WIGGLE: A new constrained molecular dynamics algorithm in Cartesian coordinates

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Abstract

The theory of conventional constrained molecular dynamics (MD) simulations is reexamined based on a projection operator approach. A new algorithm, named WIGGLE, is presented for MD simulations with internal constraints. At each time step, the algorithm utilizes the constrained accelerations derived from velocity adjustments to satisfy the hidden constraints, and provides both initial and final constrained values that are almost an order of magnitude closer to the desired values than does RATTLE. Its performance is compared with those of RATTLE and SHAKE for an octane molecule. Also presented are a formalism to additionally constrain the angular momentum about the center of mass and an expression for the local energy drift during each integration time step.
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1. Introduction

Molecular dynamics (MD) simulations are commonly used to deduce conformational changes as well as physical properties of macromolecules, the atomistic trajectories being determined by numerically integrating the related Newton equations of motion [1,2]. In order to maintain the system's stability, the integration time step routinely has to be kept small enough (less than 1 fs) to resolve such fast motions as vibrations of internal bond length coordinates. However, during certain simulation time ranges of a molecule, the

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average changes in the internal bond lengths are negligible compared to those in torsion (viz., dihedral) angles directly related to conformational changes. Thus, freezing the fast internal motions is an efficient way to increase the integration time step. Typically, freezing all bond length coordinates enables one to use a time step four times larger than that for an unconstrained MD simulation.

Since the introduction of SHAKE [3], in which atomic coordinates are iteratively adjusted to give internal bond length constraints within a specified tolerance at each time step, analyses and modifications to constrain internal degrees of freedom have been undertaken [4–26]. Another important algorithm for this purpose is RATTLE [6], in which atomic velocities are additionally adjusted, based on the velocity Verlet scheme [27], to satisfy the hidden constraints that are time derivatives of the original constraint equations. Thus, RATTLE provides more accurate constrained atomic velocities than SHAKE, in which atomic velocities are implicitly determined by the Verlet algorithm [28].

In SHAKE and RATTLE, the unconstrained accelerations obtained from forces without any constraints are used to give the initial atomic positions for the next time step. We present a new method, named WIGGLE, that uses the constrained accelerations easily derived from the adjusted atomic velocities to satisfy the hidden constraints, and provides initial constrained values for the next time step that are closer to the desired values than those in SHAKE and RATTLE.

In Section 2, the theory of constrained MD simulations is reinvestigated based on the underlying projection operator. Derivation of WIGGLE and its implementation are shown in Section 3, and it is applied to an octane molecule to test its performance compared with RATTLE and SHAKE in Section 4. Finally, a method of constraining the total angular momentum about the center of mass (Appendix A) and a specific relation for the local energy drift in a given time step (Appendix B) are presented.

2. A projection operator approach to constrained molecular dynamics

We consider an isolated molecule of p atoms whose positions x_λ ($\lambda = 1, \ldots, p$) are subject to N_c constraints $\sigma^\alpha(X) = C^\alpha$ (constant) ($\alpha = 1, \ldots, N_c$). In matrix form, the constraint equations are represented by

$$\sigma(X) = C, \tag{1}$$

where $X \equiv (x_1^1 x_1^2 x_1^3 \ldots x_p^1 x_p^2 x_p^3)^T$ with superscript 'T' representing the transpose of a matrix. Then classical atomic motion is governed by

$$m\ddot{X} = -\partial_X(V + \sigma^T \Lambda) \equiv -\partial_X V_c \equiv F_X - B_c^T \Lambda, \tag{2}$$

where m is a $3p \times 3p$ diagonal matrix containing triads of atomic masses m_λ, a dot represents differentiation with respect to time, $F_X \equiv -\partial_X V$ are forces due to the system's potential energy function V without constraints, $V_c \equiv V + \sigma^T \Lambda$ with Λ being the Lagrange undetermined parameters for constraint forces, and $B_c \equiv \partial_X \sigma$. Successive differentiation of (1) with respect to time provides the following hidden constraints:

$$\dot{\sigma} = B_c \dot{X} = 0, \tag{3}$$

$$\ddot{\sigma} = B_c \ddot{X} + \dot{X}^T B_{2c} \dot{X} = 0 \tag{4}$$

with $B_{2c} \equiv \partial_X B_c \equiv \partial_X^2 \sigma$. Using (2) and (4), for given $\dot{X}$ and F_X the parameters Λ can be determined by solving

$$G_{cc} \Lambda = B_c m^{-1} F_X + \dot{X}^T B_{2c} \dot{X}, \tag{5}$$

where $G_{cc} \equiv B_c m^{-1} B_c^T$ with the superscript '−1' representing the inverse of a nonsingular matrix. For constraints on nonredundant internal coordinates, the symmetric matrix G_{cc} is also positive definite, giving a nonsingular solution for Λ. Substituting this into (2) leads one to

$$\ddot{\mathbf{X}} = \mathbf{m}^{-1}\mathbf{F}_X - \mathbf{m}^{-1}\mathbf{B}_c^T\mathbf{G}_{cc}^{-1}(\mathbf{B}_c\mathbf{m}^{-1}\mathbf{F}_X + \dot{\mathbf{X}}^T\mathbf{B}_{2c}\dot{\mathbf{X}}) \quad \text{[from (5)]}$$
$$= \mathbf{m}^{-1}\mathbf{F}_X - \mathbf{m}^{-1}\mathbf{B}_c^T\mathbf{G}_{cc}^{-1}(\mathbf{B}_c\mathbf{m}^{-1}\mathbf{F}_X - \mathbf{B}_c\ddot{\mathbf{X}}) \quad \text{[from (4)]}$$
$$= \mathbf{m}^{-1}\mathbf{F}_X - \mathbf{m}^{-1}\mathbf{B}_c^T\mathbf{G}_{cc}^{-1}\mathbf{B}_c(\mathbf{m}^{-1}\mathbf{F}_X - \ddot{\mathbf{X}}). \tag{6}$$

Thus, for a nonsingular $\mathbf{G}_{cc}$, (2) is equivalent to

$$\mathbf{Q}\ddot{\mathbf{X}} = \mathbf{Q}\mathbf{m}^{-1}\mathbf{F}_X \tag{7}$$

with $\mathbf{Q} \equiv \mathbf{1} - \mathbf{m}^{-1}\mathbf{B}_c^T\mathbf{G}_{cc}^{-1}\mathbf{B}_c$. Since $\mathbf{Q}^2 = \mathbf{Q}$ and $\mathbf{B}_c\mathbf{Q} = \mathbf{0}$, $\mathbf{Q}$ is a projection operator from unconstrained dynamical space to the subspace, viz., the kernel of the linear operator corresponding to $\mathbf{B}_c$, that is orthogonal to the space spanned by the constrained degrees of freedom [12].

