Inertial stochastic dynamics. I. Long-time-step methods for Langevin dynamics

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Two algorithms are presented for integrating the Langevin dynamics equation with long numerical time steps while treating the mass terms as finite. The development of these methods is motivated by the need for accurate methods for simulating slow processes in polymer systems such as two-site intermolecular distances in supercoiled DNA, which evolve over the time scale of milliseconds. Our new approaches refine the common Brownian dynamics (BD) scheme, which approximates the Langevin equation in the highly damped diffusive limit. Our LTID (''long-time-step inertial dynamics'') method is based on an eigenmode decomposition of the friction tensor. The less costly integrator IBD (''inertial Brownian dynamics'') modifies the usual BD algorithm by the addition of a mass-dependent correction term. To validate the methods, we evaluate the accuracy of LTID and IBD and compare their behavior to that of BD for the simple example of a harmonic oscillator. We find that the LTID method produces the expected correlation structure for Langevin dynamics regardless of the level of damping. In fact, LTID is the only consistent method among the three, with error vanishing as the time step approaches zero. In contrast, BD is accurate only for highly overdamped systems. For cases of moderate overdamping, and for the appropriate choice of time step, IBD is significantly more accurate than BD. IBD is also less computationally expensive than LTID (though both are the same order of complexity as BD), and thus can be applied to simulate systems of size and time scale ranges previously accessible to only the usual BD approach. Such simulations are discussed in our companion paper, for long DNA molecules modeled as wormlike chains. [S0021-9606(00)50717-X]

I. INTRODUCTION

Brownian dynamics (BD) algorithms which incorporate hydrodynamic interactions[1] have been widely used to simulate relatively slow processes (up to several milliseconds) of large polymers like circular DNA of several kilobase pairs represented by elastic models.[2–9] An inertial Langevin treatment which ignores hydrodynamic interactions has also been introduced.[10–12] To our knowledge, an inertial dynamics algorithm which includes a full hydrodynamic treatment has not been applied to a wormlike chain model of a polymer.

The BD algorithm, introduced by Ermak and McCammon,[1] is based on the Langevin description of particle dynamics. A key element in the development of this algorithm is the assumption that the numerical time step, Δt, is much greater than the momentum relaxation times, τ_i, which are given by the inverses of the eigenvalues of the matrix $\mathbf{M}^{-1}\mathbf{Z}$, where $\mathbf{M}$ is the diagonal matrix of particle masses, and $\mathbf{Z}$ is the frictional interaction tensor. The accuracy of the algorithm depends on another assumption, which is often not explicitly checked: that is, the systematic interparticle force remains constant over time scales *greater* than the numerical time step.

Therefore, for BD to be applied, a time step must exist that is simultaneously greater than the momentum relaxation times and less than the time scale of fluctuations in the systematic forces. The first constraint tends to be easily satisfied for the case of elastic polymer models: Momentum relaxation times are typically in the picosecond range, and numerical time steps are usually in the range of tens to hundreds of picoseconds.[4,6,13] In contrast, the extent to which the second constraint is satisfied for these models has not been extensively studied. The influence of ignoring the inertial terms on the dynamic behavior remains unclear.

Toward this goal, we have developed a long-time-step inertial dynamics (LTID) scheme for integrating the inertial Langevin dynamics equation. In spirit, this approach is similar to the work of van Gunsteren and Berendsen,[14] but differs in that we consider hydrodynamic coupling between the particles, an essential feature for polymer dynamics. This coupling is described by the friction matrix $\mathbf{Z}$.

LTID depends on an eigenmode decomposition of $\mathbf{Z}$. Based on this decomposition we propagate the eigenmodes with numerical time steps comparable to those commonly used in BD. Thus we can generate trajectories much longer than would be possible using a traditional integrator, such as the Verlet method.[15–17] The decomposition itself consumes the majority of the trajectory computational time since the friction tensor is configuration dependent, and the decomposition must be updated as the conformation evolves. The update requires more computation than the calculation of the interparticle forces because the eigen decomposition requires

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$O(N^3)$ floating point operations, where N is the number of particles in the system. However, the traditional BD algorithm resorts to a Cholesky factorization of the diffusion tensor, which also scales as $O(N^3)$ in computational cost. (See Note added in proof.) For the DNA systems presented in the companion paper,[18] we find that LTID is more expensive than BD (requiring one order of magnitude more CPU time than BD). The added cost stems mainly from the eigenmode decomposition, which consumes more CPU time than the Cholesky factorization used in BD. Additionally, LTID requires more matrix multiplications for the position and velocity update equations.

By examining the long-time-step limiting behavior of the LTID algorithm, we derive two Brownian algorithms which approximate the LTID method but are less computationally intensive. We denote both methods as ''Brownian'' because they involve explicitly tracking only the particle positions, and not the velocities. The first method is identical to the traditional BD algorithm. We call the other ''inertial Brownian dynamics'' (IBD) because it incorporates a mass-dependent correction term into the BD method. IBD arises from a singular perturbation expansion of the Langevin equation, and involves a relatively simple modification of the standard BD algorithm. Since it is similar to traditional BD in terms of time steps allowed and computational complexity, yet accurately approximates the inertial effects for the overdamped systems which we study, IBD promises to be a valuable tool for the long-time simulation of polymer systems. As we show in Ref. 18, IBD incurs a modest computational increase of a factor of 2 compared to BD when applied to our macroscopic model of DNA. Like BD, both LTID and IBD do not produce physical meaningful velocity distributions. Rather, the effective velocity applied over a time step produces a correct description of position evolution.

In Sec. II we present the basic inertial Langevin formulation for dynamic simulations, and develop the LTID algorithm for integrating the governing equations. We then obtain both our IBD algorithm and the standard BD algorithm by examining the long-time-step limiting behavior of LTID. In Sec. III we implement these methods for a simple harmonic oscillator where analytic results are available. We find that LTID produces the expected correlation structure for inertial Langevin motion while BD is reasonable only when the system is highly overdamped. For moderate levels of overdamping, IBD captures the inertial behavior that BD ignores. We show that among the three methods, LTID is the only consistent integrator, highlighting its utility as a reference to which IBD and BD may be compared. We also show that the IBD time step cannot be arbitrarily small. It has a lower bound limited by the inertial relaxation time and an upper bound limited by the time scale of systematic force fluctuations.

In our companion paper[18] we demonstrate the implementation of these methods to a macroscopic model for DNA. Our simulations of large systems (up to 1500 base pairs) reveal properties that are sensitive to mass, such as writhing number and radius of gyration autocorrelation functions and the rate of intermolecular site juxtaposition.

