to a partial differential equation involving only the $m - 3$ internal coordinates.

Macroscopic Translational Diffusion

The translational diffusion of a body over macroscopic distances that are much larger than the body's size is governed by some representative diffusion coefficient D_t. In the preceding section, we considered a coefficient ${}^t\bar{D}_P$ that governs the average microscopic motions according to Brownian motion eq 8. As shown, points displaced from the center of diffusion have increased ${}^t\bar{D}_P$ values since their motions include additional contributions from rotational and internal motions. However, all points of a body must

diffuse over macroscopic distances at the same rate. Intuitively, if we equate D_t with any ${}^t\bar{D}_P$, these additional motions should not contribute, and the minimum value ${}^t\bar{D}_D$ should be used. To rigorously show that this is the correct choice, we reduce the complete diffusion equation governing all m degrees of freedom to the ordinary translational diffusion equation for an idealized point particle with diffusion coefficient D_t. Our approach closely follows that of ref 11 and 29.

We consider a suspension of identical flexible bodies that is sufficiently dilute to ignore interparticle effects. Let $\rho = \rho(\mathbf{r}_P,\varphi,t)$ be the density of particles at time t with position $\mathbf{r}_P$ and orientation φ. That is, there are $\rho d^3\mathbf{r} d^m\varphi$ particles with positions within volume element $d^3\mathbf{r}$ about $\mathbf{r}_P$ and orientations within $d^m\varphi$ about φ. The description that follows is equally valid for any point P in the body. Let $c = c(\mathbf{r}_P,t)$ be the particle concentration, that is, the density regardless of orientation, given by

$$c = \int \rho(\mathbf{r}_P,\varphi,t) g^{1/2}\, d^m\varphi \tag{20}$$

The equation of particle conservation can be written as

$$\partial\rho/\partial t = -\nabla\cdot{}^t\mathbf{J} - \nabla_\varphi\cdot{}^r\mathbf{J} \tag{21}$$

where ∇ is the usual del operator with Cartesian components $\partial/\partial x_i$, for $i = 1, 2, 3$, ∇_φ is the orientation del operator defined previously, and ${}^t\mathbf{J}$ and ${}^r\mathbf{J}$ are the translational and orientational flux, respectively. We assume that there are no convection currents, external forces, or torques present. The diffusive contribution to the flux is given by Fick's law according to

$$\begin{aligned} {}^t\mathbf{J} &= -{}^t\mathbf{D}_P\cdot\nabla\rho - {}^c\mathbf{D}_P{}^\dagger\cdot\nabla_\varphi\rho \\ {}^r\mathbf{J} &= -{}^c\mathbf{D}_P\cdot\nabla\rho - {}^r\mathbf{D}\cdot\nabla_\varphi\rho \end{aligned} \tag{22}$$

while the flux contribution driven by the internal potential is given as

$$\begin{aligned} {}^t\mathbf{J} &= \beta\rho\,{}^c\mathbf{D}_P{}^\dagger\cdot\mathbf{f} \\ {}^r\mathbf{J} &= \beta\rho\,{}^r\mathbf{D}\cdot\mathbf{f} \end{aligned} \tag{23}$$

Adding these contributions and substituting in the continuity equation give

$$\partial\rho/\partial t = \nabla\cdot{}^t\mathbf{D}_P\cdot\nabla\rho + \nabla\cdot{}^c\mathbf{D}_P{}^\dagger\cdot(\nabla_\varphi - \beta\mathbf{f})\rho + \nabla_\varphi\cdot{}^c\mathbf{D}_P\cdot\nabla\rho + \nabla_\varphi\cdot{}^r\mathbf{D}\cdot(\nabla_\varphi - \beta\mathbf{f})\rho \tag{24}$$

This is the complete diffusion equation for the flexible body. In contrast, the ordinary diffusion equation can be written as

$$\partial c/\partial t = D_t\nabla^2 c \tag{25}$$

where ∇^2 is the Laplacian $\nabla\cdot\nabla$, c is the particle concentration, and D_t is the particle diffusion coefficient.

We wish to integrate out the orientational dependency in eq 24, equate our results with eq 25, and obtain D_t in terms of the diffusion matrices. Of course, without knowing the orientational dependence we cannot immediately do this. As a particle moves over macroscopic distances, it randomly tumbles many times and intuition suggests that we could simply assume a Boltzmann distribution internally determined by potential V and isotropic with respect to external laboratory axes. However, it is easily seen that this immediate assumption of orientational equilibrium leads to the identification $D_t = {}^t\bar{D}_P$. That is, the resulting ordinary diffusion coefficient would depend on the particular choice of point P.

To proceed, we turn to perturbation methods. Let l be a characteristic particle size and τ a time scale characteristic of particle motion over l. We introduce dimensionless diffusion matrices according to

$${}^t\mathbf{D}_P^* = (\tau/l^2){}^t\mathbf{D}_P \qquad {}^c\mathbf{D}_P^* = (\tau/l){}^c\mathbf{D}_P \qquad {}^r\mathbf{D}^* = \tau\,{}^r\mathbf{D}$$

Let $l' \gg l$ be a characteristic macroscopic distance and $\tau' \gg \tau$ a time scale appropriate to diffusion over this distance. Then $t^* = t/\tau'$ and $\nabla^* = l'\nabla$ are dimensionless. Noting that in Brownian motion the square of the displacement is proportional to the time interval, we pick the macroscopic time scale by choosing $\tau' = \tau(l'/l)^2$. Equation 24 can then be written entirely in terms of dimensionless quantities as

$$\partial\rho/\partial t^* = \nabla^*\cdot{}^t\mathbf{D}_P^*\cdot\nabla^*\rho + \epsilon^{-1}\nabla^*\cdot{}^c\mathbf{D}_P{}^{\dagger *}\cdot(\nabla_\varphi - \mathbf{f}^*)\rho + \epsilon^{-1}\nabla_\varphi\cdot{}^c\mathbf{D}_P^*\cdot\nabla^*\rho + \epsilon^{-2}\nabla_\varphi\cdot{}^r\mathbf{D}^*\cdot(\nabla_\varphi - \mathbf{f}^*)\rho \tag{26}$$

where $\mathbf{f}^* \equiv \beta\mathbf{f}$ and $\epsilon \equiv l/l'$, with $\epsilon \ll 1$.

