Integration methods for molecular dynamics*

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Abstract

Classical molecular dynamics simulation of a macromolecule requires the use of an efficient time-stepping scheme that can faithfully approximate the dynamics over many thousands of timesteps. Because these problems are highly nonlinear, accurate approximation of a particular solution trajectory on meaningful time intervals is neither obtainable nor desired, but some restrictions, such as *symplecticness*, can be imposed on the discretization which tend to imply good long term behavior. The presence of a variety of types and strengths of interatom potentials in standard molecular models places severe restrictions on the timestep for numerical integration used in explicit integration schemes, so much recent research has concentrated on the search for alternatives that possess (1) proper dynamical properties, and (2) a relative insensitivity to the fastest components of the dynamics. We survey several recent approaches.

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1 Introduction

For classical molecular dynamics (MD) of macromolecules such as nucleic acids, proteins and polymers, atomic trajectories obey Newton's second law of motion:

$$M\frac{d^2}{dt^2}q = -\nabla_q V(q), \tag{1}$$

where q is vector containing all positions (in cartesian coordinates), M is a diagonal matrix of atomic masses with each mass replicated thrice, and $V(q)$ is the (empirical) potential energy function. Standard numerical schemes for simulating the dynamical behavior of a macromolecule are based on discrete timestepping. When the number of atoms is large, we need a fast method to calculate electrostatic interactions at each step, and we need parallelism, preferably scalable parallelism, but it is not enough to be able to take fast time steps for microsecond to millisecond dynamics: ways must be found to increase the length of the timesteps.

These systems are highly nonlinear and have the hallmarks of chaos. In particular, they exhibit sensitive dependence on perturbations. For example, numerical experiments in [1] show that tiny perturbations introduced into the trajectories are doubled about every picosecond meaning that even with double precision (about 15 digits of precision) the trajectory would be overwhelmed by the effects of roundoff error after just fifty picoseconds of simulation. Moreover, it is typical to use random values for initial velocities. Thus for long-time integrations, accuracy with respect to a particular trajectory is neither desired nor obtainable. Instead, what is sought is generic or representative behavior of the system, or in some cases good sampling of phase space.

The variety of types and strengths of terms in the potential function for a biomolecule complicates numerical simulation. These problems involve *multiple time scales*. In most cases, the primary restriction on timestep comes from the presence of the strong chemical bonds (which contribute high-frequency components to the motion). Occasionally, the word "stiff" is used to describe the problem with multiple scales, but this usage is nonstandard, and may confuse the issue. Strictly speaking, the term "stiff" implies that we are seeking particular trajectories of the system that are smoother than nearby trajectories. However, due to the ergodic nature of the differential equations for MD, no trajectory can be smoother than its neighbors for more than a short time interval. In the sequel, we will sometimes use the terms "fast modes" or "high frequency components," to refer to components of *linearized* dynamics.

The numerical integration schemes of molecular dynamics roughly divide into four categories according to their handling of these critical "fast" modes:

(i) Methods that accurately resolve the highest frequencies, e.g. explicit methods (with small timesteps), including multiple time stepping and the method LIN [47].

(ii) Methods which inaccurately resolve the highest frequencies: e.g. the implicit midpoint method with large timestep Δt. Although to date apparently not used in MD, this method has recently been employed for other problems in nonlinear dynamics, e.g. for rigid and elastic bodies [38].

(iii) Methods based on removal of the fast components through the introduction of constraints, including SHAKE [34] and RATTLE[2].

(iv) Methods which attempt to suppress the fast components, e.g. the method LI [29], which introduces dissipation via the implicit Euler scheme to enable larger timesteps and balances this with a random noise term to maintain the desired temperature.

Traditionally, numerical integrators have been analyzed in terms of their *stability* and *accuracy*. In standard usage, "stability" means boundedness with respect to perturbations, and "accuracy" means accuracy with respect to a given trajectory; these concepts are of limited practical value for the treatment of nonlinear dynamics on long time intervals, due to the sensitive dependence on initial conditions. Although it is found that classical stability and local accuracy are prerequisite for a given integrator to function well in molecular dynamics, these standard concepts are inadequate for gauging its effectiveness.

