Configurational Temperature in Membrane Simulations Using Dissipative Particle Dynamics

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The use of excessively long timesteps in dissipative particle dynamics simulations may produce simulation artifacts due to the generation of configurations which are not representative of the desired canonical ensemble. The configurational temperature, amongst other quantities, may be used to assess the extent of the deviation from equilibrium. This paper presents results for simulations of models of water, and lipid bilayer membranes, to illustrate the nature of the problems.

I. INTRODUCTION

Dissipative particle dynamics (DPD) has become a popular tool for simulating the behaviour of both simple and complex fluids. In outline, it consists of the solution of the classical equations of motion for a system of interacting particles, together with a set of stochastic and dissipative forces which control the temperature and allow one to choose the viscosity. It is usual to employ a very simple, repulsive, pair potential, often choosing the force law derived from it to vary linearly with separation within a specified cutoff range. As well as these conservative forces, the stochastic and dissipative forces also act in a pairwise fashion, so as to conserve momentum and ensure hydrodynamic behaviour. The particles represent fluid regions, rather than individual atoms and molecules: the softness and simplicity of the interactions permit the use of a long time step, compared with conventional molecular dynamics. This, and the acceleration of physical processes compared with those seen in more realistic simulations, gives an advantage of several orders of magnitude, at the cost of a very rough mapping onto specific molecular properties. The way to relate the key DPD parameters to fluid equations of state and transport coefficients, has been usefully presented by Groot and Warren.

By tuning the interactions to represent hydrophilic and hydrophobic units, and linking together the particles in a simple bead-spring fashion, the DPD method has been applied to lipid bilayer membranes. Self-assembly and phase diagrams have been investigated, stress profiles determined, and the effects of small molecules studied. Several papers have attempted to optimise the computational algorithm used to solve the DPD equations. The early emphasis was on the correct handling of the velocity-dependent dissipative forces, and ensuring the correct balance of these with the random forces, at an appropriate timestep, so as to generate the canonical ensemble. Accordingly, most attention has focused on maintaining a kinetic temperature \( T_k \) (defined in terms of the kinetic energy per degree of freedom, via the equipartition theorem) reasonably close to the desired temperature \( T \). A detailed analysis of the ideal fluid limit, as a function of timestep, has been carried out. In addition, it has become standard practice to check the pair distribution function and diffusion coefficient for dependence on the time step, as diagnostic tests.

Recently, increased attention has been paid to the suitability or otherwise of the time step for the integration of the conservative forces. This is particularly important in simulations of multi-component systems, polymers, and membranes, where some of the interaction potentials may be stronger than others, including intramolecular bond-bending and stretching terms. The usual criterion of molecular dynamics, energy conservation in the absence of random and dissipative forces, is not usually employed, and any problems may be disguised by the thermostatting. In order to generate meaningful results, it is essential to sample configurations from the canonical (Boltzmann) distribution, and any indicator of significant deviations must be taken seriously. Den Otter and Clarke were the first to point out that DPD, at the usual timesteps and state points, generates configurations for which the configurational temperature \( T_c \) differs significantly from the desired temperature \( T \) and the kinetic temperature \( T_k \).

Den Otter and Clarke estimated this quantity by calculating (for small timesteps) the average potential energy \( \langle U \rangle \) as a function of temperature in the vicinity of \( T \), and fitting the results to a quadratic curve; then, this curve was used to convert averages of \( \langle U \rangle \) measured at larger timesteps into an estimate of \( T_c \). Here a different, and more straightforward definition is used. The configurational temperature \( T_c \) is written

\[
k_B T_c = \frac{\sum_j \langle |\nabla_j U|^2 \rangle}{\sum_j \langle \nabla_j^2 U \rangle},
\]

where \( k_B \) is Boltzmann’s constant, \( \nabla_j \) the gradient, and \( \nabla_j^2 \) the laplacian, of the potential energy \( U \), with respect to the position of particle \( j \). The summations may be over all particles in the system, or restricted to a single species,
or indeed to an individual particle. The expression has long been known as a hypervirial relation \cite{22,23}. It was first introduced by Rugh \cite{24} as an independent estimate of temperature in simulations, and recommended as a diagnostic test for lack of equilibrium by Butler et al. \cite{25}.

In the context of membrane simulations, Jakobsen et al. \cite{26} observed significant differences in the kinetic temperatures of different species in DPD simulations, and recommended this as a simple diagnostic test of incorrect integration of the equations of motion. They also mentioned the possibility of monitoring the configurational temperature, but no dramatic improvements at long time step were seen, and they recommended the use of shorter time steps.