With the exception of ϵ, we assume that all terms in eq 26 are the same order of magnitude. Substituting the perturbation series

$$\rho = \rho_0 + \epsilon\rho_1^* + \epsilon^2\rho_2^* + \ldots \equiv \rho_0 + \rho_1 + \rho_2 + \ldots$$

into eq 26 and equating equal powers of ϵ yield a series of dimensionless equations that can then be rewritten in the original unstarred notation. Recognizing that the diffusion matrices are constants with regard to the operator ∇ and using the operator replacements

$$\nabla\cdot{}^c\mathbf{D}_P{}^\dagger\cdot(\nabla_\varphi - \beta\mathbf{f}) = \nabla_\varphi\cdot{}^c\mathbf{D}_P\cdot\nabla - \mathbf{d}_P\cdot\nabla$$

$$L = \nabla_\varphi\cdot{}^r\mathbf{D}\cdot(\nabla_\varphi - \beta\mathbf{f}) \tag{27}$$

we obtain two constitutive relations

$$L\rho_0 = 0 \tag{28a}$$

$$L\rho_1 = -\mathbf{d}_P\cdot\nabla\rho_0 - 2\nabla\cdot{}^c\mathbf{D}_P{}^\dagger\cdot(\nabla_\varphi - \beta\mathbf{f})\rho_0 \tag{28b}$$

plus the series

$$L\rho_{i+2} = \partial\rho_i/\partial t - \nabla\cdot{}^t\mathbf{D}_P\cdot\nabla\rho_i + \mathbf{d}_P\cdot\nabla\rho_{i+1} - 2\nabla_\varphi\cdot{}^c\mathbf{D}_P\cdot\nabla\rho_{i+1} \tag{28c}$$

for $i = 0, 1, \ldots, \infty$.

Equation 28a is satisfied by the Boltzmann solution describing internal equilibrium, namely

$$\rho_0 = Nc_0\exp(-\beta V) \tag{29}$$

where N is the normalization coefficient given in eq 6b, and $c_0 = c_0(\mathbf{r}_P,t)$ is the associated concentration. In the previous section on microscopic motions, we assumed that the configurations of an isolated particle are distributed according to Boltzmann statistics. For that assumption to hold here as $\epsilon \to 0$, it follows that the lowest order solution given by eq 29 must also be the unique solution to eq 28a.

Using eq 29 causes the second term on the right-hand side of eq 28b to vanish identically. The general solution to eq 28b is

$$\rho_1 = \mathbf{r}_{PD}\cdot\nabla\rho_0 + \psi \tag{30}$$

where ψ vanishes identically when substituted in eq 28a. To verify that the first term is, indeed, the particular solution, use the identities $\nabla_\varphi\rho_0 = \beta\mathbf{f}\rho_0$ and $\mathbf{R}_{PD}{}^\dagger = \nabla_\varphi\mathbf{r}_{PD}$ to rearrange the resulting left-hand side of eq 28b as

$$\nabla_\varphi\cdot{}^r\mathbf{D}\cdot\mathbf{R}_{PD}{}^\dagger\cdot\nabla\rho_0$$

When the action of ∇_φ is restricted within braces, this expression becomes

$$\{(\nabla_\varphi + \beta\mathbf{f})\cdot{}^r\mathbf{D}\cdot\mathbf{R}_{PD}{}^\dagger\}\cdot\nabla\rho_0$$

From eq 5b, ${}^r\mathbf{D}\cdot\mathbf{R}_{PD}{}^\dagger$ can be replaced by ${}^c\mathbf{D}_D - {}^c\mathbf{D}_P$, and from eq 13, the braces reduce to $\mathbf{d}_D - \mathbf{d}_P$, or just $-\mathbf{d}_P$, since $\mathbf{d}_D$ vanishes.

Having verified that $\mathbf{r}_{PD}\cdot\nabla\rho_0$ is a particular solution, we note that, since $\mathbf{r}_{PD}$ is body-fixed while ∇ is space-fixed, their dot product vanishes when isotropically integrated over all external angles the body makes with laboratory axes. As such, the associated concentration c_1 is solely determined by the ψ term. For most models, the only solutions of $L\psi = 0$ are proportional to the Boltzmann distribution, so $\psi = (c_1/c_0)\rho_0$. Because operator L is isotropic with respect to external laboratory axes, ψ must be also. Other than this symmetry, the functional form of ψ is not needed for the analysis below. Thus when the first-order correction is included, the distribution is anisotropic with respect to external laboratory axes. The bias depends on the dot product between the lowest order spatial gradient and the position vector between point P and the center of diffusion. If macroscopic spatial equilibrium is obtained, ρ_0 is independent of location and this anisotropy disappears.