An alternative point of view is to attempt to show that the numerically computed trajectory is close to *some* true trajectory of the physical problem (i.e., starting from perturbed initial values), but obtaining such a *shadowing* property even for relatively simple systems has so far proven very difficult, despite many attempts. Still another approach is to attempt to show that the numerical trajectory is close to some true trajectory of a *nearby system of differential equations*, preferably one with dynamical properties similar to those of the original system. This is similar to the viewpoint of *backward error analysis* introduced by J.H. Wilkinson to study the algorithms of numerical linear algebra.

An important feature of Newton's equations (1) is that they can be viewed as a Hamiltonian system, i.e. they can be put in the form $\dot{q} = \nabla_p H$, $\dot{p} = -\nabla_q H$, for some smooth energy function $H = H(q,p)$. A certain category of differential invariants, the *symplectic* invariants, is associated with a Hamiltonian system. It is sensible to consider a *symplectic discretization* which preserves the same class of invariants. Much recent interest in symplectic discretization schemes for Hamiltonian systems emanates from fundamental results establishing the "backward error" point of view (i.e., the numerical flow generated by a symplectic discretization of a Hamiltonian system is the exact flow of a nearby Hamiltonian system). The practical ramifications of symplecticness for general Hamiltonian systems or for molecular dynamics are still not completely clear, but symplectic methods have proven to be important in related problems, such as long term simulation of the solar system [46] and for the design of particle accelerators [13].

The main goals of this article are first to discuss current approaches to time discretization, in particular the popular leapfrog/Verlet integrator, and, second, to sketch some alternatives that may permit the taking of longer timesteps. The first part of the paper is concerned primarily with the issue of numerical stability and correct long time behavior, particular attention being given to symplectic integration:

2. Numerical time-stepping schemes: leapfrog/Verlet

3. Symplectic discretizations

4. Alternatives to leapfrog/Verlet

The second part of the paper addresses the computational costs associated with high frequency components of trajectories. The idea of multiple time steps is to use an overall long time step with shorter time steps only for selected interactions. We can manage with even less computation if we are willing to accept less in terms of accuracy—e.g., some kind of smoothed solution—and this is apparently possible with constrained dynamics. These ideas constitute the remaining sections:

5. Multiple time stepping

6. Constrained dynamics

2 The leapfrog/Verlet scheme

For the molecular dynamics problem, the Hamiltonian takes the form $H(q,p) = T(p) + V(q)$ where the kinetic energy $T(p) = \frac{1}{2}p^T M^{-1} p$, so the corresponding equations of motion are

$$\frac{d}{dt}q = M^{-1}p, \quad \frac{d}{dt}p = -\nabla_q V(q). \tag{2}$$

The pair $(q(t), p(t))$ specifies a point in *phase space*, a $6N$ dimensional Euclidean space where N is the number of particles. These values determine the state of the system at a time t and from these one can in principle uniquely determine the values $(q(t+\Delta t), p(t+\Delta t))$ at some later time $t+\Delta t$. This mapping from the earlier to later set of values we call the Δt-flow of the system, and it will be handy to denote it by $\phi_{\Delta t,H}$. Hence,

$$\phi_{\Delta t,H}(q(t), p(t)) = (q(t+\Delta t), p(t+\Delta t)),$$

where (q,p) solves the Hamiltonian system (2).

The purpose of an integration method is to approximate the flow $\phi_{\Delta t,T+V}$. Many popular explicit methods are obtained by *splitting*: e.g., the Strang [41] splitting gives

$$\phi_{\Delta t,T+V} = \phi_{\Delta t/2,V} \circ \phi_{\Delta t,T} \circ \phi_{\Delta t/2,V} + O(\Delta t^3). \tag{3}$$

where $\circ$ denotes composition of mappings. The idea here is to replace the generally intractable computation of the flow of the original system by a sequence of systems that are analytically integrable. For example the flow $\phi_{\Delta t/2,V}$ is obtained by solving