This paper reports simulation averages of the configurational temperature for a standard single-component DPD fluid, over a range of timesteps, using a variety of proposed DPD integration methods. The results show that, although some of these methods dramatically improve the control of the kinetic temperature $T_k$, the same improvements are not seen for the configurational temperature: deviations of $T_c$ from the desired values remain significant in all cases, at the typically recommended time steps. Results are then reported for the same membrane model used in Ref. \cite{26}: largely as a result of intramolecular bonding terms in the potential, the deviations in $T_c$ are far worse than in the simple fluid case, and may be correlated with some of the other artifacts observed before \cite{27}. The general conclusion is that the configurational temperature should be added to the list of diagnostic tests applied to DPD simulations, and that shorter timesteps should be employed in membrane simulations than hitherto.

II. DYNAMICAL ALGORITHMS

The DPD equations of motion for a simple fluid may be written \cite{1,2,19}

\begin{align}
\text{d}r_i &= \left(\frac{p_i}{m}\right)\text{d}t \\
\text{d}p_i &= \sum_{j \neq i} f_{ij}^C \text{d}t + f_{ij}^D \text{d}t + \text{d}p_i^R .
\end{align}

The particles are all assumed to have the same mass $m$. The conservative forces usually take the form

\begin{align}
f_{ij}^C &= a\omega(r_{ij})\hat{r}_{ij} \\
\text{with } \omega(r) &= \begin{cases} 1 - r/r_c & r \leq r_c \\
0 & r > r_c \end{cases} .
\end{align}

Here $r_{ij} = r_i - r_j$, $r_{ij} = |r_{ij}|$, $\hat{r}_{ij} = r_{ij}/r_{ij}$. The parameter $a$ determines the strength of the conservative interactions, and $r_c$ is the cutoff. The dissipative forces and random impulses are written

\begin{align}
f_{ij}^D &= -\gamma\omega(r_{ij})^2(v_{ij} \cdot \hat{r}_{ij})\hat{r}_{ij} \\
\text{d}p_i^R &= \sigma\omega(r_{ij})\hat{r}_{ij}\text{d}W_{ij} ,
\end{align}

where $v_{ij} = v_i - v_j$, and $p_i = mv_i$. A choice has been made here to use the same weighting function $\omega(r)$ in the specification of conservative, dissipative, and random terms. The dissipative friction $\gamma$ is related to the random impulse strength $\sigma$ by the fluctuation-dissipation theorem $\sigma^2 = 2k_B T$. The quantity $\text{d}W_{ij}$ is the time derivative of a Wiener process: over a timestep $\Delta t$, $\Delta W_{ij}$ is chosen from a normal distribution with zero mean and variance $\Delta t$, and $\Delta W_{ji} = -\Delta W_{ij}$. Units are chosen such that the particle mass $m$, cutoff $r_c$, and temperature $T$ are all unity.

Four algorithms will be discussed in this paper. The “standard” DPD algorithm consists of the following steps
\[ \tilde{p}_i := p_i + \lambda \sum_{j \neq i} f_{ij}^C \Delta t + f_{ij}^D \Delta t + \Delta p_{ij}^R \] (4a)
\[ p_i := p_i + \frac{1}{2} \sum_{j \neq i} f_{ij}^C \Delta t + f_{ij}^D \Delta t + \Delta p_{ij}^R \] (4b)
\[ r_i := r_i + (p_i/m) \Delta t \]
Calculate \( f_{ij}^C (\{r_i\}) \) (4c)
\[ p_i := p_i + \frac{1}{2} \sum_{j \neq i} f_{ij}^C \Delta t + f_{ij}^D \Delta t + \Delta p_{ij}^R \] (4d)
Calculate \( f_{ij}^D (\{r_i\}, \{p_i\}) \) (4e)

Note the auxiliary momenta \( \tilde{p}_i \), used in the calculation of dissipative forces, and predicted using a parameter \( \lambda \). The value \( \lambda = 0.5 \) conveniently makes \( \tilde{p}_i = p_i \), but \( \lambda = 0.65 \) was found by Groot and Warren \[11\] to be optimal for the particular fluid that will be studied here. This paper will use \( \lambda = 0.65 \). Note also the second computation of dissipative forces, step (4f), introduced by Gibson and Chen \[11\]. Iteration of the last two steps would lead to a self-consistent algorithm \[12\] not studied here.

The second algorithm is the so-called “Scheme II” of Peters \[17\]. At each time step, the positions and momenta are updated using the conservative forces only:
\[ p_i := p_i + \frac{1}{2} \sum_{j \neq i} f_{ij}^C \Delta t \] (5a)
\[ r_i := r_i + (p_i/m) \Delta t \]
Calculate \( f_{ij}^C (\{r_i\}) \) (5b)
\[ p_i := p_i + \frac{1}{2} \sum_{j \neq i} f_{ij}^C \Delta t . \] (5c)

Following this, for every pair \( i, j \), selected in random order, the following update is performed:
\[ p_i := p_i + f_{ij}^D \Delta t + \Delta p_{ij}^R \]
\[ p_j := p_j - f_{ij}^D \Delta t - \Delta p_{ij}^R \]
with \( f_{ij}^D = a_{ij} (v_{ij} \cdot \hat{r}_{ij}) \hat{r}_{ij} \)
and \( \Delta p_{ij}^R = b_{ij} \Delta W_{ij} \hat{r}_{ij} \).