II. THEORY AND METHODS

A. Langevin description

1. Translation

Consider the Langevin equation:

$$\mathbf{M}\dot{v}(t)+\mathbf{Z}(r(t))v(t)=f_s(t)+f_r(t), \tag{1}$$

where $v\in\Re^{3N}$ is the collective velocity vector for the N particles in the system, and $\mathbf{M}\in\Re^{3N\times 3N}$ is the diagonal mass matrix. The positive definite friction tensor $\mathbf{Z}(r(t))\in\Re^{3N\times 3N}$ is a function of the configuration, $r(t)$, and describes the hydrodynamic coupling between the particles that is transmitted through the viscous solvent. The two forces on the right-hand side of Eq. (1) describe the systematic force, f_s, or negative gradient of the potential energy function, and the random force, f_r, modeling thermal interactions with the solvent. The random force is taken to be a zero-mean white noise process with spatial correlation prescribed by

$$\langle f_r(t)\cdot f_r^T(t')\rangle=2k_BT\mathbf{Z}(r(t))\,\delta(t-t'), \tag{2}$$

according to the fluctuation–dissipation theorem,[19,20] where k_B is the Boltzmann constant and T is the absolute temperature.

We rewrite Eq. (1) in a simple form:

$$\dot{v}+\mathbf{A}v=g, \tag{3}$$

where $\mathbf{A}=\mathbf{M}^{-1}\mathbf{Z}$ and $g=\mathbf{M}^{-1}(f_s+f_r)$. In general, the friction matrix is configuration dependent. To describe the algorithm, we consider one interval of time step Δt at step n of the method, where r^n and v^n represent the position and velocity at time $n\Delta t$. We expand $\mathbf{A}$ to first order in position at the current point as

$$\mathbf{A}(r^n+\Delta r)=\mathbf{A}(r^n)+\nabla\mathbf{A}(r^n)\cdot\Delta r, \tag{4}$$

and Δr to first order ($\Delta r=v^n\Delta t$), and then substitute the latter into Eq. (3):

$$\dot{v}+[\mathbf{A}(r^n)+(\nabla\mathbf{A}(r^n)\cdot v^n)(t-\Delta t)]v=g. \tag{5}$$

The friction tensor can be defined in terms of the diffusion tensor $\mathbf{D}(r(t))$:[21]

$$\mathbf{Z}=k_BT\mathbf{D}^{-1}. \tag{6}$$

For bead models a favorable choice for $\mathbf{D}(r(t))$ is the Rotne–Prager tensor,[22] which represents a second-order approximation (in inverse powers of distance) for two beads diffusing in an incompressible fluid. This diffusion tensor remains positive definite for all molecular configurations and has a zero gradient. Since the gradient of the friction tensor is $\nabla\mathbf{Z}=k_BT\mathbf{D}^{-1}(\nabla\mathbf{D})\mathbf{D}^{-1}$, together with $\nabla\mathbf{D}(r(t))=0$, we have $\nabla\mathbf{A}(r^n)=0$ in Eq. (5). We now use the diagonal factorization of $\mathbf{A}(r^n)$: $\mathbf{A}(r^n)=\mathbf{L}\Lambda\mathbf{L}^T$ where Λ is diagonal and $\mathbf{L}$ contains the corresponding eigenvectors. Substituting this factorization into Eq. (5) produces

$$\mathbf{L}^T\dot{v}+\Lambda\mathbf{L}^Tv=\mathbf{L}^Tg. \tag{7}$$

Defining the vector $w=\mathbf{L}^Tv$, we have the governing equation for the uncoupled eigenmodes of the system:

$$\dot{w}+\Lambda w=\mathbf{L}^Tg, \tag{8}$$

or

$$e^{-\Lambda t}\frac{d}{dt}\{e^{+\Lambda t}w\}=\mathbf{L}^T g, \tag{9}$$

which can be integrated:

$$w^{n+1}=e^{-\Lambda\Delta t}w^n+e^{-\Lambda(n+1)\Delta t}\int_{n\Delta t}^{(n+1)\Delta t}e^{+\Lambda s}\mathbf{L}^T g(s)ds. \tag{10}$$

Making the approximation of a constant acceleration, g^n, acting over the Δt interval, we obtain the following equation for v:

$$v^{n+1}=\mathbf{L}e^{-\Lambda\Delta t}\mathbf{L}^T v^n+\mathbf{L}\Lambda^{-1}(\mathbf{I}-e^{-\Lambda\Delta t})\mathbf{L}^T g^n, \tag{11}$$

where $\mathbf{I}$ is the identity matrix. Integrating the velocity equation, we obtain the associated position at time step $n+1$:

$$r^{n+1}=r^n+\mathbf{L}[\Lambda^{-1}(\mathbf{I}-e^{-\Lambda\Delta t})]\mathbf{L}^T v^n+\mathbf{L}\Lambda^{-1}[\mathbf{I}\Delta t-\Lambda^{-1}(\mathbf{I}-e^{-\Lambda\Delta t})]\mathbf{L}^T g^n. \tag{12}$$

Approximating the systematic force as constant over a fixed interval is reasonable so long as the time step is small compared to the rate of change of the force. The piecewise-constant approximation of the random force, on the other hand, is never strictly valid since a white noise process has no natural time scale. However, we proceed using a discrete random force, f_r^n, which is the *average* of the white noise force acting over the interval:

$$f_r^n=\frac{1}{\Delta t}\int_{n\Delta t}^{(n+1)\Delta t}f_r(s)ds. \tag{13}$$

With $f_r(t)$ distributed according to Eq. (2), it is straightforward to show that f_r^n obeys

$$\langle(f_r^n)(f_r^m)^T\rangle=2k_BT\mathbf{Z}\delta_{nm}/\Delta t, \tag{14}$$

where δ_{nm} is the usual Kronecker delta. Since the random force is taken as the average over a discrete time step, the velocity calculated from Eq. (11) is regarded as the effective velocity acting over the interval, and is not equivalent to the instantaneous particle velocity. Thus for long time steps, v^n does not have the same thermodynamic properties as the continuous velocity $v(t)$ in Eq. (1). Nevertheless, as we shall show, position trajectories computed using Eqs. (11) and (12) accurately reproduce statistical properties expected for the inertial Langevin equation even for time steps larger than the entries of Λ^{-1}.