$$\frac{d}{dt}q = 0, \quad \frac{d}{dt}p = -\nabla_q V(q).$$

If we let

$$q(t_n) = q_n, \quad p(t_n) = p_n,$$

denote the current location in phase space, the solution is trivially

$$q(t) \equiv q_n, \quad p(t) = p_n + (t - t_n)(-\nabla_q V(q_n)),$$

and integration for an interval $\Delta t/2$ yields the new value

$$p_{n+1/2} = p_n + (\Delta t/2)(-\nabla_q V(q_n)).$$

The approximation suggested by eq. (3) is merely a formal way of expressing the very popular leapfrog/Verlet method: We begin the step with values q_n, p_n, and $F_n = -\nabla_q V(q_n)$ obtained from the previous step. Then we compute

$\phi_{\Delta t/2,V}$, "half a kick":

$$p_{n+1/2} = p_n + \frac{\Delta t}{2} F_n,$$

$\phi_{\Delta t,T}$, "drift":

$$q_{n+1} = q_n + \Delta t M^{-1} p_{n+1/2},$$

$\phi_{\Delta t/2,V}$, "half a kick":

$$\begin{aligned} F_{n+1} &= -\nabla_q V(q_{n+1}) \\ p_{n+1} &= p_{n+1/2} + \frac{\Delta t}{2} F_{n+1}. \end{aligned}$$

The physical interpretation is that two impulses of equal size are imparted to the particles just before and just after each time point t_n and that between these time points the particles just drift with constant velocity.

A contribution to the error of order Δt^3 is introduced at each step of leapfrog integration. A standard stability result shows that the accumulated error over a fixed time interval is then bounded by $K\Delta t^2$ for Δt sufficiently small. The constant K in this formula grows exponentially with the length of the time interval; for molecular dynamics applications it may be very large.

Numerical integration methods can be analyzed to determine the extent to which they possess correct long-time behavior. A detailed analysis is possible for the harmonic oscillator:

$$\frac{dq}{dt} = p, \tag{4}$$

$$\frac{dp}{dt} = -\omega^2 q. \tag{5}$$

Correct behavior for the harmonic oscillator seems to be a necessary property for success in MD simulations, even if it is not sufficient. The oscillator gives insight into the vibrational behavior of bond lengths and bond angles in MD problems.

Analytically, if we plot $p(t)$ versus $\omega q(t)$ we get a circular orbit in phase in which we have a rotation by $\omega\Delta t$ for every timestep of the solution. One step of Verlet gives instead [39]

$$\begin{bmatrix} \omega q_{n+1} \\ p_{n+1} \end{bmatrix} = D \begin{bmatrix} \cos\theta & \sin\theta \\ -\sin\theta & \cos\theta \end{bmatrix} D^{-1} \begin{bmatrix} \omega q_n \\ p_n \end{bmatrix}$$

where

$$\theta = 2\text{arcsin}\frac{\omega\Delta t}{2}$$

and

$$D = \text{diag}(1, \cos\frac{\theta}{2}),$$

provided that $\omega\Delta t \leq 2$. Thus we have for the Verlet method (i) a slight stretching (ii) followed by a rotation in error by $O((\omega\Delta t)^3)$ (ii) followed by a slight shrinking.

In a sequence of Verlet steps the intermediate stretchings and shrinkings all cancel. This does not happen though if the method or the timestep is varied. The restriction $\omega\Delta t \leq 2$, which is necessary for stability, is the weakest restriction of any conventional explicit method [11].

An important property of the Verlet method is that it is *symplectic*. We will now describe this property.

3 Symplectic discretizations

In two dimensions, a mapping is symplectic if it is *area preserving*: any bounded region is mapped to another region of equal area. In higher dimensions, symplecticness is still a geometrical property, although somewhat more difficult to state. Denote a point in $\mathbf{R}^{2m}$ by $(q^1, q^2, \ldots, q^m, p^1, p^2, \ldots, p^m)$ Consider the m projections of a two-dimensional oriented surface D onto the $q^i p^i$-coordinate planes, and then sum the oriented areas of these projections to get a number $\mu(D)$. A mapping ϕ of $\mathbf{R}^{2m}$ is symplectic if $\mu(\phi(D)) = \mu(D)$ for every 2 dimensional oriented surface D. It can be demonstrated that a consequence of this property is preservation of volume.