Now, we consider $\mathbf{X}_1 \equiv \mathbf{Q}\mathbf{X}$ and $\mathbf{Q}\mathbf{X}_1 = \mathbf{Q}^2\mathbf{X}$ at an arbitrary molecular configuration of $(\mathbf{X}, \dot{\mathbf{X}})$ with nonsingular $\mathbf{G}_{cc}$. Since $\mathbf{Q}^2 = \mathbf{Q}$, we have

$$\mathbf{0} = (\mathbf{Q}^2 - \mathbf{Q})\mathbf{X} = \mathbf{X}_1 - \mathbf{X} - \mathbf{m}^{-1}\mathbf{B}_c^T\mathbf{G}_{cc}^{-1}\mathbf{B}_c(\mathbf{X}_1 - \mathbf{X})$$
$$\Longleftrightarrow \mathbf{X}_1 = \mathbf{X} - \mathbf{m}^{-1}\mathbf{B}_c^T\mathbf{G}_{cc}^{-1}\mathbf{B}_c(\mathbf{X} - \mathbf{X}_1). \tag{8}$$

Since an infinitesimal displacement $\Delta\boldsymbol{\sigma}$ in internal constraints is nonlinearly related to a Cartesian displacement $\Delta\mathbf{X}$ in the neighborhood of $\mathbf{X}$ by

$$\Delta\boldsymbol{\sigma} = \mathbf{B}_c\Delta\mathbf{X} + \tfrac{1}{2}\Delta\mathbf{X}^T\mathbf{B}_{2c}\Delta\mathbf{X} + \cdots, \tag{9}$$

with $\boldsymbol{\sigma}_1$ being constraint values at $\mathbf{X}_1$, (8) is expressed by

$$\mathbf{X}_1 = \mathbf{X} - \mathbf{m}^{-1}\mathbf{B}_c^T\mathbf{G}_{cc}^{-1}(\boldsymbol{\sigma} - \boldsymbol{\sigma}_1) + \tfrac{1}{2}(\mathbf{X} - \mathbf{X}_1)^T\mathbf{m}^{-1}\mathbf{B}_c^T\mathbf{G}_{cc}^{-1}\mathbf{B}_{2c}(\mathbf{X} - \mathbf{X}_1) + \cdots \tag{10}$$

Setting $\boldsymbol{\sigma}_1$ to the internal constraint values $\mathbf{C}$ and considering only up to the first order terms of displacements in (10), the desired atomic coordinates satisfying (1) can be iteratively obtained from

$$\mathbf{X}_{\text{new}} = \mathbf{X}_{\text{old}} - \mathbf{m}^{-1}\mathbf{B}_{c,\text{old}}^T\mathbf{G}_{cc,\text{old}}^{-1}(\boldsymbol{\sigma}_{\text{old}} - \mathbf{C}), \tag{11}$$

where the iteration continues until a desired accuracy is reached for all constraints or to a specified number of iteration cycles N_{itr}. Similarly, setting $\dot{\boldsymbol{\sigma}}_1 \equiv \mathbf{B}_c\dot{\mathbf{X}}_1$ to $\dot{\mathbf{C}} = \mathbf{0}$ with $\dot{\mathbf{X}}_1 \equiv \mathbf{Q}\dot{\mathbf{X}}$ at $\mathbf{X}$, the desired equation to adjust atomic velocities is found to be

$$\dot{\mathbf{X}}_{\text{new}} = \dot{\mathbf{X}}_{\text{old}} - \mathbf{m}^{-1}\mathbf{B}_{c,\text{old}}^T\mathbf{G}_{cc,\text{old}}^{-1}\dot{\boldsymbol{\sigma}}_{\text{old}}. \tag{12}$$

In this case, due to the linear relation of $\mathbf{B}_c(\dot{\mathbf{X}} - \dot{\mathbf{X}}_1) = \dot{\boldsymbol{\sigma}} - \dot{\boldsymbol{\sigma}}_1$ from (3), one iteration cycle is enough for convergence to the desired values. In SHAKE, atomic velocities are not explicitly adjusted to satisfy (3) with such a process represented by (12) but are implicitly determined by the Verlet algorithm.

Meanwhile, the iterative formula (11) for coordinate adjustments can be derived in another way. Applying the Newton–Raphson method to (1), viz., considering only the first order displacement terms in (9), the resulting scheme is found to be

$$\mathbf{B}_{c,\text{old}}(\mathbf{X}_{\text{new}} - \mathbf{X}_{\text{old}}) = -(\boldsymbol{\sigma}_{\text{old}} - \mathbf{C}). \tag{13}$$

In view of the left-inverse of $\mathbf{B}_{c,\text{old}}$, for the nonredundant constraints with $N_c < 3p$, there are infinitely many solutions of (13):

$$\mathbf{X}_{\text{new}} - \mathbf{X}_{\text{old}} = -\mathbf{u}^{-1}\mathbf{B}_{c,\text{old}}^T(\mathbf{B}_{c,\text{old}}\mathbf{u}^{-1}\mathbf{B}_{c,\text{old}}^T)^{-1}(\boldsymbol{\sigma}_{\text{old}} - \mathbf{C}) \tag{14}$$

with $\mathbf{u}$ being an arbitrary nonsingular symmetric matrix [29]. However, the dynamic equations of motion (2) and (5) fix $\mathbf{u}$ to be $\mathbf{m}$, making (14) identical to (11). Our test on an octane molecule shows that the direct application of (11) slowly dissipates the system's kinetic energy, eventually freezing all atomic motions, though it

provides mathematically correct constrained values. A proper scheme for avoiding this problem, with an integration time step Δt, has to specifically incorporate coordinates at the preceding time step such as [16,25]

$$\mathbf{X}_{\text{new}}(\Delta t) = \mathbf{X}_{\text{old}}(\Delta t) - \mathbf{m}^{-1}\mathbf{B}_c^{\text{T}}(0)\mathbf{G}_{cc}^{-1}(0)\{\boldsymbol{\sigma}_{\text{old}}(\Delta t) - \mathbf{C}\}. \tag{15}$$

However, this scheme converges only for ranges in Δt less than a certain limit.