The parameters \( a_{ij} \) and \( b_{ij} \) are determined by \( T \) and \( \gamma \) (or, equivalently, \( T \) and \( \sigma \)) and by the timestep. As explained by Peters \[17\], this generates the Maxwell-Boltzmann distribution of velocities and, at short time step, solves the original DPD equations.

The third algorithm is due to Lowe \[10\]. This is not a solution of the original DPD equations, but rather a pairwise thermostat applied to a conventional integration algorithm for the conservative forces. As for the Peters method, at each step the positions and momenta are updated using steps (4a)–(5c) above, using the conservative forces only. Then, examining every pair (in random order), with probability \( P = \Gamma \Delta t \), the momenta are updated as follows:
\[ p_i := p_i + \Delta p_{ij}^R \]
\[ p_j := p_j - \Delta p_{ij}^R \]
with \( \Delta p_{ij}^R = \frac{1}{2} m \left[ \zeta \sqrt{2k_B T/m} - (v_{ij} \cdot \hat{r}_{ij}) \right] \hat{r}_{ij} \)

where \( \zeta \) is selected from a Gaussian distribution with zero mean and unit variance. This procedure reselects the relative velocity from the Maxwell-Boltzmann distribution. The key parameter is the stochastic randomization frequency \( \Gamma \).

The fourth algorithm to be considered here has been proposed by Stoyanov and Groot \[18\]. It is identical with the method of Lowe, except that the fraction \( (1 - P) \) of pairs which do not have their relative velocities stochastically reselected, are instead thermalized by a deterministic method. For each such pair, after steps (4a)–(5c) a dissipative
force is calculated
\[
f_i^D = k_\omega (r_{ij}) (v_{ij} \cdot \dot{r}_{ij}) \dot{r}_{ij}
\]
\[
f_i^D := f_i^D + f_i^D
\]
\[
f_i^D := f_i^D - f_i^D .
\]

Then, after steps [5a], [5b] the momenta are corrected by
\[
p_i := p_i + \Delta t (1 - \tilde{T}_k / T) f_i^D,
\]

where \( \tilde{T}_k \) is a kinetic temperature estimated from relative velocities at the start of the timestep. Finally, the Lowe velocity reselection process is applied to the remaining fraction \( P \) of pairs as usual. In the present work, following Ref. [15], the parameter \( k \) is set to \( k = 0.3 / \Delta t \). As for the Lowe method, the key parameter is the stochastic randomization rate \( \Gamma \) which determines \( P \). [15] associate the deterministic part of their thermostat with the Nosé-Hoover algorithm [28, 29], but in practice it seems to be more closely related to that of Berendsen et al. [30], since the “friction coefficient” is not a dynamical variable but is instead directly proportional to the temperature factor \((1 - \tilde{T}_k / T)\). This approach permits a high degree of temperature control at low, or even zero, values of \( \Gamma \), where the Lowe method is ineffective: indeed, Stoyanov and Groth report an order of magnitude improvement in \( T_k \). However, the links with a statistical ensemble, and with the DPD equations themselves, remain to be established.

III. SIMULATION MODELS AND PARAMETERS

By considering the equation of state and dynamical properties of water under ambient conditions, Groot and Warren [3] established the standard parameter set that is commonly used in algorithm tests [14, 15, 17, 18]: strength parameter \( \alpha = 25 \), number density \( \rho = 3 \), stochastic impulse strength \( \sigma = 3 \), and hence (for \( T = 1 \)) \( \gamma = 4.5 \). This is sometimes referred to as “Model B”. This paper reports results for Model B, and also for variants with \( \sigma = 1 \) and \( \sigma = 6 \), using both the DPD and Peters methods. For the Stoyanov-Groot and Lowe algorithms, stochastic collision rates \( \Gamma = 0, 0.2, 4 \) and the maximum possible \( \Gamma = 1 / \Delta t \) (corresponding to \( P = 1 \), completely reselecting all velocities every timestep) are investigated. A system size of \( N = 250 \) particles in a cubic box with periodic boundary conditions is used throughout.