2. Rotation

For simplicity, we present the Langevin formulation of rotational dynamics for the case where no direct frictional coupling exits between particle rotations or between rotations and translations. The dynamics of each rotational degree of freedom is given by

$$m_i\dot{\Omega}_i+\xi_i\Omega_i=\tau_{s,i}+\tau_{r,i}, \tag{15}$$

where m_i is the rotational moment of inertial, ξ_i is the rotational friction constant, Ω_i is the angular velocity, $\tau_{s,i}$ is the systematic torque, and $\tau_{r,i}$ is a random torque with zero mean and variance described by

$$\langle\tau_{r,i}(t)\tau_{r,j}(t')\rangle=2k_BT\xi_i\delta_{ij}\delta(t-t'). \tag{16}$$

With no coupling between the various modes and a constant torque acting over the nth time step, the solution to Eq. (15) is immediate:

$$\Omega_i^{n+1}=\Omega_i^n e^{-(\xi_i/m_i)\Delta t}+\frac{1}{\xi_i}[1-e^{-(\xi_i/m_i)\Delta t}](\tau_{s,i}^n+\tau_{r,i}^n). \tag{17}$$

B. Three algorithms

1. Long-time step inertial dynamics (LTID)

The basic LTID algorithm for translation follows directly from Eqs. (11) and (12):

$$v^{n+1}=\mathbf{L}e^{-\Lambda\Delta t}\mathbf{L}^T v^n+\mathbf{L}\Lambda^{-1}(\mathbf{I}-e^{-\Lambda\Delta t})\times\mathbf{L}^T\mathbf{M}^{-1}(f_s^n+f_r^n), \tag{18}$$

and

$$r^{n+1}=r^n+\mathbf{L}[\Lambda^{-1}(\mathbf{I}-e^{-\Lambda\Delta t})]\mathbf{L}^T v^n+\mathbf{L}\Lambda^{-1}[\mathbf{I}\Delta t-\Lambda^{-1}(\mathbf{I}-e^{-\Lambda\Delta t})]\mathbf{L}^T\mathbf{M}^{-1}(f_s^n+f_r^n), \tag{19}$$

where f_s^n is the systemic force and f_r^n is chosen from $\langle(f_r^n)(f_r^m)^T\rangle=2k_BT\mathbf{Z}\delta_{nm}/\Delta t$.

The angular velocity update equation is given by Eq. (17), and the rotational update equation is obtained from integrating the rotational velocity equation over the finite time step:

$$\Delta\Theta_i^n=\frac{m_i}{\xi_i}[1-e^{-(\xi_i/m_i)\Delta t}]\Omega_i^n+\frac{1}{\xi_i}\left[\Delta t-\frac{m_i}{\xi_i}(1-e^{-(\xi_i/m_i)\Delta t})\right](\tau_{s,i}^n+\tau_{r,i}^n). \tag{20}$$

Here $\Delta\Theta_i^n$ represents the finite angular rotation about the ith rotational degree of freedom over the nth time step. The random torque is chosen based on $\langle(\tau_r^n)^2\rangle=2k_BT\xi_i/\Delta t$.

2. Inertial Brownian dynamics (IBD)

In the limit $e^{-\lambda_i\Delta t}\to 0$ for all the λ_i entries of Λ, Eqs. (11) and (12) can be reduced to

$$r^{n+1}=r^n+\mathbf{L}\Lambda^{-1}\mathbf{L}^T\Delta t\, g^n+\mathbf{L}\Lambda^{-2}\mathbf{L}^T(g^{n-1}-g^n), \tag{21}$$

or

$$r^{n+1}=r^n+\frac{\mathbf{D}}{k_BT}\left[f^n\Delta t+\frac{\mathbf{MD}}{k_BT}(f^{n-1}-f^n)\right], \tag{22}$$

where the diffusion matrix, $\mathbf{D}$, is equal to $k_BT\mathbf{Z}^{-1}$.[21] As for LTID, $f^n=f_s^n+f_r^n$ where f_s^n is the systematic force and f_r^n is chosen from $\langle(f_r^n)(f_r^m)^T\rangle=2k_BT\mathbf{Z}\delta_{nm}/\Delta t$.

Equation (22) augments the Ermak and McCammon update formula[1] with an inertial correction term. Equation (22) is also a discretization of the differential equation, Eq. (A3), which arises from a perturbative expansion of the Langevin equation (see Appendix A). For the case of a single-variable (scalar) Langevin equation, IBD can be compared to the algorithm of van Gunsteren and Berendsen.[14] In Appendix B,

we show that for a special choice of Δt, the IBD and the van Gunsteren and Berendsen algorithms have a similar form.

The rotational update of Eq. (20) in the limit $e^{-(\xi_i/m_i)\Delta t}\to 0$ reduces to

$$\Delta\Theta_i^n=\frac{1}{\xi_i}\left[\Delta t(\tau_{s,i}^n+\tau_{r,i}^n)+\frac{m_i}{\xi_i}(\tau_{s,i}^{n-1}+\tau_{r,i}^{n-1}-\tau_{s,i}^n-\tau_{r,i}^n)\right], \tag{23}$$

where the random torque is chosen as for LTID.

3. Brownian dynamics (BD)

The third method we consider is the standard BD scheme, which comes from a stronger restriction on the time step, Δt. In the limit $\max_i\{\lambda_i^{-1}\}/\Delta t\to 0$, Eqs. (11) and (12) reduce to the standard Ermak and McCammon method:

$$r^{n+1}=r^n+\frac{\mathbf{D}}{k_BT}f^n\Delta t. \tag{24}$$

Note that the usual BD formulation

$$r^{n+1}=r^n+\frac{\mathbf{D}}{k_BT}f_s^n\Delta t+R^n, \tag{25}$$

with the random displacement covariance structure $\langle R^n(R^m)^T\rangle=2\Delta t\,\delta_{nm}\mathbf{D}$, is equivalent to Eq. (24) since $\langle f_r^n(f_r^m)^T\rangle=2k_BT\mathbf{Z}\delta_{nm}/\Delta t$ and $\mathbf{Z}=k_BT\mathbf{D}^{-1}$. Equivalently, we can arrive at Eq. (24) by setting the entries in the mass matrix in Eq. (22) to zero.

For this case, the rotational update equation reduces to

$$\Delta\Theta_i^n=\frac{\Delta t}{\xi_i}(\tau_{r,i}^n+\tau_{s,i}^n). \tag{26}$$

C. One-dimensional oscillator

To compare the behavior of our long-time-step methods to that of the traditional BD algorithm, we study the example of a one-dimensional oscillator.