The iteration process of (15) and (12) does not require matrix inversion for $\mathbf{G}_{cc}^{-1}$ but solving linear equations related to $\mathbf{G}_{cc}$, e.g. for the scheme of (15)

$$\mathbf{G}_{cc}\boldsymbol{\Gamma} = \boldsymbol{\sigma} - \mathbf{C}. \tag{16}$$

For a symmetric positive definite matrix $\mathbf{G}_{cc}$, this can be solved by either a direct matrix method of Cholesky decomposition or an iterative (Jacobi, Gauss–Seidel, successive over-relaxation, preconditioned conjugate gradient, etc.) method [30,31]. Although the efficiency of the preconditioned conjugate gradient method is well-known [30], (16) can also be efficiently solved by the truncated series expansion method around the identity matrix [19]. Following this, with $\mathbf{D}$ being the diagonal matrix of its αth elements defined by $d^{\alpha} \equiv 1/\sqrt{G_{cc}^{\alpha\alpha}}$, the inverse matrix $\mathbf{G}_{cc}^{-1}$ can be approximated by [19]

$$\mathbf{G}_{cc}^{-1} = \mathbf{D}(\mathbf{D}\mathbf{G}_{cc}\mathbf{D})^{-1}\mathbf{D} = \mathbf{D}(\mathbf{1} - \mathbf{P})^{-1}\mathbf{D} \cong \mathbf{D}\left(\sum_{n=0}^{N_{\text{ord}}} \mathbf{P}^n\right)\mathbf{D}, \tag{17}$$

where the nonzero elements of the symmetric matrix $\mathbf{P}$ are given only for $\alpha \neq \beta$ by

$$P^{\alpha\beta} = -d^{\alpha}G_{cc}^{\alpha\beta}d^{\beta}. \tag{18}$$

However, with its accuracy depending on the largest power N_{ord}, the expansion of (17) is valid only when all eigenvalues of $\mathbf{P}$ are smaller than unity in absolute magnitude.

Alternatively, the matrix formulations (15) and (12) can be transformed, respectively, into direct iterative methods using diagonal elements of $\mathbf{G}_{cc}$: for the αth constraint

$$x_{\lambda,\text{new}}^k(\Delta t) = x_{\lambda,\text{old}}^k(\Delta t) - \frac{1}{m_{\lambda}}[\mathbf{B}_c(0)]_{\lambda^k}^{\alpha} \frac{\sigma_{\text{old}}^{\alpha}(\Delta t) - C^{\alpha}}{G_{cc}^{\alpha\alpha}(0)} \tag{19}$$

$$\dot{x}_{\lambda,\text{new}}^k = \dot{x}_{\lambda,\text{old}}^k - \frac{1}{m_{\lambda}}[\mathbf{B}_{c,\text{old}}]_{\lambda^k}^{\alpha} \frac{\dot{\sigma}_{\text{old}}^{\alpha}}{G_{cc,\text{old}}^{\alpha\alpha}}, \tag{20}$$

where the iteration converges as long as $\mathbf{G}_{cc}$ is a diagonally dominant matrix. Note that for constraints on internal coordinates the corresponding diagonal elements of $\mathbf{G}_{cc}$ depend only on constraint values and atomic masses [32], which, since constant in time, can be computed at the first time step and stored for efficient use in later time steps.

3. Derivation and implementation of WIGGLE

The new constrained MD scheme, WIGGLE, is based on the idea of utilizing the constraint parameters $\boldsymbol{\Lambda}(\Delta t)$ determined from the velocity adjustments for $\dot{\mathbf{X}}(\Delta t)$, rather than being put to zero and readjusted for $\mathbf{X}(2\Delta t)$ as in RATTLE, so as to keep the initial atomic positions for the next time step as close as possible to the desired constrained molecular geometry. RATTLE [6], which is based on the velocity Verlet scheme, can be expressed by

$$\mathbf{X}(\Delta t) = \mathbf{W}(\Delta t) - \frac{\Delta t^2}{2}\mathbf{m}^{-1}\mathbf{B}_c^{\text{T}}(0)\boldsymbol{\Lambda}(0) \tag{21}$$

$$\dot{\mathbf{X}}(\Delta t) = \dot{\mathbf{Z}}(\Delta t) - \frac{\Delta t}{2}\mathbf{m}^{-1}\mathbf{B}_c^{\text{T}}(\Delta t)\boldsymbol{\Lambda}(\Delta t), \tag{22}$$

with $\mathbf{W}(\Delta t)$ and $\dot{\mathbf{Z}}(\Delta t)$ being initial positions and velocities defined, respectively, by:

$$\mathbf{W}(\Delta t) \equiv \mathbf{X}(0) + \Delta t \dot{\mathbf{X}}(0) + \frac{\Delta t^2}{2} \mathbf{m}^{-1} \mathbf{F}_X(0) \tag{23}$$

$$\dot{\mathbf{Z}}(\Delta t) \equiv \dot{\mathbf{X}}(0) + \frac{\Delta t}{2} \ddot{\mathbf{X}}(0) + \frac{\Delta t}{2} \mathbf{m}^{-1} \mathbf{F}_X(\Delta t), \tag{24}$$

where atomic accelerations $\ddot{\mathbf{X}}$ are subject to (2) at each time step. However, instead of (23), WIGGLE adopts

$$\mathbf{W}(\Delta t) \equiv \mathbf{X}(0) + \Delta t \dot{\mathbf{X}}(0) + \frac{\Delta t^2}{2} \ddot{\mathbf{X}}(0), \tag{25}$$