For their tests of DPD simulations of membranes, Jakobsen et al. [20] adopted the model of Shillcock and Lipowsky [6]. Each lipid molecule has the form of a 7-bead chain \( HT \), with repulsion parameters between hydrophilic “head” beads (H), hydrophobic “tail” beads (T), and “water” beads (W) as follows: \( \alpha_{WW} = \alpha_{HH} = \alpha_{TT} = 25 \), \( \alpha_{HW} = 35 \), \( \alpha_{HT} = 50 \), \( \alpha_{TW} = 75 \). Successive lipid beads are connected by harmonic springs, and a simple bond-bending potential favours linearity:
\[
\begin{align*}
    u_{\text{stretch}}(r_{ij}) &= \frac{1}{2} k_{\text{stretch}} (r_{ij} - \ell_0)^2 & \text{with } k_{\text{stretch}} = 128, \ell_0 = 0.5 \\
    u_{\text{bend}}(r_{ij}, r_{jk}) &= k_{\text{bend}} (1 - r_{ij} \cdot r_{jk}) & \text{with } k_{\text{bend}} = 20.
\end{align*}
\]

The present paper uses this model but follows Jakobsen et al. [20] in choosing all stochastic impulse strengths to be the same, \( \sigma = 3 \), in the DPD and Peters algorithms. For comparison, results obtained using the Stoyanov-Groot method with \( \Gamma = 0 \), and using the Lowe thermostat with \( \Gamma = 1 / \Delta t \), are reported. A smaller system is used here than in the previous papers [6, 20]: \( N_{\text{lipid}} = 100 \) lipid chains plus \( N_{\text{water}} = 2500 \) water beads, making \( N = 3200 \) beads in all. A cuboidal box, with periodic boundaries, was employed. Transverse box dimensions were fixed so as to give an overall number density \( \rho = 3 \), and an area per lipid \( 2A / N_{\text{lipid}} = 0.617 \), close to the state of zero surface tension. The chains were pre-formed into a flat bilayer, and allowed to equilibrate before any measurements were made.

The time unit \( \tau = r_c \sqrt{m/k_B T} \) is defined in terms of the other fixed parameters. In these units, for the water model described above, Groot and Warren [3] recommend timesteps in the range \( \Delta t = 0.04 \ldots 0.06 \), so as to achieve an accuracy of order 1% in \( T_k \); the present paper investigates time steps in the range \( 0.005 \leq \Delta t \leq 0.06 \). Total simulation times for the water runs were \( t_{\text{run}} = 2000 \), and for the membrane runs were \( t_{\text{run}} = 10000 \). Formulae for the Laplacians used to calculate the configurational temperature for this model are given in the Appendix.

IV. RESULTS

Figures 1 and 2 show the measured temperatures for the four chosen algorithms, in simulating the water model at various choices of thermostatting strength. With an appropriate choice of parameters, it is indeed possible to achieve a
kinetic temperature $T_k$ within 1% of the desired value at a timestep $\Delta t = 0.05$; the Stoyanov-Groot method performs well in this regard at all values of $\Gamma$, and the Lowe thermostat is good at high values of $\Gamma$. The more recently-developed thermostats all seem less sensitive to variations in $\sigma$ or $\Gamma$ than the basic DPD algorithm. However, it can be seen that the error in the configurational temperature $T_c$ is an order of magnitude worse than that in $T_k$, being around 10% at $\Delta t = 0.05$, and this is not dramatically affected by the choice of algorithm: the “best” (Stoyanov-Groot at $\Gamma = 0$) reduces the error by 30–40% compared to the “worst” (all of the methods, at high stochastic thermalization rate). Also, for quite small stochastic damping $\Gamma = 0.5$ (i.e. $P = 0.025$ at $\Delta t = 0.05$), the Stoyanov-Groot method becomes similar in performance to the other methods.
FIG. 3: Membrane simulations using (a) DPD algorithm with $\lambda = 0.65$, $\sigma = 3.0$, (b) Peters scheme II with $\sigma = 3.0$. Temperatures as functions of timestep $\Delta t$. Circles: H (head) and T_6 (tail) beads. Squares: T_1 and T_5 beads. Diamonds: T_2, T_3 and T_4 beads. Triangles: W (water) beads. The lines are to guide the eye. Statistical errors are approximately the same size as the plotting symbols.

FIG. 4: Membrane simulations using (a) Stoyanov-Groot thermostat with $\Gamma = 0$, (b) Lowe thermostat with $\Gamma = 1/\Delta t$. Temperatures as functions of timestep $\Delta t$. Symbols as for Fig. 3.