1. Langevin dynamics

Consider the Langevin description of the one-dimensional oscillator:

$$\begin{aligned}&m\ddot{x}+\zeta\dot{x}+ax=f_r,\\&\langle f_r(t)f_r(t+\tau)\rangle=2k_BT\zeta\delta(t-\tau),\end{aligned} \tag{27}$$

where m is the mass, ζ is the friction coefficient, and a is the strength of the harmonic potential. The friction coefficient is related to the usual Langevin damping constant, $\gamma=\zeta/m$, where γ has units of inverse time. Here, $f_r(t)$ is a white noise process with variance given above. Introducing the nondimensional distance r and time s given by

$$r=(a/k_BT)^{1/2}x,\quad s=(a/\zeta)t, \tag{28}$$

Eq. (27) reduces to

$$\begin{aligned}&k\ddot{r}+\dot{r}+r=w,\\&\langle w(s)w(s+\sigma)\rangle=2\delta(s-\sigma),\end{aligned} \tag{29}$$

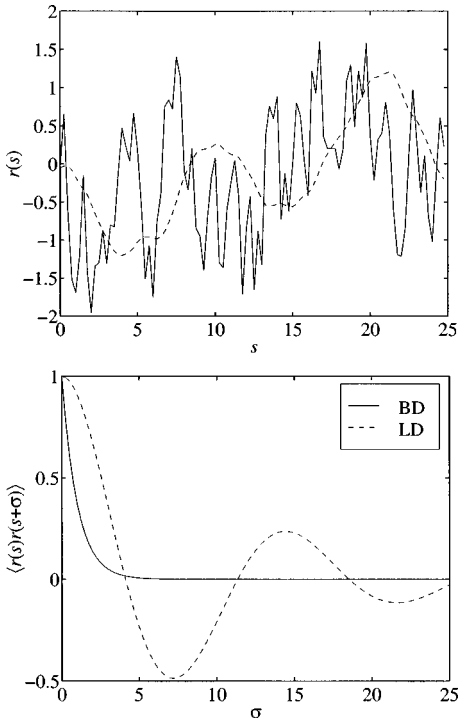

FIG. 1. Comparison of position trajectories and autocorrelation functions for Brownian and Langevin motions for a one-dimensional harmonic oscillator. For the Brownian process (solid lines) $k=0$, and for the Langevin process (dashed lines) $k=5$. The lower panel plots $\langle r(s)r(s+\sigma)\rangle_{\mathrm{LD}}$ and $\langle r(s)r(s+\sigma)\rangle_{\mathrm{BD}}$, the position autocorrelation functions for LD and BD trajectories, respectively.

where σ is an arbitrary time variable. The nondimensional mass parameter k is related to the dimensional parameters by $k=ma/\zeta^2$. Particles governed by Eq. (29) have equilibrium position and velocity distributions described by $\langle r^2\rangle=1$ and $\langle\dot{r}^2\rangle=1$.

2. Brownian dynamics

The Brownian description of the same system:

$$\dot{r}+r=w \tag{30}$$

produces the same position distribution, $\langle r^2\rangle=1$, but the velocity is distributed according to

$$\begin{aligned}\langle\dot{r}(s)\dot{r}(s+\sigma)\rangle&=\langle r(s)r(s+\sigma)\rangle+\langle w(s)w(s+\sigma)\rangle\\&=\langle r(s)r(s+\sigma)\rangle+2\delta(s-\sigma),\end{aligned} \tag{31}$$

where $\langle r(s)r(s+\sigma)\rangle$ denotes the position autocorrelation function. Thus the velocities generated from a Brownian simulation are not physically meaningful. Yet a trajectory of positions generated based on BD will be statistically indistinguishable from one generated by LD in the highly damped limit, $k=ma/\zeta^2\to 0$.

For finite k, the difference between the Langevin and Brownian trajectories can be striking. In Fig. 1 a Brownian trajectory ($k=0$) is compared to a Langevin trajectory with $k=5$. Both the Langevin and Brownian data sample the same canonical position distribution. Yet $r(s)$ fluctuates much more rapidly for the Brownian case.

3. Autocorrelation functions

A statistical measure of the difference between the Brownian and Langevin motions is the position autocorrelation function, $\langle r(s)r(s+\sigma)\rangle$. It can be shown that $\langle r(s)r(s+\sigma)\rangle$ for the Langevin system is given by the impulse response function of Eq. (29):

$$\langle r(s)r(s+\sigma)\rangle_{\mathrm{LD}}=\frac{l_2e^{l_1\sigma}-l_1e^{l_2\sigma}}{l_2-l_1}, \tag{32}$$

where

$$l_{1,2}=-\frac{1}{2k}(1\pm\sqrt{1-4k}). \tag{33}$$

Similarly the position autocorrelation for BD is the impulse response of a first-order system:

$$\langle r(s)r(s+\sigma)\rangle_{\mathrm{BD}}=e^{-\sigma}. \tag{34}$$

It is straightforward to verify that $\langle r(s)r(s+\sigma)\rangle_{\mathrm{LD}}$ reduces to $\langle r(s)r(s+\sigma)\rangle_{\mathrm{BD}}$ for $k\ll 1$.

Plotted in the lower panel of Fig. 1 is $\langle r(s)r(s+\sigma)\rangle$ for the Brownian and for the Langevin motion. For this choice of k, the Langevin system is underdamped and the response function, a decaying sinusoid, differs markedly from the Brownian autocorrelation. In what follows we compare the correlation structure predicted by LTID, IBD, and BD to the analytic forms of the above-given autocorrelation functions.

III. NUMERICAL SIMULATIONS

A. Algorithms for a one-dimensional oscillator

For this nondimensional scalar example, the LTID algorithm can be implemented as follows. An initial estimate of the position update is made for the nth time step:

$$\begin{aligned} r^{n+1,*}&=r^n+k(1-e^{-\Delta s/k})v^n\\ &\quad+[\Delta s-k(1-e^{-\Delta s/k})](f_s^n+w^n), \end{aligned} \tag{35}$$

where $f_s^n=-r^n$ is the systematic force at the nth time and the random force is chosen from $\langle (w^n)^2\rangle=2/\Delta s$. Using the position $r^{n+1,*}$ we calculate the force $f_s^{n,*}=-(r^n+r^{n+1,*})/2$ to use in the final update:

$$\begin{aligned} v^{n+1}&=e^{-\Delta s/k}v^n+(1-e^{-\Delta s/k})(f_s^{n,*}+w^n),\\ r^{n+1}&=r^n+k(1-e^{-\Delta s/k})v^n\\ &\quad+[\Delta s-k(1-e^{-\Delta s/k})](f_s^{n,*}+w^n). \end{aligned} \tag{36}$$

The above-mentioned method is second-order in its treatment of the systematic force. (It is straightforward to verify its second-order accuracy for the harmonic oscillator equation in the absence of thermal forces.)