which is closer to the desired constrained molecular geometry than (23) since (25) uses constrained atomic accelerations $\ddot{\mathbf{X}}$ rather than the unconstrained ones $\mathbf{m}^{-1}\mathbf{F}_X$ in (23). In this case, the vector of constraint parameters $\mathbf{\Lambda}(0)$ in (21), which is to be determined so that the $\mathbf{X}(\Delta t)$ satisfy the given constraint relations of (1), is different from the one defined in (2 and 5) at $\mathbf{X}(0)$. Since (25) itself supports a dynamics in Cartesian coordinates, the resulting $\mathbf{W}(\Delta t)$ from accurate $\dot{\mathbf{X}}(0)$ and $\ddot{\mathbf{X}}(0)$ is already a good approximation to the atomic positions for the next time step. Any position adjustment from this to $\mathbf{X}(\Delta t)$ during the time step Δt induces the velocity of $\{\mathbf{X}(\Delta t) - \mathbf{W}(\Delta t)\}/\Delta t$ that has to be additionally incorporated into (22). Thus, instead of (24), the initial WIGGLE velocities are given by

$$\dot{\mathbf{Z}}(\Delta t) \equiv \dot{\mathbf{X}}(0) + \frac{1}{\Delta t}\{\mathbf{X}(\Delta t) - \mathbf{W}(\Delta t)\} + \frac{\Delta t}{2}\ddot{\mathbf{X}}(0) + \frac{\Delta t}{2}\mathbf{m}^{-1}\mathbf{F}_X(\Delta t) = \dot{\mathbf{q}}(\Delta t) + \frac{\Delta t}{2}\mathbf{m}^{-1}\mathbf{F}_X(\Delta t) \tag{26}$$

with $\dot{\mathbf{q}}(\Delta t) \equiv \{\mathbf{X}(\Delta t) - \mathbf{X}(0)\}/\Delta t$. Although the accurate $\ddot{\mathbf{X}}(\Delta t)$ for $\mathbf{W}(2\Delta t)$ in the next time step is determined from solving (2 and 5), an effective alternative to this can be obtained from

$$\ddot{\mathbf{X}}(\Delta t) = \frac{2}{\Delta t}\{\dot{\mathbf{X}}(\Delta t) - \dot{\mathbf{q}}(\Delta t)\}, \tag{27}$$

which is derived from applying (26) to (22) and using (2), with $\dot{\mathbf{X}}(\Delta t)$ being the adjusted atomic velocities satisfying the hidden constraints.

In the first part of WIGGLE, the parameters $\mathbf{\Lambda}(0)$ in (21) can be iteratively determined as in RATTLE and SHAKE so that the resulting $\mathbf{X}(\Delta t)$ satisfy (1) within a specified limit:

$$\mathbf{\Lambda}_{\text{new}}(0) = \mathbf{\Lambda}_{\text{old}}(0) - \frac{2}{\Delta t^2}[\mathbf{B}_{c,\text{old}}(\Delta t)\mathbf{m}^{-1}\mathbf{B}_c^{\mathrm{T}}(0)]^{-1}\{\boldsymbol{\sigma}_{\text{old}}(\Delta t) - \mathbf{C}\}. \tag{28}$$

This is derived from the Taylor expansion of $\boldsymbol{\sigma}(\mathbf{X}(\Delta t))$ to the terms in Δt^2 with respect to $\mathbf{W}(\Delta t)$ [3] and is equivalent to the iterative position adjustments of

$$\mathbf{X}_{\text{new}}(\Delta t) = \mathbf{X}_{\text{old}}(\Delta t) - \mathbf{m}^{-1}\mathbf{B}_c^{\mathrm{T}}(0)[\mathbf{B}_{c,\text{old}}(\Delta t)\mathbf{m}^{-1}\mathbf{B}_c^{\mathrm{T}}(0)]^{-1}\{\boldsymbol{\sigma}_{\text{old}}(\Delta t) - \mathbf{C}\}. \tag{29}$$

Although (29) provides atomic positions closer to the desired constrained geometry than does (15), it requires computing $\mathbf{B}_c$ at each iteration cycle and also dealing with the nonsymmetric matrix $\mathbf{B}_{c,\text{old}}(\Delta t)\mathbf{m}^{-1}\mathbf{B}_c^{\mathrm{T}}(0)$ [16,25]. The worst possibility is that the diagonal elements of $\mathbf{B}_{c,\text{old}}(\Delta t)\mathbf{m}^{-1}\mathbf{B}_c^{\mathrm{T}}(0)$ may take zero values, thus, giving a singularity in (29), while those of the symmetric $\mathbf{G}_{cc}$ are positive definite for constraints on nonredundant internal coordinates. Specifically, for the αth distance type constraint of

$$\boldsymbol{\sigma}^{\alpha}(\mathbf{X}) = (\mathbf{x}_v - \mathbf{x}_\mu)^2 \equiv \mathbf{x}_{\mu v}^2 \equiv r_{\mu v}^2 = C^{\alpha}, \tag{30}$$

$[\mathbf{B}_{c,\text{old}}(\Delta t)\mathbf{m}^{-1}\mathbf{B}_c^{\mathrm{T}}(0)]^{\alpha\alpha}$ is zero when $\mathbf{x}_{\mu v,\,\text{old}}(\Delta t) \cdot \mathbf{x}_{\mu v}(0) = 0$, while $G_{cc}^{\alpha\alpha} = 4C^{\alpha}(1/m_\mu + 1/m_v)$ is nonzero constant in time. Although a modified scheme based on the nonlinear Newton iteration has been introduced to avoid this kind of singularity [23], the iterative method of (19) is an efficient alternative. In order to adjust positions for the αth constraints, it allows us to use the following singularity free expressions:

$$\mathbf{x}_{\mu,\text{new}}(\Delta t) = \mathbf{x}_{\mu,\text{old}}(\Delta t) + \frac{1}{m_\mu} \frac{\mathbf{x}_{\mu\nu}(0)\left\{r^2_{\mu\nu,\text{old}}(\Delta t) - C^\alpha\right\}}{2C^\alpha(1/m_\mu + 1/m_\nu)} \tag{31}$$

$$\mathbf{x}_{\nu,\text{new}}(\Delta t) = \mathbf{x}_{\nu,\text{old}}(\Delta t) - \frac{1}{m_\nu} \frac{\mathbf{x}_{\mu\nu}(0)\left\{r^2_{\mu\nu,\text{old}}(\Delta t) - C^\alpha\right\}}{2C^\alpha(1/m_\mu + 1/m_\nu)}. \tag{32}$$