For the membrane simulations, temperatures for each of the bead types (species) are reported in Figs 3 and 4. There are several points of interest. Firstly, the kinetic temperatures for different species are different, as already noted [26]. The discrepancies between $T_k$ and $T$ for the lipid beads are somewhat worse than in the case of simple water at the same timesteps, of order a few percent. The configurational temperatures are also different for the different species. For the lipid beads, they are all in much poorer agreement with the desired temperature, than for the water: at $\Delta t = 0.05$, $T_c$ is too high by 80–90% for some of the tail beads. This indicates a serious departure from equilibrium. Secondly, numbering the tail beads T_1–T_6 with T_1 next to the head bead, the results for both $T_k$ and $T_c$ divide naturally into groups: \{H, T_6\}, \{T_1, T_5\}, \{T_2, T_3, T_4\}, and \{W\}. Within each group, the temperatures agree, almost to within the statistical error bars, and no attempt is made to distinguish them in the figures. This suggests
FIG. 5: Density and temperature profiles in the bilayer region for membrane simulations using the Peters thermostat. Top two panels show configurational and kinetic temperatures as functions of timestep. Solid lines: $\Delta t = 0.05$. Dashed lines: $\Delta t = 0.03$. Dot-dashed lines: $\Delta t = 0.01$. Bottom panel shows, for reference, the local density, measured at $\Delta t = 0.01$. Solid lines: H beads. Long dashes: T beads. Short dashes: W beads.

that the intramolecular stretching and bending potential terms (which are the same within each group) are the dominant factors in the problems of maintaining equilibrium; in the following section, some support will be given to this view, but it is also argued that the intermolecular potentials make a contribution. Of the four algorithms studied, the DPD, Peters, and heavily-thermostatted Lowe method perform in a similar way to each other. The behaviour of the Stoyanov algorithm is unusual: although $T_c$ is quite close to $T$ up to $\Delta t = 0.03$, $T_k$ shows an instability. As $\Delta t$ increases, the water temperature falls dramatically below $T$, while the other species become much too hot. This effect makes the simulation unphysical for $\Delta t = 0.05$.

Density and temperature profiles are shown in Fig. 5 selecting the Peters thermostat as being representative. Jakobsen et al. [26] report a time step dependence of the density profiles, specifically a change in the (small) concentrations of head group beads in the interior of the bilayer. The present simulations do not confirm such a systematic effect; however, the transverse dimensions of the system are much smaller than those of Ref. [26], so the relevant statistics and timescales may prevent resolution of the effect here. The temperature profiles are as expected from Figs 3 and 4, with the most dramatic indicators of lack of equilibrium in the regions occupied by tail beads $\{T_2, T_3, T_4\}$. A comparison of the different algorithms at fixed timestep $\Delta t = 0.03$ is given in Fig 6. In the lipid tail region the Lowe thermostat (with the parameter $\Gamma$ set to the maximum allowed value) gives the worst $T_c$, about 20% too high, while the Stoyanov thermostat (with $\Gamma = 0$) gives the best, about 8% too high; however the performance order is
FIG. 6: Density and temperature profiles in the bilayer region for membrane simulations at $\Delta t = 0.03$ using the different thermostats. Top two panels show configurational and kinetic temperatures. Solid lines: Lowe thermostat with $\Gamma = 1/\Delta t$. Long dashes: Peters thermostat with $\sigma = 3$. Short dashes: DPD algorithm with $\sigma = 3$. Dash-dotted line: Stoyanov-Groot thermostat with $\Gamma = 0$. Bottom panel shows, for reference, the local density, measured at $\Delta t = 0.01$. Solid lines: H beads. Long dashes: T beads. Short dashes: W beads.

reversed for $T_k$ with the Lowe thermostat (by construction) being perfectly accurate and the Stoyanov thermostat being overdamped by about 5%. The behaviour in the water region does not give a good indicator of the lack of equilibrium within the membrane.

It is of interest to compare these profiles with the pressure tensor results which were also previously found to exhibit an anomaly \cite{26}. The pressure profiles are calculated in the Irving-Kirkwood convention \cite{31} using a method essentially the same as that described by Goetz and Lipowsky \cite{32}. The results for the Peters thermostat are shown in Fig. 7. The component $P_N$ normal to the bilayer is not constant, contrary to what must hold for a system at equilibrium \cite{26}. For $\Delta t = 0.05$ the error is comparable in magnitude to the physically interesting quantity, the difference $P_N - P_T$ between normal and transverse components, whose integral gives the surface tension. There is some cancellation of errors, since the anomaly appears in both components \cite{26}; however, such an error is clearly undesirable. The point to be made here is that the configurational temperature profiles of Fig. 6 are echoed in the pressure profiles of Fig. 7.
It is evident that the configurational temperature gives a different perspective, from the kinetic temperature, on simulation equilibrium, even for simple fluids. Also the intramolecular bond stretching and bending potentials used in membrane simulations have a direct effect on the stability of the algorithm, which can be estimated via $T_c$, amongst other indicators.