Equations 29 and 30 are valid for any flexible body. To continue this section, we assume that there are not boundaries for the space of orientational coordinates. As such, the left-hand side and the last term on the right-hand side of eq 28c vanish identically when integrated over all orientations. For $i = 0$, we obtain

$$\partial c_0/\partial t = \int \nabla\cdot{}^t\mathbf{D}_P'\cdot\nabla\rho_0 g^{1/2}\, \mathrm{d}^m\varphi \tag{31}$$

with ${}^t\mathbf{D}_P'$ defined as

$${}^t\mathbf{D}_P' = {}^t\mathbf{D}_P - \tfrac{1}{2}(\mathbf{d}_P\mathbf{r}_{PD} + \mathbf{r}_{PD}\mathbf{d}_P) \tag{32}$$

Since ρ_0 given by eq 29 is isotropic with regard to external axes, eq 31 becomes

$$\partial c_0/\partial t = (1/3)\,\overline{\mathrm{Tr}\ {}^t\mathbf{D}_P'}\nabla^2 c_0 \tag{33}$$

with the overbar symbol defined by eq 6. Although ${}^t\mathbf{D}_P'$ depends upon the particular point P being used, its Boltzmann average does not. From eq 7 and 32

$$(1/3)\,\overline{\mathrm{Tr}\ {}^t\mathbf{D}_P'} = {}^t\bar{D}_P - (1/3)\overline{\mathbf{d}_P\cdot\mathbf{r}_{PD}} \tag{34a}$$

or from eq 15

$$(1/3)\,\overline{\mathrm{Tr}\ {}^t\mathbf{D}_P'} = {}^t\bar{D}_D \tag{34b}$$

so that c_0 obeys the ordinary diffusion equation

$$\partial c_0/\partial t = {}^t\bar{D}_D\nabla^2 c_0 \tag{35}$$

regardless of which point P is being used.

In the limit that ϵ vanishes, i.e., for macroscopic distances, we identify eq 35 with eq 25 and find that, indeed, all points in the body diffuse according to the ordinary diffusion equation with the same coefficient D_t given as $D_t = {}^t\bar{D}_D$. This is our desired result. Even though we used a perturbation approach, our result becomes exact in the limit of macroscopic distances.

Experimentally, a macroscopic distance is one for which ϵ is sufficiently small to ignore possible higher order corrections. Unlike c_0, subsequent expressions for c_i, with $i > 0$, generally depends on the particular point P. That is, rotational and internal motions about the center of diffusion enter into the results. However, if we use the center of diffusion, it is easy to show that we again regain the ordinary diffusion equation for c_1 involving ${}^t\bar{D}_D$. To order ϵ then, the translational motions of the center of diffusion are governed by D_t. At order ϵ^2, the ordinary diffusion equation no longer applies to even the center of diffusion. At this order, it is no longer possible to treat translational motions independently of the details of orientational relaxation from the particle initial conditions involved.

Internal Boundary Conditions

In preceding expressions requiring integration by parts, we assumed that the orientational degrees of freedom constitute an unbounded space. This assumption can be made without any loss of generality, because the internal potential V can always be chosen to obtain a distribution limited to certain flexible configurations. However, the presence of unbounded domains often becomes unwieldy when numerical methods are used, and, in practice, impenetrable barriers are usually imposed to restrict internal configurations.

We now assume that internal boundaries are present. All orientational averages, such as those involved in defining ${}^t\bar{D}_P$, are, of course, restricted to the allowed internal configurations. ${}^t\bar{D}_P$ still has its minimum value at that unique point that is defined for any flexible body by eq 10. Equations 10 and 11 are general results that hold for any flexible body. However, subsequent redefinitions of the center of diffusion in eq 12 and 13 must be augmented, since integration by parts was used, and there will now be surface terms present. Retracing the steps leading to eq 13 generates an additional boundary condition: if $\mathbf{n}$ is some m-dimensional unit vector field normal to the boundary, then ${}^t\bar{D}_P$ can have a minimum value at some point P only if

$$\mathbf{n}\cdot{}^c\mathbf{D}_P = 0 \tag{36}$$

vanishes everywhere along the boundary. That is, the center of diffusion is now defined by condition that $\mathbf{d}_P$ vanish for all allowed internal configurations, and that, along any configurational boundaries, the normal projection of ${}^c\mathbf{D}_P$ vanishes.

When the complete diffusion equation is considered, there is now the additional requirement that the flux ${}^r\mathbf{J}$ across any internal boundary must vanish, where ${}^r\mathbf{J}$ is given by eq 22 and 23. A perturbation expansion of $\mathbf{n}\cdot{}^r\mathbf{J} = 0$ yields

$$\mathbf{n}\cdot{}^r\mathbf{D}\cdot(\nabla_\varphi - \beta\mathbf{f})\rho_0 = 0 \tag{37a}$$

$$\mathbf{n}\cdot{}^r\mathbf{D}\cdot(\nabla_\varphi - \beta\mathbf{f})\rho_i = -\mathbf{n}\cdot{}^c\mathbf{D}_P\cdot\nabla\rho_{i-1} \tag{37b}$$

on the boundary, for $i = 1, 2, \ldots, \infty$. Equation 37a is identically satisfied by eq 29 for ρ_0. Substituting eq 29 for ρ_0 and eq 30 for ρ_1 in eq 37b and using eq 5b lead to the condition $\mathbf{n}\cdot{}^c\mathbf{D}_D\cdot\nabla\rho_0 = 0$, which is satisfied by eq 36. Thus, internal boundary conditions imposed on the orientational flux are satisfied by the previous solutions through order ϵ regardless of the choice of point P being used.

Equations 31 and 33 for $\partial c_0/\partial t$ still apply when eq 37 is used to eliminate any flux through internal boundaries. However, the tensor ${}^t\mathbf{D}_P'$ involved there is now no longer given by eq 32, which holds only if surface terms vanish, but according to the more general expression

$${}^t\mathbf{D}_P' = {}^t\mathbf{D}_P + (1/6)(\mathbf{R}_{PD}\cdot{}^c\mathbf{D}_P + {}^c\mathbf{D}_P{}^\dagger\cdot\mathbf{R}_{PD}{}^\dagger) \tag{38}$$

which holds for any flexible body. Taking the trace of eq 38 and using eq 11, we again obtain eq 35. That is, c_0 still obeys the ordinary diffusion equation with diffusion coefficient ${}^t\bar{D}_D$, without regard to which point P is being used or whether internal boundaries are present. The comments that follow eq 35 also remain true. In particular, the center of diffusion still characterizes the translational motion of a body through order ϵ^1.