The Δt-flow $\phi_{\Delta t,H}$ of a Hamiltonian system is always μ-preserving, hence symplectic. In the context of flows of Hamiltonian systems, the invariant $\mu(D)$ is referred to as the Poincaré integral invariant.

The geometric definition of symplecticness can be replaced by an algebraic one. Let $\Phi = \Phi(x)$ denote the Jacobian matrix of a mapping $\phi : \mathbf{R}^{2n} \to \mathbf{R}^{2n}$. ϕ is symplectic if

$$\Phi(x)^T J \Phi(x) \equiv J,$$

where J is the $2m \times 2m$ skew-symmetric "symplectic structure matrix:"

$$J = \left[\begin{array}{cc} 0 & I \\ -I & 0 \end{array} \right].$$

For demonstrating symplecticness of complicated mappings, it is sometimes convenient to use the language of differentials: a mapping is said to be symplectic if it preserves the "2-form" $dp \wedge dq = \sum_{i=1}^{m} dp^i \wedge dq^i$. (The algebra of exterior products of differentials can then be used to simplify the calculations.)

A discretization of (2) can be viewed as a mapping $\psi_{\Delta t}$ of phase space that approximates the flow map $\phi_{\Delta t,H}$. Since, as we have seen, the symplecticness of the flow map of an Hamiltonian system is such a strong condition, it is natural to seek discretizations which also possess this property. Recently, a great deal of work on symplectic discretizations has been undertaken (see e.g. [36] for a survey). Much of the motivation for this work comes from the following backward error argument: if a symplectic discretization is applied to approximate the Δt-flow $\phi_{\Delta t,H}$, then the numerical map $\psi_{\Delta t}$ is exactly the Δt-flow of a perturbed Hamiltonian:

$$\psi_{\Delta t} \equiv \phi_{\Delta t,\tilde{H}},$$

where (with r the order of the method)

$$\tilde{H} = H + \Delta t^r H_r + \Delta t^{r+1} H_{r+1} + \cdots$$

for some functions H_i, $i \geq r$.

The sense in which $\tilde{H}$ is "close" to H is complicated. In particular, the formal series expansion for $\tilde{H}$ need not converge.

An interesting theorem due to Ge and Marsden [16] states roughly that for a generic Hamiltonian system, a symplectic method cannot exactly conserve the energy unless it is a reparameterization in time of the true flow. In the Verlet method, the perturbed Hamiltonian ($\tilde{H}$) corresponding to the discretization is affected in both the kinetic energy and potential energy terms, causing the mass matrix M to cease to be diagonal. The magnitude of energy fluctuations in actual simulation is caused by this perturbation and is thus a useful indicator of accuracy.

The Verlet method also conserves the angular momentum [48].

Another strong property possessed by the flow of a Hamiltonian system such as (2) is time-reversibility. This means that if we integrate forward τ units in time from point A to point B, then replace t by $-t$ and p by $-p$ in the differential equations and integrate τ units starting from B, we arrive back at point A. A similar property can be defined for a discretization scheme (for example, the leapfrog/Verlet scheme is reversible), and may also be of importance for long term dynamics [9].

From the form of typical methods such as leapfrog, there is no reason why the stepsize Δt may not vary with the timestep number. For example, we could imagine adjusting the Δt from step to step according to some estimate of the local discretization error. However, the results are less than satisfactory in practical implementations [10]. This can be explained in terms of the nearby Hamiltonian: when we vary the stepsize in a symplectic integrator the effect is the same as if we would solve a different modified Hamiltonian system over each timestep. Thus it is no longer possible to say that the numerical solution coincides with the solution of one and the same nearby Hamiltonian.

4 Alternatives to leapfrog/Verlet

Various alternatives to leapfrog for numerical integration in molecular dynamics have been proposed and implemented over the years. These include multistep schemes and Runge-Kutta methods.[1] A survey of MD experiments using various methods is found in [5]. One can also look for efficient splitting methods based on alternatives to the Strang splitting. One general approach is based on the idea of multiple time stepping, which we discuss in section 5.