Some insight into the information contained in $T_c$ may be obtained by considering a very simple model: the 1-D harmonic oscillator, with hamiltonian

$$\mathcal{H} = \frac{p^2}{2m} + \frac{1}{2}kx^2 \equiv K(p) + U(x).$$

It is known [33, 34] that the velocity Verlet algorithm conserves exactly a “shadow hamiltonian” which we may write in the form

$$\mathcal{H}^\dagger(x, p) = \frac{p^2}{2m} + \frac{1}{2}kx^2(1 - \phi) \equiv K(p) + U^\dagger(x)$$

where $\phi = \frac{1}{4}(k/m)\Delta t^2$. 

V. ANALYSIS AND DISCUSSION

FIG. 7: Density and pressure profiles in the bilayer region for membrane simulations using the Peters thermostat. Top panel: normal component $P_N$ as a function of timestep: Solid lines: $\Delta t = 0.05$. Dashed lines: $\Delta t = 0.03$. Dot-dashed lines: $\Delta t = 0.01$. Middle panel: surface tension integrand, $P_N - P_T$, measured at $\Delta t = 0.01$. Bottom panel: local density, measured at $\Delta t = 0.01$. Solid lines: H beads. Long dashes: T beads. Short dashes: W beads.
TABLE I: Laplacian $\nabla^2 U$ for beads in lipid chain calculated for isolated chain at $T = 0$, as an equilibrium simulation average at $T = 1$ for an isolated chain, from the full condensed phase simulation at $T = 1$, and from a fit to the measured $T_c$, Fig. 4b, assuming a locally isotropic harmonic potential. Figures in parentheses represent the estimated error in the last digit.

| Bead | single chain | condensed phase |
|------|--------------|-----------------|
|      | $T = 0$     | $T = 1$         | Fit          |
| H    | 288 273(2)  | 491(1) 1157(1)  |
| T₁   | 1056 853(6) | 1132(1) 1893(1) |
| T₂   | 1216 970(5) | 1272(1) 2272(1) |
| T₃   | 1216 986(7) | 1266(2) 2327(1) |
| T₄   | 1216 972(8) | 1264(2) 2277(1) |
| T₅   | 1056 865(8) | 1116(2) 1884(1) |
| T₆   | 288 267(3)  | 438(1) 1123(1)  |
| W    | 122.8(1) 479(1) |

A dynamical algorithm which alternates periods of velocity Verlet with velocity reselection from the canonical ensemble at temperature $T$ (analogous to the “Lowe” algorithm of DPD) will actually generate momenta from the correct Maxwell-Boltzmann distribution $\exp(-K/k_B T)$ and configurations from the “shadow distribution” $\exp(-U^2/k_B T)$. An immediate consequence is

$$\frac{1}{2}k_B T = \langle p^2 / 2m \rangle = \left\langle \frac{1}{2} k x^2 (1 - \phi) \right\rangle.$$

Since the force $f = -k x$ and $\partial^2 H / \partial x^2 = k$, the kinetic and configurational temperatures are

$$k_B T_k = \langle p^2 / m \rangle = k_B T$$

$$k_B T_c = \frac{\langle f^2 \rangle}{\langle \partial^2 H / \partial x^2 \rangle} = \frac{k_B T}{1 - \phi}.$$

For a 3D isotropic harmonic oscillator $U = \frac{1}{2} k |r|^2$, $f = -k r$, the same formula applies, with $k = \frac{1}{2} \nabla^2 U$, and it is straightforward to extend it to the anisotropic case. The effect of an over-large time step is to reduce the effective force constant dictating the configurational distribution, increase the mean squared displacement, and (in proportion) increase the mean squared force which gives the value of $T_c$. The above equation is a reasonable first approximation to the curves shown in Figs 4a, 4b. For the lipids, assuming that the intramolecular bond potentials are approximately harmonic, a given fractional error in $T_c$ for each bead may approximately translate into a corresponding fractional error in mean-squared displacement which, when compounded along the chain, becomes a more significant error in overall flexibility.

It is tempting to try to estimate these contributions to $T_c$, for the isolated lipid chain. In the harmonic approximation, the appropriate force constants may be evaluated, taking the lipids to be in their minimum energy configuration, and counting all the bonds in which a bead participates. In Table I the sum (over $x$, $y$ and $z$ directions) of these predicted force constants (for $k_{\text{stretch}} = 128$, $\ell_0 = 0.5$, $k_{\text{bend}} = 20$) are compared with measured average Laplacians from simulations of a single chain at $T = 1$, and simulations of the full fluid system at $T = 1$, both conducted at short timesteps. The figures partly explain the close similarity in configurational temperatures within the groups of beads mentioned in the previous section, in terms of intramolecular potentials. There is some reduction in the average Laplacians due to fluctuations of the single chain at $T = 1$ compared with $T = 0$. However, in the full condensed phase simulation, this is more than compensated by an intermolecular contribution of order 200–250 in these reduced units, so part of this coincidence is due to the similar environments, and identical repulsion parameters between like beads, for this particular model.