The use of an impenetrable barrier is entirely consistent with the notion that all internal dynamics are governed by an internal potential. That is, an internal boundary can be considered as a limiting internal potential in which V is represented by a step function across the bounding

surface. The generalized force $\mathbf{f}$ then has an additional component along the boundary that is normal to the surface and that involves a Dirac δ function. If we remove this additional component from the associated $\mathbf{d}_P$ vector and use the delta function property in the various orientational integrations, the results are equivalent to those obtained here in which we simply imposed a boundary.

Allowing for the presence or absence of internal boundaries, we can summarize the properties of an isolated flexible body as follows. The macroscopic diffusion coefficient D_t is equivalent to ${}^t\bar{D}_D$, where the overbar average is extended over all allowed orientations and the center of diffusion, point D, is the unique point in every body with the least average Brownian motion. The center of diffusion is the only point where $\mathbf{d}_P$ vanishes for all allowed configurations and $\mathbf{n}\cdot{}^c\mathbf{D}_P$ vanishes at any configurational boundaries.

Rigid-Body Approximation and Bounds on D_t

A useful approximation to D_t follows in which each configuration of a flexible body is considered as a rigid body. The diffusion coefficient of each configuration is found by rigid-body formulas, using the appropriate rigid-body center of diffusion for that body, denoted point D'. Averaging over all configurations, the resulting translational diffusion coefficient, denoted D_t', will generally differ from D_t, since the dynamic aspects of flexibility, involving translational coupling to internal motions, have been left out. In the Appendix, we show that these coupling effects are inherently beneficial, at least within the framework of low Reynold's number hydrodynamics used to generate diffusion coefficients. That is, $D_t \geq D_t'$, with the equality holding only if the coupling terms evaluated at point D' are identically zero for all configurations. One model for which these terms do indeed vanish is the elastic dumbbell considered by Zimm[16] in which two identical beads are connected along an axis by a spring. By symmetry, the translational motions of the dumbbell's midpoint are independent of distance changes between beads. If the beads are not identical, this decoupling no longer occurs. More realistic models would be expected to have a preponderance of asymmetric configurations in which internal motions cannot be decoupled from the translational motions of point D'. In general, then, the rigid-body approximation underestimates the actual macroscopic diffusion coefficient of a flexible body.

Since using any point P of a flexible body other than the actual center of diffusion overestimates its macroscopic diffusion, we know that ${}^t\bar{D}_P \geq D_t$, with ${}^t\bar{D}_P$ given by eq 9. Although the center of mass, point M, is not directly involved in diffusive behavior, it may remain close enough to the center of diffusion for ${}^t\bar{D}_M$ to provide a good approximation to D_t. Another useful point is the rigid-body center of diffusion at each configuration, point D', whose location is algebraically determined by eq 17 and 19. Point D' would have the slowest microscopic motions in a rigid body but not in the actual flexible body. As shown in the example that follows, the difference between ${}^t\bar{D}_M$ and D_t' is slight while that between ${}^t\bar{D}_{D'}$ and D_t' is even smaller. This suggests that D_t may be determined from these bounds to an adequate accuracy in most if not all cases without actually having to solve the complicated partial differential equation determining the location of a flexible body's center of diffusion.

Application to a Hinged Rod

As a simple example with 1 degree of internal freedom, we consider a long rod that has a frictionless hinge at its center and undergoes planar bending. Bead-model methods will be used in order to provide a realistic hydrodynamic treatment that includes hydrodynamic interactions between rod halves (for a general review of these methods, see ref 12). Each rod half is represented by a collinear array of identical touching beads. As shown in Figure 1, the rod halves attach at a point O midway between the centers of their end beads. This connection avoids interpenetration of the beads as the rod bends by angle α from a straight rod at $\alpha = 0°$ to form a side-by-side hairpin at $\alpha = \pm 180°$. Right-handed axes 1, 2, and 3 are placed along the symmetry axes of the body, with axis 3 normal to the plane containing the rod halves and axis 2 lying between them.

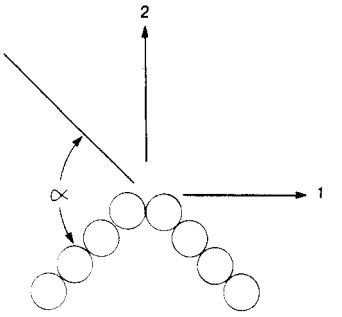

Figure 1. Bead model of a hinged rod bent at its center by angle α. Right-handed axes 1, 2 and 3 are located at the contact point O between the two rod halves. Axis 3 is normal to the bending plane, while axis 2 bisects the angle between rod halves.

The three translational degrees of freedom are represented by point P's displacements Δx^i along axes 1, 2, and 3. For the 4 orientational degrees of freedom, the first 3 are represented by rigid rotational displacements $\Delta\phi^i$ about axes 1, 2, and 3 and the last by bending displacements $\Delta\alpha$. By symmetry, these are principal axes for rotations and translations, and bending motions are not coupled to rotations. As such, the 3×3 matrix ${}^t\mathbf{D}_P$ and the 4×4 matrix ${}^r\mathbf{D}$ are diagonal. By symmetry, the center of diffusion must lie along axis 2, and we restrict further considerations of positional dependence along this axis. The 4×3 matrix ${}^c\mathbf{D}_P$ then yields only three nonzero coefficients: ${}^cD_P{}^{13}$, involving coupling between rotations about axis 1 and point P's translations along axis 3; ${}^cD_P{}^{31}$, involving coupling between rotations about axis 3 and point P's translations along axis 1; and ${}^cD_P{}^{42}$, involving coupling between bending and point P's translations along axis 2. For convenience, let $D^{\alpha\alpha} \equiv {}^rD^{44}$ and ${}^cD_P{}^{\alpha 2} \equiv {}^cD_P{}^{42}$.