For the IBD algorithm we use the same first- and second-order estimates of the systematic force acting over the nth step: $f_s^n=-r^n$ and $f_s^{n,*}=-(r^n+r^{n+1,*})/2$. The initial position update is given by

$$\begin{aligned} r^{n+1,*}&=r^n+f_s^n\Delta s+k(f_s^{n-1,*}-f_s^n)\\ &\quad+d_r^n+k(d_r^{n-1}-d_r^n)/\Delta s, \end{aligned} \tag{37}$$

where $\langle (d_r^n)^2\rangle=2\Delta s$. The final update is given by

$$\begin{aligned} r^{n+1}&=r^n+f_s^{n,*}\Delta s+k(f_s^{n-1,*}-f_s^{n,*})\\ &\quad+d_r^n+k(d_r^{n-1}-d_r^n)/\Delta s. \end{aligned} \tag{38}$$

The BD algorithm is given by

$$r^{n+1,*}=r^n+f_s^n\Delta s+d_r^n \tag{39}$$

and

$$r^{n+1}=r^n+f_s^{n,*}\Delta s+d_r^n, \tag{40}$$

where d_r^n is chosen from the same distribution as for IBD.

B. Choice of time step

Since we wish to compare the behavior of our long-time-step methods to that of BD, we choose the time steps for our simulations to be optimal for the BD algorithm, balancing efficiency with accuracy. Substitution of Eq. (40) into Eq. (39) yields

$$r^{n+1}=r^n-\tfrac{1}{2}[r^n+r^n(1-\Delta s)+d_r^n]\Delta s+d_r^n. \tag{41}$$

For the mean square position we obtain

$$\langle (r^n)^2\rangle=\frac{1-\Delta s+\frac{1}{4}(\Delta s)^2}{1-\Delta s+\frac{1}{2}(\Delta s)^2-\frac{1}{8}(\Delta s)^3}. \tag{42}$$

We note that for accurate reproduction of the canonical position distribution, the size of the time step Δs is not related to the characteristic times of the Langevin system, given by $1/|l_i|$. The choice of time step $\Delta s=1/4$ results in $\langle (r^n)^2\rangle=0.9825$, allowing us to obtain accurate solutions with the largest possible time step.

The appeal of the BD algorithm is that it allows time steps much greater than the smallest characteristic time of the Langevin equation. Standard discretizations of the inertial Langevin equations (such as the Verlet methods[15–17] or Runge–Kutta methods) requires time steps around $1/|4l_1|$. For $k=0.01$, the smallest eigenvalue of the Langevin equation is $l_1\approx 100$. Thus a reasonable time step for BD is 100 times greater than a reasonable time step for Verlet.

For the less extreme cases, e.g., $k=0.1$, the required Verlet time step of around $1/|4l_1|\approx 0.03$ is still much smaller than the BD time step of 1/4. For this value of k, however, the behavior of the Langevin system, as measured by the position autocorrelation, is noticeably different from that of the BD system. We shall show that our new algorithms allow us to reproduce the behavior of the inertial Langevin system while using time steps equal to or greater than those used for BD.

C. The highly overdamped case, $k=0.01$

In the limit of small k, we expect the Brownian and Langevin formulations to be indistinguishable. The Langevin equation is highly damped and the Brownian approximation is sufficient to describe motions governed by the inertial Langevin equation.

Plotted in the upper panel of Fig. 2 are the results from BD, IBD, and LTID simulations at $k=0.01$. Results are based on trajectories of 10^6 steps using $\Delta s=1/4$. On the left

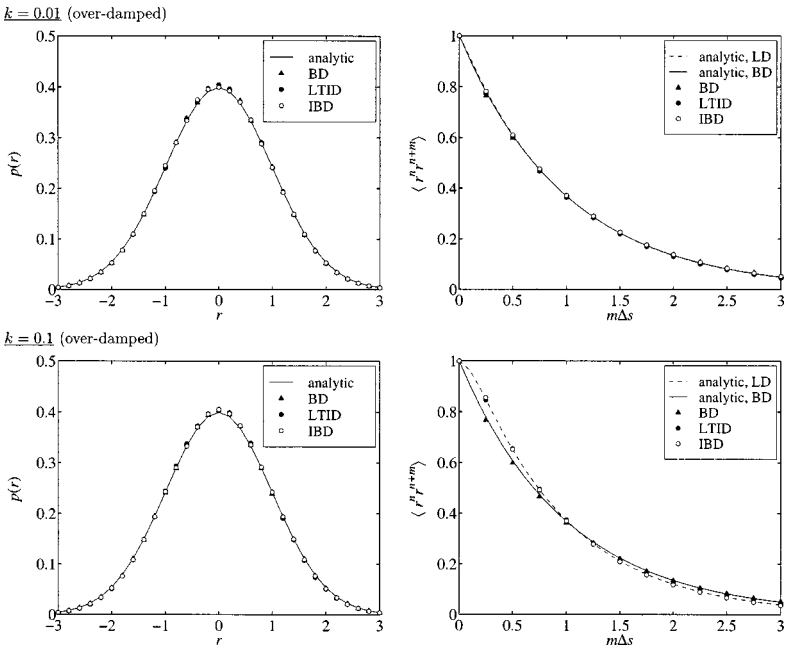

FIG. 2. Comparison of predicted position distributions and autocorrelation functions for LTID, IBD, and BD for overdamped oscillators: $k=0.01$ (top), and $k=0.1$ (bottom). Predicted probability distributions of position (left) are compared to the analytic result, $e^{-r^2/2}/\sqrt{2\pi}$, shown as solid line. The calculated autocorrelation functions for the position trajectories (right) are compared to the theoretical LD and BD correlation functions [Eqs. (32) and (34)], plotted as dashed and solid lines, respectively. Results are based on trajectories of length 10^6 time steps $\Delta s=0.25$.

is the probability distribution of position, $p(r)$, calculated by each algorithm. The canonical distribution function $e^{-r^2/2}/\sqrt{2\pi}$ is shown as the solid line.

In the right-hand panel the autocorrelation function $\langle r^n r^{n+m}\rangle$ for the trajectories calculated from each algorithm is plotted. The continuous autocorrelations $\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{LD}}$ and $\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{BD}}$ [Eqs. (32) and (34)] are shown as the dashed and solid lines, respectively. The autocorrelation for BD and LD are nearly identical and each algorithm closely reproduces the analytical forms of $p(r)$ and $\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{LD}}$ nearly exactly. For these results the effective mass is negligible and the extra work involved in LTID and IBD compared to BD is unnecessary.