The simulated fluids are not actually harmonic, and so the above analysis should not be over-interpreted. The final column of Table I shows the results of fitting eqn (7b) to the Lowe thermostat results shown in Fig. 1b. The fits are excellent, but the fitted parameters are all significantly larger than would have been expected. Partly, this can be explained by the anisotropy of the local harmonic potential: the stiffest potentials will dominate the breakdown of the algorithm. However one should also remember that the real shadow hamiltonian is more complicated than a simple harmonic potential, and will not split in the same way into a kinetic part plus a renormalized configurational part.

Some effort has been made to develop practical methods to estimate the shadow Hamiltonian for complex systems 33, 34. Knowledge of this function may help not only the monitoring of algorithm performance, but also the
implementation of more efficient algorithms such as hybrid Monte Carlo \cite{37}. This method differs from DPD in the rejection of moves so as to guarantee that the desired ensemble is sampled. Returning to the points made by Hafskjold et al. \cite{27}, it is notable that smoothness of the potential is a highly desirable feature in the accurate construction of shadow hamiltonians. To illustrate this, Engle et al. \cite{36} considered a simple harmonic oscillator potential, modified by splitting into two halves at the minimum, with a flat piece inserted between them. The consequent lack of smoothness was shown to degrade conservation of the shadow hamiltonian. Such a potential is a possible one-dimensional model system for the numerical aspects of DPD dynamics: the oscillation back and forth represents the motion of a DPD bead out of the repulsive quadratic potential of a neighbour, and into the repulsive range of a different neighbour. In the absence of an improved algorithm to handle the DPD conservative forces, using a shorter timestep for them seems the best approach \cite{17}.

VI. CONCLUSIONS

The essential conclusion of this paper is that stiffer potentials, and stronger conservative forces, require shorter timesteps. This is hardly a new point, and is increasingly being recognised in the DPD community \cite{17,26,27}, where the principal danger is that the effects of an over-long timestep may be disguised by the thermostat. It is recommended here that the configurational temperature $T_c$ be measured and reported in DPD simulations, along with other indicators that the system is not at equilibrium, so as to address this danger. $T_c$ is easy to calculate, and appears to be sensitive to some of the artifacts that appear in other properties such as the pressure tensor profile in membranes.

The degree of accuracy of sampling required will, no doubt, vary from one application to another. For the standard water model, Groot and Warren \cite{3} recommended timesteps $\Delta t \approx 0.05$, so as to achieve an accuracy of order 1% in $T_k$. Applying the same criterion to $T_c$ would lead to a revised recommendation, $\Delta t \approx 0.015$. Modern thermostats are dramatically better at controlling $T_k$, and give modest improvements in $T_c$. Stoyanov and Groot \cite{18} note, for instance, that their new method keeps $T_k$ within the desired 1% range even for $\Delta t = 0.09$; however, such a timestep would result in an error in $T_c$ between 24% and 44% depending on $\Gamma$. Also, for multicomponent systems such as lipid membranes, there may be substantial imbalances in the distribution of $T_k$ and $T_c$ between the different species. Such large discrepancies indicate lack of equilibrium, i.e. configurations are being sampled incorrectly.

It would, no doubt, be possible to devise thermostats that control the value of $T_c$ as well as $T_k$, and that act separately on the different types of bead. In such a case, it becomes important to measure other, independent, quantities as a function of time step, and to bear in mind that no single quantity acts as an indicator of equilibrium.

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Appendix

The calculation of the Laplacian for each of the potential terms used in this study proceeds as follows. The DPD repulsive potential between $i$ and $j$, with $\mathbf{r}_{ij} = \mathbf{r}_i - \mathbf{r}_j$, takes the form (assuming $r_{ij} \leq r_c$)

$$u = \frac{1}{2} \left( \frac{\alpha}{r_c} \right) (r_{ij} - r_c)^2.$$

The gradients (the negatives of which are the conservative forces of eqn (3a)) are

$$\nabla_i u = -\nabla_j u = \alpha \left( \frac{r_{ij}}{r_c} - 1 \right) \hat{r}_{ij},$$

and the Laplacians are

$$\nabla_i^2 u = \nabla_j^2 u = \alpha \left( \frac{3}{r_c} - \frac{2}{r_{ij}} \right).$$