To evaluate these diffusion coefficients, we apply bead-model methods developed for segmentally flexible bodies.[14] This approach can be summarized as follows: the hydrodynamic drag of an isolated bead i' of radius a is given by the usual Stokes factor $\zeta_{i'} = 6\pi\eta a$, where η is the solvent viscosity, and hydrodynamic interactions between bead pairs j' and k' are represented by a modified Oseen tensor $\mathbf{T}_{j'k'}$ first derived by Rotne and Prager.[30,31] For a spatial arrangement of n beads corresponding to the hinged rod at some particular α, we load a $3n \times 3n$ "supermatrix" $\mathbf{Q}$ with off-diagonal 3×3 blocks $\mathbf{Q}_{j'k'} = \zeta_{j'}\mathbf{T}_{j'k'}$ and diagonal 3×3 blocks $\mathbf{Q}_{i'i'} = \mathbf{I}$. Inverting $\mathbf{Q}$ yields a $3n \times 3n$ supermatrix $\mathbf{S}$. $\mathbf{S}$ is decomposed into 3×3 blocks $\mathbf{S}_{i'j'}$ that are used to generate matrices $\mathbf{A}_{ij}$, $\mathbf{C}_{ij}$, $\mathbf{D}_{ij}$, for $i, j = 1, 2$, that characterize the complete hydrodynamics of the two rod halves regardless of the nature of their attachment. By the use of displacement representation described above, these matrices are then projected on the allowed degrees of freedom to generate the 7-dimensional hydrodynamic resistance tensor $\mathbf{K}$ for the hinged rod. At low Reynold's numbers, a generalized Stokes–Einstein relation holds. We thus invert $\mathbf{K}$ and obtain the 7-dimensional diffusion

tensor $\mathbf{D} = kT\mathbf{K}^{-1}$ that contains the desired components.

For simplicity, this procedure is carried out at the hinge, point O. The nonzero components of ${}^{t}\mathbf{D}_P$ and ${}^{c}\mathbf{D}_P$ can be obtained at other points along axis 2 by using the transformation relations given in eq 5. Let $\hat{\mathbf{2}}$ be a unit vector along axis 2, so $\mathbf{r}_{OP} = y_{OP}\hat{\mathbf{2}}$. The needed nonzero components of the 3×4 matrix $\mathbf{R}_{OP}$ can be expressed as

$$R_{OP}{}^{31} = -R_{OP}{}^{13} = y_{OP}$$

$$R_{OP}{}^{24} = \dot{y}_{OP}$$

where $\dot{y}_{OP} \equiv \partial y_{OP}/\partial\alpha$.

In the absence of any internal potential, we assume an equilibrium ensemble of hinged rods would be uniformly distributed over α. As such, we take $g^{1/2}$ to be an ignorable constant, a choice which reduces ∇_α to $\partial/\partial\alpha$ in all expressions. With $g^{1/2}$ constant, the orientational average $\bar{h}$ of any function $h(\alpha)$ becomes

$$\bar{h} = \int_{\alpha_1}^{\alpha_2} h(\alpha) \exp[-\beta V(\alpha)]\, d\alpha \Big/ \int_{\alpha_1}^{\alpha_2} \exp[-\beta V(\alpha)]\, d\alpha \tag{39}$$

where α is generally bounded between two limits α_1 and α_2. Recalling the definition

$${}^{t}\bar{D}_P \equiv (1/3)\overline{({}^{t}D_P{}^{11} + {}^{t}D_P{}^{22} + {}^{t}D_P{}^{33})}$$

and using eq 9, we can express ${}^{t}\bar{D}_P$ for any point P in terms of quantities evaluated at the hinge according to

$${}^{t}\bar{D}_P = {}^{t}\bar{D}_O + (1/3)\overline{[({}^{r}D^{11} + {}^{r}D^{33})y_{OP}{}^2 + D^{\alpha\alpha}\dot{y}_{OP}{}^2]} + (2/3)\overline{[({}^{c}D_O{}^{13} - {}^{c}D_O{}^{31})y_{OP} + {}^{c}D_O{}^{\alpha 2}\dot{y}_{OP}]} \tag{40}$$

For the center of diffusion, point D, this expression further reduces (see eq 11) so that the macroscopic diffusion coefficient can be expressed as

$$D_t = {}^{t}\bar{D}_O - (1/3)\overline{[({}^{r}D^{11} + {}^{r}D^{33})y_{OD}{}^2 + D^{\alpha\alpha}\dot{y}_{OD}{}^2]} \tag{41}$$

Equation 16 for y_{OD} also simplifies. From symmetry, $\mathbf{d}_P = d_P\hat{\mathbf{2}}$. To evaluate d_P, we note that rotations are decoupled from internal bending, so $\nabla_\varphi \cdot {}^{c}\mathbf{D}_P$ is the sum of a rigidlike term given in eq 17, and a term $\partial {}^{c}D_P{}^{\alpha 2}/\partial\alpha$. Equation 13 yields

$$d_P = {}^{c}D_P{}^{31} - {}^{c}D_P{}^{13} + \beta f {}^{c}D_P{}^{\alpha 2} + \partial {}^{c}D_P{}^{\alpha 2}/\partial\alpha \tag{42}$$

where $f = -\partial V(\alpha)/\partial\alpha$. Equation 16 similarly partitions into rigid and internal portions. Using eq 18 to evaluate the rigid portion, we have

$$D^{\alpha\alpha}\ddot{y}_{OD} + (\beta f D^{\alpha\alpha} + \partial D^{\alpha\alpha}/\partial\alpha)\dot{y}_{OD} - ({}^{r}D^{11} + {}^{r}D^{33})y_{OD} = -d_O \tag{43}$$

where $\ddot{y}_{OD} \equiv \partial^2 y_{OD}/\partial\alpha^2$.