Thus, the expression of $\mathbf{x}_{\mu\nu,\text{old}}(\Delta t) \cdot \mathbf{x}_{\mu\nu}(0)$ in the corresponding equations in the early SHAKE [3] and RAT-TLE [6] can be efficiently replaced by C^α. For constraints only on distances such as (30), the cross terms of $\mathbf{G}_{cc}$, given by $G^{\alpha\beta}_{cc} = 4\mathbf{x}_{\nu\mu} \cdot \mathbf{x}_{\nu\lambda}/m_\nu$ for $\alpha \neq \beta$, are nonzero only for constraints adjacent to each other with m_ν being the mass of the shared atom.

In the second part of WIGGLE, $\mathbf{\Lambda}(\Delta t)$ in (22) is adjusted from zero so that atomic velocities $\dot{\mathbf{X}}(\Delta t)$ at the adjusted atomic positions satisfy the hidden constraints with the initial velocities given by (26). This can also be used for a RATTLE scheme since the same expression is derivable from substituting (24) into (22). Note that, in the RATTLE process with $\dot{\mathbf{Z}}(\Delta t)$ defined by (24), any changes of $\mathbf{\Lambda}(0)$ in (21) for the adjustment of $\mathbf{X}(\Delta t)$ induce changes in $\dot{\mathbf{Z}}(\Delta t)$. However, using (26), we can avoid such subsequent adjusting of the initial atomic velocities from $\dot{\mathbf{X}}(0) + \Delta t \mathbf{m}^{-1}\mathbf{F}_X(0)/2$ at each position adjustment for $\mathbf{X}(\Delta t)$ in the conventional RATTLE [6] process. Due to the linearity of (3), the velocity adjustment can be accomplished in an iteration cycle. Applying $\mathbf{B}_c(\Delta t)$ to the right-hand side of (22) and imposing $\dot{\boldsymbol{\sigma}}(\Delta t) = \mathbf{0}$, the desired $\mathbf{\Lambda}(\Delta t)$ is found to be

$$\mathbf{\Lambda}(\Delta t) = \frac{2}{\Delta t}[\mathbf{G}_{cc}(\Delta t)]^{-1}\mathbf{B}_c(\Delta t)\dot{\mathbf{Z}}(\Delta t). \tag{33}$$

Substituting this into (22), the constrained velocities are found to be

$$\dot{\mathbf{X}}(\Delta t) = \dot{\mathbf{Z}}(\Delta t) - \mathbf{m}^{-1}\mathbf{B}^{\mathrm{T}}_c(\Delta t)[\mathbf{G}_{cc}(\Delta t)]^{-1}\mathbf{B}_c(\Delta t)\dot{\mathbf{Z}}(\Delta t) = \mathbf{Q}(\Delta t)\dot{\mathbf{Z}}(\Delta t), \tag{34}$$

where $\mathbf{Q}$ is the projection matrix defined in (7). Successive application of $\mathbf{Q}$ to the previously adjusted velocities corresponds to the matrix iteration of (12). In the case of imposing only distance type constraints of (30), the iterative scheme of (20) leads to

$$\dot{\mathbf{x}}_{\mu,\text{new}}(\Delta t) = \dot{\mathbf{x}}_{\mu,\text{old}}(\Delta t) + \frac{1}{m_\mu} \frac{\mathbf{x}_{\mu\nu}(\Delta t)\left\{\dot{\mathbf{x}}_{\mu\nu,\text{old}}(\Delta t) \cdot \mathbf{x}_{\mu\nu}(\Delta t)\right\}}{C^\alpha(1/m_\mu + 1/m_\nu)} \tag{35}$$

$$\dot{\mathbf{x}}_{\nu,\text{new}}(\Delta t) = \dot{\mathbf{x}}_{\nu,\text{old}}(\Delta t) - \frac{1}{m_\nu} \frac{\mathbf{x}_{\mu\nu}(\Delta t)\left\{\dot{\mathbf{x}}_{\mu\nu,\text{old}}(\Delta t) \cdot \mathbf{x}_{\mu\nu}(\Delta t)\right\}}{C^\alpha(1/m_\mu + 1/m_\nu)}. \tag{36}$$

An explicit WIGGLE scheme consists of the following:

(i) Routine for the first time step:
   (a) Given $\mathbf{X}_0$, $\dot{\mathbf{X}}_0$; compute $\mathbf{F}_{X0} \equiv -\partial_{\mathbf{X}_0}V$.
   (b) Set $\dot{\mathbf{Z}}_0 = \dot{\mathbf{X}}_0$ and adjust $\dot{\mathbf{X}}_0$ in (22) to satisfy (3), if necessary.
   (c) Solve (5) and (2) for $\ddot{\mathbf{X}}_0$.
   (d) Set $\mathbf{W}_1 = \mathbf{X}_0 + \Delta t(\dot{\mathbf{X}}_0 + \Delta t\ddot{\mathbf{X}}_0/2)$.
   (e) Adjust $\mathbf{X}_1$ in (21) from $\mathbf{W}_1$ to satisfy (1).
   (f) Set $\dot{\mathbf{q}}_1 = (\mathbf{X}_1 - \mathbf{X}_0)/\Delta t$.

(ii) Routine for the $(k + 1)$th time step $(k > 0)$:
   (a) Compute $\mathbf{F}_{Xk} \equiv -\partial_{\mathbf{X}_k}V$.
   (b) Set $\dot{\mathbf{Z}}_k = \dot{\mathbf{q}}_k + \Delta t\mathbf{m}^{-1}\mathbf{F}_{Xk}(\Delta t)/2$.
   (c) Adjust $\dot{\mathbf{X}}_k$ in (22) from $\dot{\mathbf{Z}}_k$ to satisfy (3).
   (d) Set $\mathbf{W}_{k+1} = \mathbf{X}_k + \Delta t(2\dot{\mathbf{X}}_k - \dot{\mathbf{q}}_k)$.