D. The moderately overdamped case, $k=0.1$

Analogous results for the case of $k=0.1$ are presented in the lower panel of Fig. 2. Once again, these results are based on trajectories of 10^6 steps with $\Delta s=1/4$. For this case the system is still overdamped, yet the BD response function differs from that of LD. The computed $\langle r^n r^{n+m}\rangle$ from IBD and LTID closely follows $\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{LD}}$ (dashed line) while the computed $\langle r^n r^{n+m}\rangle$ from BD follows $\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{BD}}$. Here, although the system is over damped, the effects of mass are not negligible and BD does not produce the inertial correlation structure.

It is interesting to note that for $k=0.1$ and the time step of $\Delta s=1/4$ used here, $e^{-\Delta s/k}=e^{-2.5}\approx 0.082$. Hence, the restriction for IBD, namely $e^{-\Delta s/k}\approx 0$, is not necessarily excessively strict. Clearly for this case the value $e^{-\Delta s/k}\approx 0.082$ is small enough for IBD to produce accurate results. (A systematic study of how the accuracy of BD depends upon time step is presented in Sec. III G.)

E. Critically damped case, $k=0.25$

For $k=0.25$, we find that IBD behaves poorly with $\Delta s=1/4$ (see the following). For this choice of Δs the parameter $e^{-\Delta s/k}$ is approximately 0.37. To decrease $e^{-\Delta s/k}$, we choose a larger time step. For these results, a time step of 1/2 is used for the IBD algorithm, resulting in $e^{-\Delta s/k}=e^{-2}$. For BD and LTID we use $\Delta s=1/4$ as before.

At $k=0.25$ the Langevin system is critically damped. Results for this system are presented in the upper panel of Fig. 3. The critically damped Langevin autocorrelation function differs considerably from that of BD. Again, LTID and IBD follow $\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{LD}}$. Since IBD uses a large time step, the autocorrelation function is sampled at a lower resolution for IBD than for BD and LTID.

F. Underdamped case, $k=0.5$

In the bottom panel of Fig. 3 are presented results for the slightly underdamped case, $k=0.5$. Here we use $\Delta s=1/4$ for BD and LTID as for the earlier cases and set $\Delta s=1$ for IBD. Again, $\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{LD}}$ is reproduced by LTID and IBD. Note that IBD predicts a narrow position distribution compared to the analytic result, $e^{-r^2/2}/\sqrt{2\pi}$.

G. Error analysis

The position variance predicted by each algorithm is reported in Table I for $k=0.01$, 0.1, 0.25, and 0.5. The computed $\langle r^2\rangle$ is close to 1 for all cases except IBD at $k=0.5$.

The time steps used for IBD, $(\Delta s)_{\mathrm{IBD}}$, are reported in the Table I, as well as $1/|4l_1|$, a reasonable time step for Verlet or Runge–Kutta methods. For the overdamped cases ($k=0.01$, $k=0.1$), the values of $1/|4l_1|$ are much smaller than 1/4, the time step used by BD, IBD, and LTID. For $k=0.25$ and $k=0.5$ the values of $1/|4l_1|$ are closer to 1/4, yet we use values of $(\Delta s)_{\mathrm{IBD}}$ greater than 1/4 for these cases.

As mentioned, application of the IBD method requires using a time step that is larger than k. To explore the effects of Δs on the behavior of IBD, we return to the critically damped case, $k=0.25$. The behavior will be similar for smaller values of k. But the criterion that $e^{-\Delta s/k}$ is small is

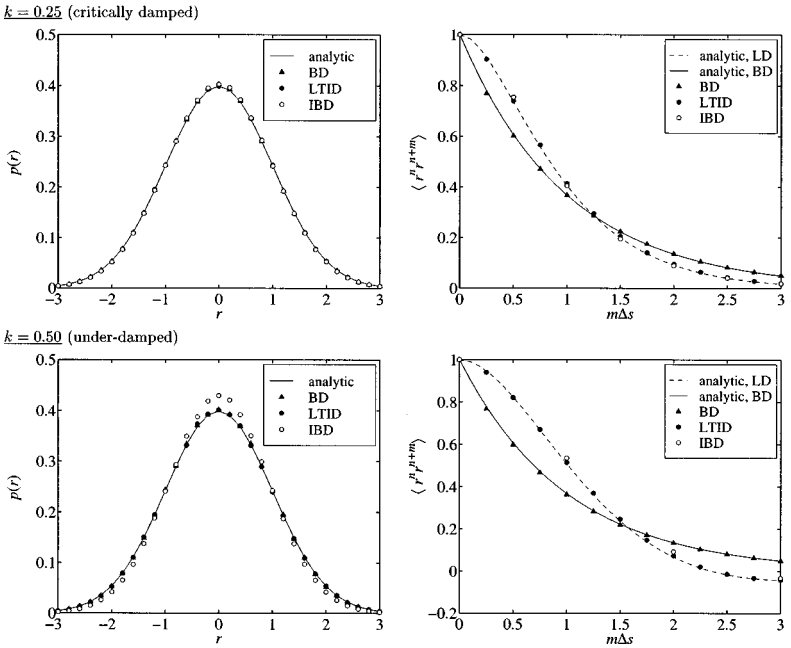

FIG. 3. Comparison of position distributions and autocorrelation functions for critically damped and underdamped oscillators. See the caption to Fig. 2. Results for critical damping ($k=0.25$) and underdamping ($k=0.5$) are shown in the upper and lower panels, respectively. Results are based on trajectories of length 10^6 using time steps $\Delta s=0.25$ for LTID and BD. For IBD, $\Delta s=0.5$ for $k=0.25$ and $\Delta s=1.0$ for $k=0.5$.

more easily satisfied for small k and the restrictions on Δs are not as severe. For larger values, the system is underdamped and IBD does not behave well.

Plotted in the upper panel of Fig. 4 are the position distributions predicted by IBD for several choices of Δs. Choosing Δs much smaller than 1/2 results in relatively broad distributions, while larger Δs results in relatively narrow distributions. In the lower panel is plotted the difference between the computed autocorrelations $\langle r^n r^{n+m}\rangle$ and the analytic result $\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{LD}}$. This difference is greatest at $m=0$. Only for $\Delta s=1/2$ does $\langle r^n r^{n+m}\rangle$ approximate the correct correlation structure.

In the upper panel of Fig. 5 we compare the realized variance $\langle r^2\rangle$ from each algorithm as a function of time step. We see that $\langle r^2\rangle$ asymptotically approaches 1 as Δs decreases for BD and LTID, while the variance explodes at small time steps for IBD. For the proper choice of Δs (around 0.5) $\langle r^2\rangle\approx 1$.