For α bounded between α_1 and α_2, we have the additional boundary condition that ${}^{c}D_D{}^{\alpha 2}$ vanish at these limits. From eq 5b, $\dot{y}_{OD}$ is then given at α_1 and α_2 according to

$$\dot{y}_{OD} = -{}^{c}D_O{}^{\alpha 2}/D^{\alpha\alpha} \tag{44}$$

A general approach to locating the center of diffusion is to impose two boundaries and start with some trial value for y_{OD} at α_1, such as that corresponding to the center of mass. With eq 44 for $\dot{y}_{OD}$ at α_1, numerically integrate eq 43 to obtain a trial solution for y_{OD} from $\alpha = \alpha_1$ to $\alpha = \alpha_2$. This trial solution will generally not satisfy eq 44 at α_2. Readjust the initial trial value of y_{OD} at α_1 and start again, proceeding until satisfactory agreement is obtained with the required boundary condition at α_2. If an internal potential $V(\alpha)$ is present and is intended to be the sole restoring force, then α_1 and α_2 should be place at regions of high potential where the Boltzmann factor would be quite small and there would be negligible effect of introducing additional cutoffs.

Table I
Various Translational Diffusion Coefficients for Several Centrally Hinged Rod Models[a]

α_0, deg	D_t	D_t'	${}^{t}\bar{D}_{D'}$	${}^{t}\bar{D}_M$	${}^{t}\bar{D}_O$
			Without Spring Potential[b]		
5	1.000	1.000	1.000	1.008	2.191
45	1.001	1.001	1.001	1.010	2.156
90	1.004	1.004	1.005	1.019	2.109
135	1.020	1.019	1.022	1.038	2.123
180	1.063	1.060	1.067	1.077	2.215
			With Spring Potential[c]		
5	1.000	1.000	1.000	1.008	2.191
45	1.001	1.001	1.001	1.011	2.156
90	1.009	1.008	1.009	1.023	2.130
135	1.025	1.024	1.027	1.040	2.148
180	1.038	1.036	1.040	1.052	2.169

[a] Coefficients normalized to D_t for straight rigid rod. [b] $f = 0$, $-\alpha_0 \le \alpha \ge +\alpha_0$. [c] $\beta f = K\alpha$, $-\infty \le \alpha \ge +\infty$, K chosen to give same $\bar{\alpha}$ as $f = 0$ case with corresponding α_0.

An interactive Fortran program was used to determine the location of the center of diffusion and obtain orientational averages. The diffusion coefficients are evaluated from the bead-model procedure at approximately 25 discreetly spaced α values. Cubic spline interpolation is used so that all coefficients in eq 43 and 44 appear to the calling routines as smooth continuous functions of α from 0° to 180°.[32] By standard practice, the second-order differential equation for y_{OP} in eq 43 is replaced by a pair of coupled first-order equations. These equations are integrated simultaneously with a fourth-order Runge–Kutta method in which step size can be decreased to satisfy desired error tolerances. For all cases treated here, the potential as well as any restrictions on bending are symmetric about $\alpha = 0°$, so that $y(\alpha)_{OD} = -y(-\alpha)_{OD}$ and $-\alpha_1 = \alpha_2 \equiv \alpha_0$, with α_0 assumed positive. As such, we integrate eq 43 from $\alpha = \alpha_0$ to 0° and replace the boundary requirement at $\alpha = -\alpha_0$ with the equivalent requirement that $y_{OD} = 0$ at $\alpha = 0°$.[33] The program was run on an IBM-XT equipped with an 8087 numeric data-processing chip with a compiler that supports the 8087 and allows all calculations to be done in double precision (approximately 15-digit accuracy) with negligible increase in computation time.

Various results are summarized in Table I. As indicated, the top set are obtained without any internal potential present ($f = 0$) for several values of α_0. In the bottom set, a spring potential is present with $\beta f = -K\alpha$. Taking $K = 8/(\pi\alpha_0{}^2)$ gives a distribution average of α over all angles from 0 to ∞ equal to that obtained for a given α_0 in the top set. For comparative purposes, this corresponding value of α_0 has been indicated in the bottom set rather than the K value used. Finally, with the spring potential present, the α value used to start the solution for y_{OD} is taken as 180° to prevent interpenetration of the rod halves. When the results are compared, there is seen to be little difference between a hinged rod freely bending within a restricted range or bending in the presence of the corresponding equivalent elastic restoring force.

For simplicity, all diffusion coefficients are normalized to the D_t value obtained for the straight rigid rod with $\alpha = 0°$. Column 2 gives the desired macroscopic diffusion coefficient values for the flexible rod. D_t increases as α_0 increases, primarily because of the enhanced hydrodynamic shielding between rod halves for configurations with large α. The actual increase is slight, with the maximum being only 6.3% greater than that for the straight rigid rod. Column 3 gives the rigid-body approximation results.[34] As seen, D_t' is an excellent approximation to D_t, with the

maximum difference being only 0.3%. As required, D_t' is also found to be less than D_t, although this difference is often below the level of precision in Table I.

The last three columns give translational diffusion coefficients governing the average microscopic displacements of selected points in the flexible hinged rod. For the rigid-body center of diffusion, point D', eq 19 yields

$$y_{OD'} = -({}^cD_O{}^{13} - {}^cD_O{}^{31})/({}^rD^{11} + {}^rD^{22})$$

For the center of mass, point M, $y_{OM} = -10a \sin(\alpha/2)$, since each rod half has 10 beads of radius a. The coefficients evaluated at points D' and M provide excellent approximations to D_t, with the maximum difference being only 0.4% using ${}^t\bar{D}_{D'}$ and 1.4% using ${}^t\bar{D}_M$. As required, these two coefficients are always found to be greater than D_t, although this difference is often below the level of precision in Table I. Finally, the microscopic motions of the hinge are seen to be substantially greater than these other points with ${}^t\bar{D}_O$ values at least twice as large as any of the other coefficients.