The formulae for the bond stretching potential of eqn (6a) are identical, with the replacements $r_c \to \ell_0$ and $\alpha \to k_{\text{stretch}} \ell_0$.\[352x352]
For the angle-bending potential of eqn (63) between successive beads \(i, j, k\), define \(c_{ij} = r_{ij} \cdot r_{ij}, c_{jk} = r_{jk} \cdot r_{jk}, c_{ijk} = r_{ij} \cdot r_{jk}\). The gradients of these scalar products with respect to individual positions are:

\[
\begin{align*}
\nabla_i c_{ij} &= 2r_{ij} \\
\nabla_j c_{ij} &= -2r_{ij} \\
\nabla_k c_{ij} &= 0
\end{align*}
\]

\[
\begin{align*}
\nabla_i c_{jk} &= 0 \\
\nabla_j c_{jk} &= 2r_{jk} \\
\nabla_k c_{jk} &= -2r_{jk}
\end{align*}
\]

\[
\begin{align*}
\nabla_i c_{ijk} &= r_{jk} \\
\nabla_j c_{ijk} &= r_{ij} - r_{jk} \\
\nabla_k c_{ijk} &= -r_{ij}.
\end{align*}
\]

The Laplacians are

\[
\begin{align*}
\nabla_i^2 c_{ij} &= 6 \\
\nabla_i^2 c_{jk} &= 6 \\
\nabla_i^2 c_{ijk} &= 0
\end{align*}
\]

The potential has the form \(u_{\text{bend}} = k_{\text{bend}}(1 - C)\), where

\[
C = \cos \theta_{ijk} = r_{ij}^{-1/2} r_{jk}^{-1/2} c_{ijk}.
\]

The necessary gradients are

\[
\begin{align*}
\nabla_i C &= (\nabla_i c_{ij}^{-1/2}) c_{jk} c_{ij}^{-1/2} c_{ij} + c_{ij}^{-1/2} (\nabla_i c_{ij}^{-1/2}) c_{ijk} + r_{ij}^{-1/2} (\nabla_i c_{ijk}) \\
&= c_{ij}^{-1/2} r_{jk} - \frac{c_{ijk}}{c_{ij}} r_{ij}
\end{align*}
\]

\[
\begin{align*}
\nabla_j C &= (\nabla_j c_{ij}^{-1/2}) c_{jk}^{-1/2} c_{ij} + c_{ij}^{-1/2} (\nabla_j c_{ij}^{-1/2}) c_{ijk} + c_{ij}^{-1/2} c_{jk}^{-1/2} (\nabla_j c_{ijk}) \\
&= c_{ij}^{-1/2} c_{jk}^{-1/2} \left( 1 + \frac{c_{ijk}}{c_{ij}} \right) r_{ij} - \left( 1 + \frac{c_{ijk}}{c_{jk}} \right) r_{jk}
\end{align*}
\]

\[
\begin{align*}
\nabla_k C &= (\nabla_k c_{ij}^{-1/2}) c_{jk}^{-1/2} c_{ij} + c_{ij}^{-1/2} (\nabla_k c_{ij}^{-1/2}) c_{ijk} + c_{ij}^{-1/2} c_{jk}^{-1/2} (\nabla_k c_{ijk}) \\
&= c_{ij}^{-1/2} c_{jk}^{-1/2} \left( c_{ijk} r_{jk} - r_{ij} \right)
\end{align*}
\]

The Laplacians are given by

\[
\begin{align*}
\nabla_i^2 C &= \left( \nabla_i^2 c_{ij}^{-1/2} \right) c_{jk}^{-1/2} c_{ij} + c_{ij}^{-1/2} \left( \nabla_i^2 c_{ij}^{-1/2} \right) c_{ijk} + c_{ij}^{-1/2} \left( \nabla_i^2 c_{ijk} \right) \\
&= -2c_{ij}^{-3/2} c_{jk}^{-1/2} c_{ijk} \\
\nabla_j^2 C &= \left( \nabla_j^2 c_{ij}^{-1/2} \right) c_{jk}^{-1/2} c_{ij} + c_{ij}^{-1/2} \left( \nabla_j^2 c_{ij}^{-1/2} \right) c_{ijk} + c_{ij}^{-1/2} c_{jk}^{-1/2} \left( \nabla_j^2 c_{ijk} \right) \\
&= -2c_{ij}^{-3/2} \left( c_{ijk} + c_{ij} c_{jk} + c_{ij} c_{jk} \right) \\
\nabla_k^2 C &= \left( \nabla_k^2 c_{ij}^{-1/2} \right) c_{jk}^{-1/2} c_{ij} + c_{ij}^{-1/2} \left( \nabla_k^2 c_{ij}^{-1/2} \right) c_{ijk} + c_{ij}^{-1/2} c_{jk}^{-1/2} \left( \nabla_k^2 c_{ijk} \right) \\
&= -2c_{ij}^{-3/2} \left( c_{ijk} + c_{ij} c_{jk} + c_{ij} c_{jk} \right)
\end{align*}
\]

All of the above results should be multiplied by \((-k_{\text{bend}})\) to give the gradients and Laplacians for the bending potential of eqn (63).

It is worth emphasizing that the dissipative and random terms in the DPD equations (2) play no role in the calculation of Laplacians and squared forces which go into the configurational temperature, eqn (1).

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