We define a mean-square measure of error in the autocorrelation function as

$$E(\Delta s)=\sum_{m=0}^{\infty}\left[\langle r^n r^{n+m}\rangle-\langle r(s)r(s+m\Delta s)\rangle_{\mathrm{LD}}\right]^2\Delta s. \tag{43}$$

TABLE I. The mean square displacement $\langle r^2\rangle$ predicted by LTID, IBD, and BD for various choices of k. Data are based on trajectories of 10^6 steps with time steps of $\Delta s=1/4$ (BD and IBD) and k-dependent time steps for IBD (penultimate column). Also reported is $1/|4l_1|$, the approximate time step required by Verlet or Runge–Kutta methods, which is up to two orders of magnitude smaller than Δs used in our algorithms.

k	$\langle r^2\rangle$ (BD)	$\langle r^2\rangle$ (LTID)	$\langle r^2\rangle$ (IBD)	$(\Delta s)_{\mathrm{IBD}}$	$1/\lvert 4l_1\rvert$
0.01	0.9836	0.9733	0.9779	0.25	0.0025
0.10	0.9843	0.9698	0.9723	0.25	0.0282
0.25	0.9831	0.9778	0.9653	0.5	0.1250
0.50	0.9850	0.9903	0.8582	1.0	0.1768

This error is plotted versus Δs in the lower panel of Fig. 5 for $k=0.25$. For BD, $\langle r^n r^{n+m}\rangle$ never approaches the expected curve for Langevin dynamics, even in the limit of small time step. For small Δs, the error associated with BD approaches

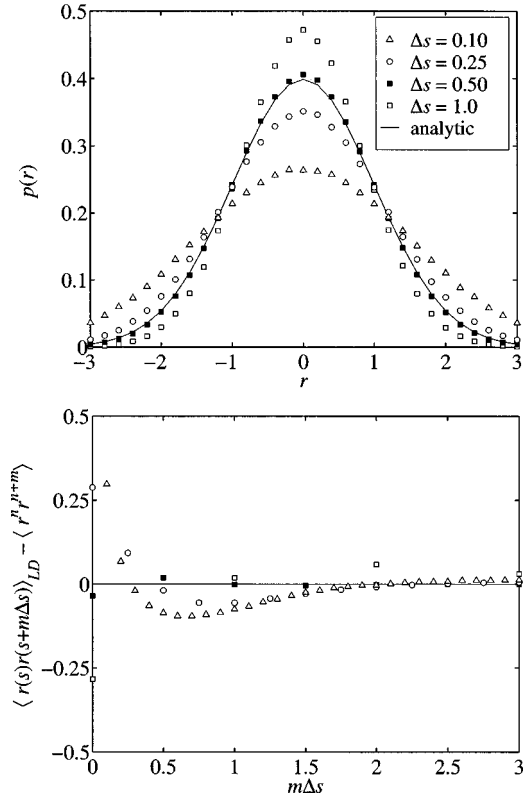

FIG. 4. Calculated IBD position distributions at critical damping ($k=0.25$) at various time steps (0.10, 0.25, 0.50, and 1.0), upper panel, and the difference between the computed correlation, $\langle r^n r^{n+m}\rangle$, and the exact result for the continuous Langevin equation, $\langle r(s)r(s+m\Delta s)\rangle$, Eq. (32), lower panel. The solid line in the upper panel indicates the Boltzmann distribution, $e^{-r^2/2}/\sqrt{2\pi}$. Results are based on trajectories of 10^6 time steps.

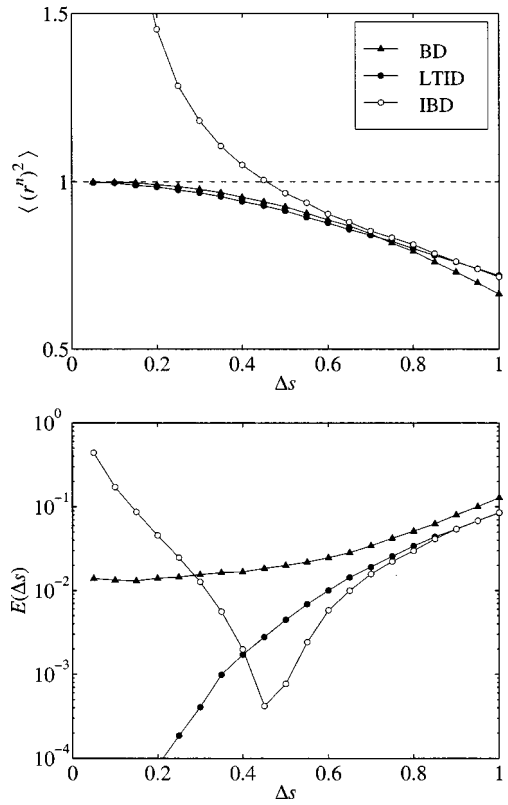

FIG. 5. Computed variance of position, $\langle (r^n)^2 \rangle$, and error, $E(\Delta s)$, in the correlation function, for each algorithm as a function of Δs. The function $E(\Delta s)$, Eq. (43), in the lower panel, is the mean-square difference between the computed position autocorrelation and the exact result for the continuous Langevin equation. Results are based on trajectories of length 10^6 time steps.

$$\lim_{\Delta s \to 0} E(\Delta s) = \int_0^\infty [\langle r(s) r(s+m\Delta s) \rangle_{\mathrm{BD}} - \langle r(s) r(s+m\Delta s) \rangle_{\mathrm{LD}}]^2 d\sigma = \tfrac{1}{72}. \quad (44)$$

The IBD error blows up both for large and for small Δs. However, near an optimal choice of Δs, the IBD error is smaller than the LTID error and more than one order of magnitude smaller than the BD error. The error for LTID, in the limit of small Δs, becomes arbitrarily small. Therefore, with respect to the inertial correlation structure, only LTID is a consistent method in that the error goes to zero with the time step.

Neither BD nor IBD is a consistent discretization of the Langevin equation. In Appendix A we present the continuous differential equation [Eq. (A3)] of which IBD is a consistent discretization.

IV. DISCUSSION AND RECOMMENDATIONS

Over the past two decades, the Brownian dynamics algorithm[1] and variations thereof have represented some of the most powerful and efficient methods available for computing long-time trajectories of large polymer systems governed by Eq. (1). By reevaluating the approximations made in the development of the standard BD algorithm and returning to the inertial description of particle dynamics, we have developed algorithms for integrating Eq. (1) which do not neglect the influence of particle mass on the system dynamics.