Discussion and Conclusion

Following earlier studies on rigid bodies, we have shown that flexible macromolecules also have a well-defined center of diffusion. In terms of microscopic Brownian motions that are small on the scale of body size, this point undergoes the slowest average translational displacements. The location of the center of diffusion was shown to be determined by a second-order partial differential equation with boundary conditions imposed along any internal boundaries.

Using perturbation methods, we identified D_t, the coefficient characterizing macroscopic translational diffusion, with ${}^t\bar{D}_P$ evaluated at the center of diffusion. Although this finding was anticipated on intuitive grounds from the minimum properties of the microscopic coefficients, the perturbation analysis constitutes a rigorous proof. For not fully macroscopic conditions, we showed that corrections to the ordinary diffusion equation with coefficient D_t appear at order ϵ^2 for the center of diffusion but may appear to order ϵ for other points, where ϵ is the ratio of body size to the diffusion distance involved.

Using a rigid-body approximation, we also showed that the dynamic effects of flexibility, those involving the coupling of internal motions to translational motions, give positive contributions to D_t. That is, considering each configuration of the flexible body as a rigid body, determining its macroscopic diffusion coefficient using rigid-body methods, and then configurationally averaging over the same internal distribution result in a coefficient that generally underestimates D_t.

As an example, we evaluated the diffusive behavior of a frictionless centrally hinged rod under a variety of bending restrictions. Bead-model methods were used in order to properly treat hydrodynamic interactions between rod halves. Flexibility was shown to have little effect on D_t. For the bead model used with 10 beads on each arm, D_t increased at most 7% from that for a straight rigid rod with 20 beads. These results with increased D_t primarily reflect enhanced hydrodynamic shielding between rod halves at large bending angles. In fact, these results differ in sign from earlier estimates in which hydrodynamic interactions between rod halves were ignored in the long-rod limit.[8]

In all cases, the D_t values for the hinged rod were determined within less than 1% by upper and lower bounds. The lower bound was obtained from the rigid-body approximation, while the upper bound was obtained from the evaluation of ${}^t\bar{D}_P$ at either the center of mass or the rigid-body center of diffusion that would be used for a corresponding rigid bent rod. These bounds suggest that, for most practical purposes, D_t may be estimated to an excellent degree without having to actually solve the partial differential equation defining the center of diffusion of a flexible body.

Finally, we comment on the validity of two assumptions underlying this work: dynamic interchangeability and Boltzmann statistics. In order that a macromolecule be correctly characterized by one coefficient D_t, it must be able to sample all its internal configurations on a time scale shorter than that involved in a macroscopic measurement. Thus, polymers that can become quite entangled may be beyond this treatment. A generalization of this work would be to assign each distinct set of interchanging configurations its own D_t. For simplicity, we have employed the usual assumption that classical Boltzmann statistics govern allowed internal configurations. This may not be true for models employing quantum mechanical distributions or models allowing unbounded potentials with multistable internal distributions. However, the qualitative findings of this paper can be shown to remain the same if the Boltzmann distribution is replaced by any arbitrary steady-state internal distribution.

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Appendix: Proof of Rigid-Body Approximation Inequality

We wish to prove that $D_t \geq D_t'$, where D_t is the macroscopic translational diffusion coefficient for a flexible body and D_t' is obtained from a rigid-body approximation. In this approximation, each flexible body configuration is considered as a rigid body whose macroscopic translational diffusion coefficient follows from rigid-body formulas. Let the diffusion coefficient governing the average microscopic motions of any point P in a rigid body be denoted ${}^tD_P'$. Averaging this coefficient over the configurational distribution gives $D_t' = {}^t\bar{D}_{D'}$, where point D' is the rigid-body center of diffusion. On the other hand, $D_t = {}^t\bar{D}_D$, where point D is the actual center of diffusion for a flexible body. Also, ${}^t\bar{D}_{P'} \geq {}^t\bar{D}_{D'}$ holds for any other point P in a rigid body, including point D, so if ${}^t\bar{D}_D \geq {}^t\bar{D}_{D'}$, then $D_t \geq D_t'$. By definition

$${}^t\bar{D}_D = (1/3)\,\overline{\mathrm{Tr}\ {}^t\mathbf{D}_D(\text{flexible})}$$

$${}^t\bar{D}_{D'} = (1/3)\,\overline{\mathrm{Tr}\ {}^t\mathbf{D}_D(\text{rigid})}$$

where ${}^t\mathbf{D}_D$(flexible) and ${}^t\mathbf{D}_D$(rigid) are the 3×3 matrices governing the translational motions of point D for a flexible and rigid body with the same configuration. Thus, to show that $D_t \geq D_t'$, we prove that Tr ${}^t\mathbf{D}_D$(flexible) $\geq$ Tr ${}^t\mathbf{D}_D$(rigid) holds at any configuration.

At low Reynold's numbers, the hydrodynamics of a body are represented by a symmetric resistance tensor $\mathbf{K}$ of appropriate dimensionality. We can always represent the allowed degrees of freedom such that the first three describe the translational displacements of point D, the second three describe rigid orientational displacements, while any n remaining describe internal displacements. As such, $\mathbf{K}$ respectively partitions into 3×3 matrices ${}^{tt}\mathbf{K}$, ${}^{rr}\mathbf{K}$, and ${}^{rt}\mathbf{K}$ governing translational motions, rotational motions, and rotational–translational coupling, $n \times 3$ matrices ${}^{it}\mathbf{K}$ and ${}^{ir}\mathbf{K}$ governing internal–translational coupling and internal–rotational coupling, and an $n \times n$ matrix ${}^{ii}\mathbf{K}$ governing internal motions. Explicitly