(e) Adjust $\mathbf{X}_{k+1}$ in (21) from $\mathbf{W}_{k+1}$ to satisfy (1).
(f) Set $\dot{\mathbf{q}}_{k+1} = (\mathbf{X}_{k+1} - \mathbf{X}_k)/\Delta t$.
(g) Go to (a) with $k = k + 1$.

The above (c) and (d) procedures in the first time step can be simplified by $\mathbf{W}_1 = \mathbf{X}_0 + \Delta t(\dot{\mathbf{X}}_0 + \Delta t\mathbf{m}^{-1}\mathbf{F}_{X0}/2)$, as in the RATTLE scheme, which avoids both computing $\mathbf{B}_{2c}$ and solving (5).

4. Application to octane

Some simulation results on an isolated octane molecule are listed in Table 1. Computations were done on a single node (512 MB of memory and 1.2 GHz processing speed) of a LINUX cluster, using the SDFF

Table 1
Results from constrained dynamics for an isolated octane molecule

	N_{itr}; N_{ord}[b]	E (kcal/mol)	Temperature (K)	δ_i[c] (Å)	δ_f[c] (Å)	CPU (s)
W-DI[a]	1	45.34 ± 0.12	296.0 ± 38.8	6.97×10^{-4}	9.89×10^{-6}	395.08
	2	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	8.68×10^{-8}	395.55
	3	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	5.59×10^{-10}	395.95
W-CD	1	45.34 ± 0.12	295.7 ± 37.9	6.80×10^{-4}	2.35×10^{-6}	402.30
	2	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	1.17×10^{-8}	403.05
	3	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	7.11×10^{-11}	404.57
W-CG	1	45.34 ± 0.12	295.8 ± 38.3	6.83×10^{-4}	2.68×10^{-6}	396.28
	2	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	8.22×10^{-8}	396.73
	3	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	3.03×10^{-9}	397.11
W-SE	1; 2	45.35 ± 0.12	295.8 ± 38.4	6.82×10^{-4}	2.71×10^{-6}	395.43
	1; 4	45.34 ± 0.12	295.7 ± 37.9	6.80×10^{-4}	2.35×10^{-6}	395.55
	1; 6	45.34 ± 0.12	295.7 ± 37.9	6.80×10^{-4}	2.35×10^{-6}	395.67
	2; 2	45.31 ± 0.12	295.5 ± 39.2	6.79×10^{-4}	1.55×10^{-8}	395.72
	2; 4	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	1.17×10^{-8}	395.85
	2; 6	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	1.17×10^{-8}	395.96
	3; 2	45.31 ± 0.12	295.5 ± 39.2	6.79×10^{-4}	1.05×10^{-10}	396.14
	3; 4	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	7.11×10^{-11}	396.28
	3; 6	45.31 ± 0.12	295.5 ± 39.2	6.80×10^{-4}	7.11×10^{-11}	396.39
R-DI	1	45.27 ± 0.12	293.5 ± 38.9	5.18×10^{-3}	8.02×10^{-5}	395.36
	2	45.31 ± 0.12	295.5 ± 38.1	5.12×10^{-3}	5.78×10^{-7}	395.81
	3	45.31 ± 0.12	295.6 ± 39.2	5.10×10^{-3}	3.54×10^{-9}	396.32
R-SE	1; 4	45.19 ± 0.13	294.0 ± 38.0	5.02×10^{-3}	1.61×10^{-5}	395.44
	2; 4	45.31 ± 0.12	295.5 ± 39.2	5.04×10^{-3}	7.52×10^{-8}	395.76
	3; 4	45.31 ± 0.12	295.5 ± 39.2	5.04×10^{-3}	4.54×10^{-10}	396.19
S-DI	1	45.57 ± 0.13	298.0 ± 40.2	1.03×10^{-2}	1.62×10^{-4}	394.64
	2	45.63 ± 0.11	293.7 ± 39.4	1.02×10^{-2}	1.12×10^{-6}	395.10
	3	45.63 ± 0.11	296.3 ± 39.7	1.01×10^{-2}	6.79×10^{-9}	395.43
S-SE	1; 4	45.37 ± 0.17	295.1 ± 38.9	1.00×10^{-2}	3.15×10^{-5}	394.86
	2; 4	45.62 ± 0.11	295.7 ± 37.9	1.01×10^{-2}	1.41×10^{-7}	395.38
	3; 4	45.63 ± 0.11	294.9 ± 38.4	9.99×10^{-3}	7.38×10^{-10}	395.82

[a] W, WIGGLE; R, RATTLE; S, SHAKE; DI, direct iteration; CG, conjugate gradient; SE, series expansion.
[b] N_{itr}, number of iteration cycles; N_{ord}, number of the highest power in SE method.
[c] δ_i and δ_f = average initial and final deviation, respectively, from the desired constrained length (1.08 Å) of each C–H bond.

force field for hydrocarbon chains optimized to reproduce ab initio structures, energies, and vibrational frequencies [33]. Only the C–H bonds were constrained (to 1.08 Å), since some C–C stretching frequencies are within the range of some angle bending frequencies. Instead of the constraint equations of (30), the actual bond distance constraints of $\sqrt{\mathbf{x}_{\mu\nu}^2} = r_{\mu\nu} = C^\alpha$ were used. The system's temperature was slowly increased from zero to room temperature by scaling atomic velocities to give a temperature change of 5 K at each 200 time steps if the average temperature was outside a specified range from the desired temperature, resulting in atomic velocities corresponding to an average temperature of 301.2 K. Unless the initial linear and angular momenta are zero, such scaling in Cartesian velocities usually introduces artificial changes in translational and rotational energy [34,35]. From this velocity set, we removed the angular momentum about the center of mass by using the method presented in Appendix A, obtaining the initial atomic velocity set to be applied to the octane molecule. Data shown in Table 1 are averaged over 5000 steps starting from the second step with $\Delta t = 2$ fs, except for CPU times which are measured for 100,000 steps. The CPU time for a given computation routine depends on the computer, compiler, and options. Our calculations also showed an inherent fluctuation of about 1 s during the repeated simulations, and the CPU times are averaged from five different runs.