We have shown that, for a simple harmonic oscillator, the difference between the Langevin and Brownian descriptions increases as the effective damping decreases. The measure of effective damping, $1/k = \zeta^2/ma$ can be regarded as a ratio of two time scales:

$$\frac{1}{k} = \frac{(\zeta/a)}{(m/\zeta)}, \quad (45)$$

where m/ζ is the characteristic time for inertial relaxation in the absence of other forces, and ζ/a is the characteristic time for relaxation in the absence of inertia. Thus the effective level of damping for polymer systems depends not only on the inertial relaxation times, but also on the potential energy function. A polymer surrounded by a highly viscous (Stokes) fluid will require treatment by an inertial algorithm when the potential energy function is such that the systematic force fluctuates on a time scale similar to the inertial relaxation times.

Since the LTID method consistently reproduces the inertial correlation structure, it can be used to probe the inertial behavior of polymer systems governed by Eq. (1). Unfortunately, LTID is more computationally expensive than BD. (The computational costs associated with BD, IBD, and LTID are presented for large DNA systems in the companion paper.[18]) The IBD method, on the other hand, is much cheaper than LTID.

Yet neither IBD nor BD is a consistent integrator for Langevin dynamics (i.e., with errors $\to 0$ as $\Delta t \to 0$). While for the overdamped simple harmonic oscillator we were able to find time steps for which the error associated with IBD was small, rendering IBD attractive for this simple system, determination of the appropriate IBD time step for a large nonlinear system is not guaranteed.

Specifically, we recommend using LTID, BD, and IBD in concert for systems where the importance of inertial effects is not known *a priori*. LTID can serve to generate a reference for the statistical properties of Langevin trajectories. Any deviation from the reference, predicted by a BD algorithm, suggests that IBD may be considered. In that case, an appropriate time step should be sought for which the configuration distribution is properly sampled and the inertial correlation structure is reproduced.

In our companion paper[18] we follow these recommendations in studying a bead model of supercoiled DNA. We find that, indeed, BD fails to predict the inertial behavior of equilibrium thermal fluctuations. In addition, we find an appropriate time step (100 ps) for IBD for this system. For reference, typical BD time steps used for similar DNA models range from 4 to 600 ps.[4,6,9] For our DNA systems, the increased computational cost of IBD over BD is a modest factor of 2 (for the same time step). By exploiting the computational efficiency of IBD, we compute inertial Langevin trajectories of several milliseconds in length, time scales appropriate for investigation of the slow process of intermolecular site juxtaposition.[18]

Note added in proof. Since completing this work, we have examined intriguing suggestions by Fixman [Macromolecules **19**, 1204 (1986)] on using a vector polynomial expansion rather than a Cholesky factorization procedure for defining the Langevin random forces characterized by a covariance matrix which is the configuration-dependent hydrodynamics tensor. We find that approximation of the correlated random force vector based on an expansion in terms of Chebyshev polynomials can produce a dramatic reduction in complexity from $O(N^3)$ where N is the system size to near $O(N^2)$ dependence for very large N. One drawback of the Chebyshev expansion is that the factors are not available for reuse if desired (e.g., to allow updating the hydrodynamics tensor less frequently than every time step). Still, the advantages/disadvantages of the matrix factorization versus vector polynomial expansion should be weighed appropriately for the application at hand. We describe this algorithmic advance in a forthcoming article, T. Schlick *et al.*, special issue of Computing in Science and Engineering devoted to computational chemistry (2000).

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APPENDIX A: ALTERNATIVE DERIVATION OF IBD

Consider the following differential equation:

$$\frac{m}{\zeta}\dot{v}+v=\frac{f}{\zeta}, \tag{A1}$$

which is the scalar case of the Langevin equation, except that here we consider $f(t)$ to be some continuous process. We consider a long-time (outer) expansion for the velocity, $v=v_0+v_1+O([m/\zeta]^2)$, where m/ζ is a small parameter. The zero-order term, $v_0=f/\zeta$, is the Brownian velocity, and $v_1=O(m/\zeta)$. Substituting this expansion into Eq. (A1), and neglecting terms higher than first order, we obtain

$$v=v_0+v_1=\frac{1}{\zeta}\left[f-\frac{m}{\zeta}\dot{f}\right]. \tag{A2}$$

For the general case, this equation becomes

$$\dot{r}=\frac{\mathbf{D}}{k_BT}\left[f-\frac{\mathbf{MD}}{k_BT}\dot{f}\right]. \tag{A3}$$

The IBD algorithm represents a numerical approximation of this differential equation. Since Eq. (A3) involves the time derivative of the force, this expansion is not valid when the force includes a white noise. However, proceeding innocently, and discretizing Eq. (A3) with the white noise thermal force described by Eq. (2), we arrive at the IBD algorithm for Langevin dynamics. That the discontinuous white noise cannot be differentiated explains our observation that IBD solutions blow up in the small-time-step limit. IBD is well-behaved and produces accurate results only for finite time steps.

APPENDIX B: IBD ALGORITHM FOR SINGLE-VARIABLE LANGEVIN EQUATION

For the scalar case the IBD algorithm can be written as

$$r^{n+1}=r^n+\frac{1}{\zeta}\left[f_s^n\Delta t-\frac{m}{\zeta}(f_s^n-f_s^{n-1})\right]+R^n-\frac{m}{\zeta}(R^n-R^{n-1})/\Delta t, \tag{B1}$$

where R^n obeys

$$\langle R^nR^p\rangle=2k_BT\delta_{np}\Delta t/\zeta. \tag{B2}$$

Here, ζ is the friction coefficient and m is the particle mass. If we choose $\Delta t=2m/\zeta$, Eq. (B1) reduces to

$$r^{n+1}=r^n+\frac{1}{\zeta}\left[f_s^n\Delta t-\frac{\Delta t}{2}(f_s^n-f_s^{n-1})\right]+R^n-\frac{m}{\zeta}(R^n-R^{n-1})/\Delta t, \tag{B3}$$

which approximates

$$r^{n+1}=r^n+\frac{1}{\zeta}\left[f_s^n\Delta t-\frac{(\Delta t)^2}{2}\dot{f}_s^n\right]+R^n-\frac{m}{\zeta}(R^n-R^{n-1})/\Delta t. \tag{B4}$$

The form of Eq. (B4) is similar to the van Gunsteren and Berendsen algorithm[14] for Brownian dynamics which is given by

$$r^{n+1}=r^n+\frac{1}{\zeta}\left[f_s^n\Delta t+\frac{(\Delta t)^2}{2}\dot{f}_s^n\right]+R^n. \tag{B5}$$

This similarity is incidental. In Eq. (B5), the $(\Delta t)^2$ term comes from expanding the force as a power series. For Eq. (B4), in contrast this term has the opposite sign and acts as an inertial correction term to compensate for a force that fluctuates on the time scale of Δt.

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