$$\mathbf{K} = \begin{matrix} {}^{tt}\mathbf{K} & {}^{tr}\mathbf{K} & {}^{ti}\mathbf{K} \\ {}^{rt}\mathbf{K} & {}^{rr}\mathbf{K} & {}^{ri}\mathbf{K} \\ {}^{it}\mathbf{K} & {}^{ir}\mathbf{K} & {}^{ii}\mathbf{K} \end{matrix}$$

where ${}^{tr}\mathbf{K} = {}^{rt}\mathbf{K}^{\dagger}$, ${}^{ti}\mathbf{K} = {}^{it}\mathbf{K}^{\dagger}$, ${}^{ri}\mathbf{K} = {}^{ir}\mathbf{K}^{\dagger}$, and † denotes matrix transpose. Since $\mathbf{K}$ is symmetric and positive-definite (positive principal values), so are ${}^{tt}\mathbf{K}$, ${}^{rr}\mathbf{K}$, and ${}^{ii}\mathbf{K}$. Applying the generalized Stokes–Einstein relation $\mathbf{D} = kT\mathbf{K}^{-1}$ generates the symmetric diffusion tensor $\mathbf{D}$ governing the $6 + n$ allowed degrees of freedom, of which the needed matrix ${}^{t}\mathbf{D}_D$ forms the upper left 3×3 block.

For the rigid body $n = 0$. Using partitioning theorems for matrix inversion[35]

$$ {}^{t}\mathbf{D}_D(\text{rigid}) = kT\,{}^{t}\mathbf{H}^{-1} $$

$$ {}^{t}\mathbf{D}_D(\text{flexible}) = kT({}^{t}\mathbf{H}^{-1} + \mathbf{E}) $$

where

$$ \mathbf{E} = {}^{t}\mathbf{H}^{-1}\cdot{}^{c}\mathbf{H}^{\dagger}\cdot\mathbf{Z}^{-1}\cdot{}^{c}\mathbf{H}\cdot{}^{t}\mathbf{H}^{-1} $$

$$ \mathbf{Z} = {}^{i}\mathbf{H} - {}^{c}\mathbf{H}\cdot{}^{t}\mathbf{H}^{-1}\cdot{}^{c}\mathbf{H}^{\dagger} $$

and

$$ {}^{t}\mathbf{H} = {}^{tt}\mathbf{K} - {}^{tr}\mathbf{K}\cdot{}^{rr}\mathbf{K}^{-1}\cdot{}^{rt}\mathbf{K} $$

$$ {}^{i}\mathbf{H} = {}^{ii}\mathbf{K} - {}^{ir}\mathbf{K}\cdot{}^{rr}\mathbf{K}^{-1}\cdot{}^{ri}\mathbf{K} $$

$$ {}^{c}\mathbf{H} = {}^{it}\mathbf{K} - {}^{ir}\mathbf{K}\cdot{}^{rr}\mathbf{K}^{-1}\cdot{}^{rt}\mathbf{K} $$

Since $\mathbf{K}$ is positive-definite, so are the symmetric matrices ${}^{t}\mathbf{H}$ and ${}^{i}\mathbf{H}$. By construction, symmetric matrix $\mathbf{E}$ is then positive semidefinite (nonnegative principal values). Thus, Tr $\mathbf{E} \geq 0$, from which we conclude that Tr ${}^{t}\mathbf{D}_D$(flexible) $\geq$ Tr ${}^{t}\mathbf{D}_D$(rigid) indeed holds for an arbitrary configuration. Q.E.D.

References and Notes

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(32) Since ${}^{r}D^{11}$ and ${}^{c}D_O{}^{13}$ blow up at $\alpha = 0°$, some care is needed to carry out their interpolations without introducing spurious spline wiggles. For $\alpha \leq 15°$, both coefficients are replaced by limiting forms proportional to $\sin^{-2}(\alpha/2)$ and $\sin^{-1}(\alpha/2)$, respectively, which match discrete values at $\alpha = 15°$. The spline fit is made to discreet α values $\geq 15°$, with first derivatives matching those of the limiting forms at 15°. Graphics routines were used to verify that the resulting functions, as well as all other needed diffusion coefficients, appear smooth over all α.
(33) Since ${}^{r}D^{11}$ and ${}^{c}D_O{}^{13}$ blow up at $\alpha = 0°$, the final value is actually obtained at a small positive angle $\epsilon < 1°$. For a particular choice of f and/or α_0, the calculated D_t obtained by trial and error has a clear minimum about a particular $y_{OD}(\epsilon)$, consistent with that expected for the center of mass or the rigid-body center of diffusion at ϵ. To the level of precision required for D_t in Table I, this procedure gives results indistinguishable from those obtained at $\epsilon = 0°$.
(34) These results use the same bead configuration considered as a rigid-body. The needed diffusion coefficients are obtained from the methods of ref 14 as follows. With the same displacement representation for rotations and translations, the matrices $\mathbf{A}_{ij}$, $\mathbf{C}_{ij}$, and $\mathbf{D}_{ij}$ are now projected onto the allowed 6 degrees of freedom to generate a hydrodynamic tensor $\mathbf{K}$. Inverting $\mathbf{K}$ gives a six-dimensional diffusion tensor $\mathbf{D} = kT\mathbf{K}^{-1}$ with nonzero components ${}^{t}D_P{}^{ii}$ and ${}^{r}D^{ii}$; for $i = 1, 2, 3$, ${}^{c}D_P{}^{13}$ and ${}^{c}D_P{}^{31}$ for some point P on axis 2. Except for ${}^{t}D_P{}^{22}$, these coefficients agree with those used in the flexible 7-dimensional case. As is easily shown, ${}^{t}D_P{}^{22}$(rigid) = ${}^{t}D_P{}^{22}$(flexible) $- ({}^{c}D_P{}^{\alpha 2})^2/D^{\alpha\alpha}$.
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