The first part of Table 1 is for the WIGGLE (W) process for different methods of solving the related linear equations: direct iteration (DI) based on (19) and (20), Cholesky decomposition (CD) with (15) and (16), conjugate gradient (CG) method, and the series expansion (SE) method of (17). Specifically, the CG method we used was preconditioned by diagonal elements of $\mathbf{G}_{cc}$ with a tolerance of 10^{-7} for the weighted square of the residual [30]. However, there were no convergence criteria imposed in other methods except for N_{itr} or N_{ord}. We observed that W-DI and W-SE perform almost equally and they are slightly more efficient than W-CD and W-CG. However, both the DI and SE methods were found to be nonconvergent for constraining all nonredundant bond angles in addition to all bond lengths. In the WIGGLE simulations, the rms fluctuations in the angular momentum about the center of mass were found to be less than 10^{-12} in the 5000 steps.

The second and third parts of Table 1 are for RATTLE (R) and SHAKE (S), respectively. In the RATTLE process, we have simplified the procedure, based on (26). The average initial deviation δ_i from the desired constrained bond length is almost an order of magnitude smaller in WIGGLE for a given N_{itr} or N_{ord} than in RATTLE. A similar trend is also observed in the average final deviation δ_f from the constrained values. The CPU times spent in the SHAKE processes, which skip the velocity adjustments for the hidden constraints, is smaller than those of RATTLE and WIGGLE. However, differences in the computational cost among WIGGLE, RATTLE, and SHAKE for a single octane molecule are negligible compared to the dominant CPU time of 394.57 s spent on calculating energies and forces only, which is almost the same as that of S-DI with $N_{\text{itr}} = 1$.

5. Concluding remarks

The proposed constrained MD scheme, WIGGLE, provides both initial and final constrained values that are an order of magnitude closer to the desired values than those in RATTLE. This is because, in determining the initial new atomic positions for the next time step, WIGGLE utilizes the constrained accelerations derived from velocity adjustments to satisfy the hidden constraints, while RATTLE and SHAKE use the unconstrained accelerations from forces without any constraints. Since the SHAKE scheme involves no adjustments of atomic velocities required in WIGGLE and RATTLE, it uses less CPU time than WIGGLE and RATTLE. However, the differences in pure algorithmic efficiency among WIGGLE, RATTLE, and SHAKE are negligible compared to the dominant computational cost in calculating energies and forces. As in the case for SHAKE and RATTLE, WIGGLE also conserves the system's angular momentum if the potential energy and constraint equations are invariant under external rotations [36].

Appendix A. Constraining angular momentum

It is useful to investigate an efficient method to remove a system's angular momentum $\mathbf{L}$ about the center of mass $\mathbf{R}_{cm}$ from a given set of atomic velocities or to carry out complete dynamic processes that keep $\mathbf{L}$ constant at an initial value $\mathbf{C}_L$. We present an efficient method to accomplish this, different from the previous approaches [10,37] that are based on the Eckart condition. With $\mathbf{y}_\lambda \equiv \mathbf{x}_\lambda - \mathbf{R}_{cm}$, the constraint equations to be dealt with can be expressed by

$$\mathbf{L}(\mathbf{X}, \dot{\mathbf{X}}) = \sum_{\lambda=1}^{p} m_\lambda \mathbf{y}_\lambda \times \dot{\mathbf{x}}_\lambda = \mathbf{C}_L. \tag{a1}$$

In order to derive equations of motion that contain atomic accelerations under the constraints of (a1), one requires only the first derivative of (a1) with respect to time [38]

$$\dot{\mathbf{L}}(\mathbf{X}, \dot{\mathbf{X}}) = [\partial_{\dot{\mathbf{X}}} \mathbf{L}]\ddot{\mathbf{X}} = \sum_{\lambda=1}^{p} m_\lambda \mathbf{y}_\lambda \times \ddot{\mathbf{x}}_\lambda = \mathbf{0}, \tag{a2}$$

since $[\partial_{\mathbf{X}} \mathbf{L}]\dot{\mathbf{X}} = \mathbf{0}$. In the case of the additional internal constraints of (1), the resulting equations of motion have the same form as (2) with [9,22]

$$\mathbf{B}_c \equiv \begin{pmatrix} \partial_{\mathbf{X}} \boldsymbol{\sigma} \\ \partial_{\dot{\mathbf{X}}} \mathbf{L} \end{pmatrix} \tag{a3}$$

$$\mathbf{G}_{cc}\boldsymbol{\Lambda} \equiv \mathbf{B}_c \mathbf{m}^{-1}\mathbf{F}_X + \begin{pmatrix} \dot{\mathbf{X}}^{\mathrm{T}}[\partial_{\mathbf{X}}^2 \boldsymbol{\sigma}]\dot{\mathbf{X}} \\ [\partial_{\mathbf{X}} \mathbf{L}]\dot{\mathbf{X}} \end{pmatrix} = \mathbf{B}_c \mathbf{m}^{-1}\mathbf{F}_X + \begin{pmatrix} \dot{\mathbf{X}}^{\mathrm{T}}[\partial_{\mathbf{X}}^2 \boldsymbol{\sigma}]\dot{\mathbf{X}} \\ \mathbf{0} \end{pmatrix}. \tag{a4}$$

With I_{cm}^{ij} being elements of the inertia tensor about the center of mass, the corresponding new terms in $\mathbf{G}_{cc} \equiv \mathbf{B}_c \mathbf{m}^{-1}\mathbf{B}_c^{\mathrm{T}}$ are found to be:

$$G_{cc}^{ij} = \sum_{\lambda=1}^{p} m_\lambda (\mathbf{y}_\lambda^2 \delta^{ij} - y_\lambda^i y_\lambda^j) = I_{cm}^{ij}, \tag{a5}$$

$$G_{cc}^{i\alpha} = (\partial_{\dot{\mathbf{X}}} L^i)\mathbf{m}^{-1}(\partial_{\mathbf{X}} \boldsymbol{\sigma}^\alpha)^{\mathrm{T}} = \sum_{\lambda=1}^{p} (\mathbf{y}_\lambda \times \partial_{\mathbf{x}_\lambda} \boldsymbol{\sigma}^\alpha)^i = 0. \tag{a6}$$

This results from the orthogonality of internal constraints to external rotations [39].