Multistep methods make use of the previously computed timesteps and function values to improve the approximation. The explicit "Gear methods"

[1] The term "multistep method" should not be confused with "multiple time stepping" discussed in the following section.

implemented in many molecular dynamics codes are an example of a type of multistep method. These methods are not symplectic or reversible, and it is not clear that the extra order obtained is relevant, since they exhibit relatively poor long term stability of energy. Also of interest in the family of multistep methods are the higher order symmetric schemes (the cousins of position Verlet/Störmer's rule) [21]. These have recently been applied with great success in long-term simulations of the motion of the solar system [30]. The chief advantage of using these multistep methods is that high accuracy can be obtained with minimal cost measured in terms of force evaluations. It has not been shown that multistep methods can be symplectic in the strict sense of the term, but the symmetric methods are time-reversible.

Higher order multistep schemes will likely offer only moderate improvements in efficiency *for the accuracies needed in MD*, e.g., 40% decrease in computing time [25].

Runge-Kutta methods involve a sequence of intermediate "stage" calculations which are then combined in such a way as to obtain desirable features such as high order of accuracy, stability or symplecticness. The standard explicit fourth order method uses four stages. It is well known that to achieve order $p > 4$ with an explicit RK scheme, more than $p+1$ stages are necessary [17]. Since each stage involves a force evaluation, it is probably not advantageous to consider very high order RK methods for molecular dynamics calculations, particularly since high-order of accuracy is not necessarily the critical feature.

Implicit methods require the solution of a system of nonlinear equations at each timestep. For example, the implicit midpoint method can be written

$$q_{n+1} = q_n + \Delta t M^{-1}\frac{p_n + p_{n+1}}{2}, \tag{6}$$

$$p_{n+1} = p_n - \Delta t \nabla_q V(\frac{q_n + q_{n+1}}{2}). \tag{7}$$

It can be shown that this method is symplectic, time-reversible and second order accurate. Implicit methods are typically employed with the hope of circumventing stability restrictions and enabling much larger timesteps. A family of higher order implicit methods (Gauss-Legendre Runge-Kutta schemes [17]) with similar properties have been used, although for molecular dynamics applications the advantages of these higher order schemes appear to be outweighed by increased implementation costs. Some work on the implementation of these methods for molecular dynamics has been undertaken by [19].

The stability of the implicit midpoint method on the harmonic oscillator (4)-(5) can be thoroughly analyzed. A short calculation shows that with q_{n+1} and p_{n+1} computed from (6)-(7), they satisfy

$$\begin{bmatrix} \omega q_{n+1} \\ p_{n+1} \end{bmatrix} = \begin{bmatrix} \cos\theta & \sin\theta \\ -\sin\theta & \cos\theta \end{bmatrix} \begin{bmatrix} \omega q_n \\ p_n \end{bmatrix},$$

with θ defined by

$$\theta = 2\mathrm{arctan}\frac{\omega\Delta t}{2}.$$

As for the leapfrog scheme, we have a rotation through an angle θ which is in error by $O(\Delta t^3)$. In this case, there is no stretching or shrinking (the implicit midpoint method preserves quadratic invariants).

Of interest is the behavior of this method for large $\omega\Delta t$. We can see that as $\Delta t\omega \to \infty$, $\theta \to \pi$. This means that for large $\omega\Delta t$, the frequency gets completely distorted. There is no stability restriction on Δt, but the high frequencies are not accurately represented unless Δt is proportionately small.

In the case of generic linear systems, the foregoing analysis applies independently to each of the fundamental modes. This means that the equations can be decoupled into essentially the equations of a set of independent harmonic oscillators. This means that if we are only interested in the slowest modes, we can resolve these by using a large timestep. The high frequency components will be incorrectly resolved, but this causes no difficulty since they are decoupled from the lower modes.