Therefore, instead of (12), the desired atomic velocities can be adjusted from a given set of initial values by using

$$\dot{\mathbf{X}}_{new} = \dot{\mathbf{X}}_{old} - \mathbf{m}^{-1}\mathbf{B}_{c,old}^{\mathrm{T}}\mathbf{G}_{cc,old}^{-1}\begin{pmatrix} \dot{\boldsymbol{\sigma}} \\ \mathbf{L} - \mathbf{C}_L \end{pmatrix}, \tag{a7}$$

since $[\partial_{\dot{\mathbf{X}}} \mathbf{L}]\dot{\mathbf{X}} = \mathbf{L}$. Since internal constraints are orthogonal to the external rotations, the process for velocity adjustments can be separated between internal and external constraints. Thus, either before or after adjusting velocities only for internal constraints with (12), the process for angular momentum constraints can be carried out for all atomic velocities by

$$\dot{\mathbf{x}}_{\lambda,\text{new}} = \dot{\mathbf{x}}_{\lambda,\text{old}} + \mathbf{y}_\lambda \times \mathbf{S}, \tag{a8}$$

with $\mathbf{S}$ being the solution vector of $\mathbf{I}_{cm}\mathbf{S} = \mathbf{L} - \mathbf{C}_L$. An equivalent equation to (a8) can also be found elsewhere [40]. Because the angular momentum constraints are to be used in the adjustments of atomic velocities, they should be excluded from the process of adjusting atomic positions.

Appendix B. Energy drift

The stability of a numerical algorithm is closely related to its capability of long time simulations for a dynamical system. For a general constrained Cartesian integration scheme, it is therefore of interest to compute even an approximate change in the system's total energy during an integration time step and to determine the factors affecting the system's stability. This is because a local energy drift in each time step will eventually affect the global stability depending on whether the local error is cumulative or not for many integration steps.

As a general numerical integration scheme for (2), we consider

$$\mathbf{X}(\Delta t) = \mathbf{X}(0) + \Delta t \alpha \dot{\mathbf{X}}(0) + \Delta t^2 \left\{ \beta \ddot{\mathbf{X}}(0) + \gamma \ddot{\mathbf{X}}(\Delta t) \right\} \tag{b1}$$

$$\dot{\mathbf{X}}(\Delta t) = \dot{\mathbf{X}}(0) + \Delta t \left\{ \varepsilon \ddot{\mathbf{X}}(0) + \omega \ddot{\mathbf{X}}(\Delta t) \right\}, \tag{b2}$$

where α, β, γ, ε, and ω are appropriate constants, and variables $\mathbf{X}(0)$, $\dot{\mathbf{X}}(0)$, and $\ddot{\mathbf{X}}(0)$ are assumed to satisfy (2)–(5) with suitable constraint force parameters $\mathbf{\Lambda}(0)$. The WIGGLE scheme presented in Section 3 can also be modified for an arbitrary set of α, β, γ, ε, and ω. With the kinetic energy T being given by

$$T = \tfrac{1}{2}\dot{\mathbf{X}}^{\mathrm{T}}\mathbf{m}\dot{\mathbf{X}}, \tag{b3}$$

the system's total energy, $E \equiv T + V_c$, at $\mathbf{X}(\Delta t)$ can be Taylor expanded with respect to $\mathbf{X}(0)$ by

$$E(\Delta t) = E(0) + \Delta t E^{(1)}(0) + \frac{\Delta t^2}{2}E^{(2)}(0) + \frac{\Delta t^3}{6}E^{(3)}(0) + \cdots \tag{b4}$$

In view of (b1), since $\ddot{\mathbf{X}}(\Delta t)$ is expanded as

$$\ddot{\mathbf{X}}(\Delta t) = \ddot{\mathbf{X}}(0) + \Delta t \alpha [(\dot{\mathbf{X}}^{\mathrm{T}}\partial_{\mathbf{X}})\ddot{\mathbf{X}}](0) + \cdots \tag{b5}$$

the coefficients $E^{(1)}$ and $E^{(2)}$ are found to be, respectively

$$E^{(1)} = \alpha\dot{\mathbf{X}}^{\mathrm{T}}\left\{ \alpha\partial_{\mathbf{X}}V_c + (\varepsilon + \omega)\mathbf{m}\ddot{\mathbf{X}} \right\} = (\alpha - \varepsilon - \omega)\dot{\mathbf{X}}^{\mathrm{T}}\partial_{\mathbf{X}}V_c \tag{b6}$$

$$E^{(2)} = \left\{ 2(\beta + \gamma) - (\varepsilon + \omega)^2 \right\}\ddot{\mathbf{X}}^{\mathrm{T}}\partial_{\mathbf{X}}V_c + \alpha(\alpha - 2\omega)\dot{\mathbf{X}}^{\mathrm{T}}[\partial_{\mathbf{X}}^2 V_c]\dot{\mathbf{X}}, \tag{b7}$$

where the constrained equations of motion (2) are used. These contributions will be zero if $\alpha = \varepsilon + \omega = 2\omega$ and $2(\beta + \gamma) = \alpha^2$, and (b4) is then found to be

$$E(\Delta t) = E(0) + \frac{\Delta t^3}{12}\left\{ 3\alpha(4\gamma + \alpha^2)\ddot{\mathbf{X}}^{\mathrm{T}}[\partial_{\mathbf{X}}^2 V_c]\dot{\mathbf{X}} - \alpha^3\dot{\mathbf{X}}^{\mathrm{T}}[(\dot{\mathbf{X}}^{\mathrm{T}}\partial_{\mathbf{X}})(\partial_{\mathbf{X}}^2 V_c)]\dot{\mathbf{X}} \right\}(0) + \cdots \tag{b8}$$

The Δt^3 term in (b8) represents the smallest energy drift during an integration time step for the dynamical scheme of (b1) and (b2), including the velocity Verlet scheme [27] ($\alpha = 1$, $\beta = \varepsilon = \omega = 1/2$, $\gamma = 0$). If the constraint forces are too inaccurate to hold for (2), then the first order term of (b6) may destroy the system's stability.

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