On the other hand, the situation for nonlinear problems is much more complex. No simple decoupling of the modes of the problem is possible, and the possibility exists that errors induced in the high frequency components of the linearization may contaminate the numerical solution—particularly over longer time intervals.

Actually, difficulties can arise even in relatively simple planar nonlinear problems for which only one linear mode is present. In Figure 1 we have indicated the result of an experiment with a simple modification of the harmonic oscillator with potential $V(q) = \omega^2 q^2/2 + \epsilon q^4/4$, where $\omega = 10$ and $\epsilon = 1$. Applying the implicit midpoint method for various values of the stepsize, we compute the energy error at each timestep and then plot the energy error vs. both time and the stepsize. This results in a jagged surface that becomes smoother for smaller timesteps. Note that for values of the stepsize near $\Delta t = .2$, one observes very large variations in the total energy. We refer to this phenomena as "stepsize resonance." Although a detailed analysis of these resonances is beyond the scope of the current article, the existence of the resonances should raise a red flag regarding the use of implicit methods in order to lengthen the stepsize.

5 Multiple time stepping

In molecular dynamics simulations, the highest frequencies in the system are due to the bond stretching and bond-angle bending potentials, which

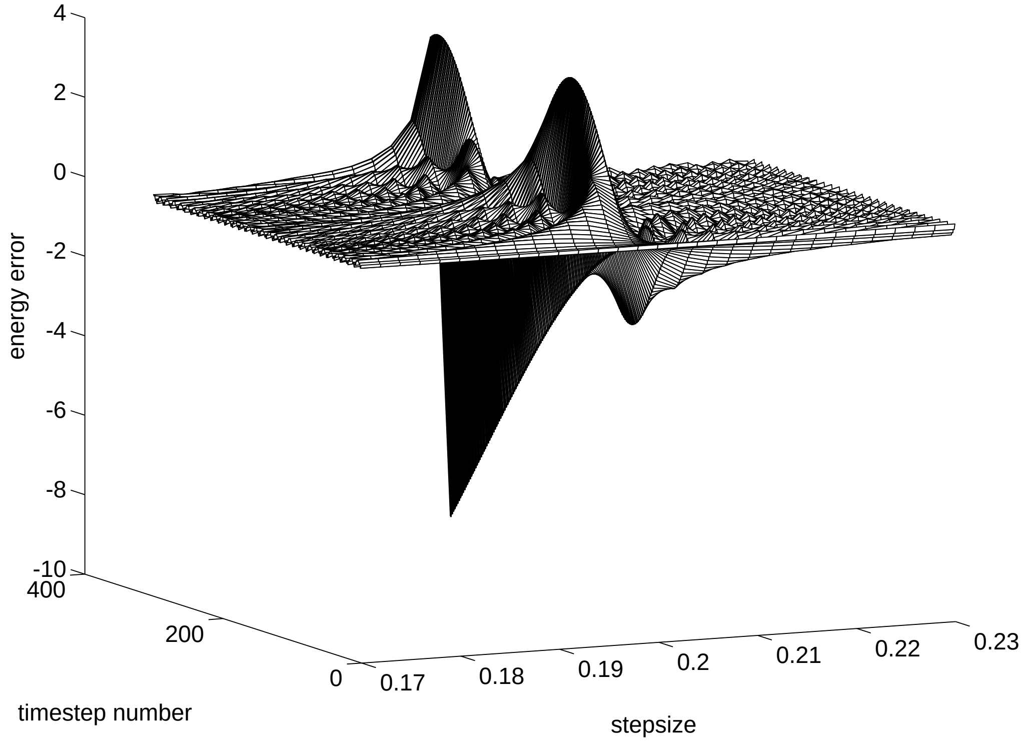

Figure 1: Stepsize resonance for a simple model problem. The graph indicates the energy error in the computed solution with a given stepsize and at a given timestep number.

can be written in the form

$$V_{\text{bond}}(q) \;=\; \frac{1}{2}\sum_i k_i g_i(q) g_i(q). \tag{8}$$

Here the functions g_i stand for $g_i(q) = r - r_0$ in case of bond stretching and for $g_i(q) = \phi - \phi_0$ in case of bond-angle bending. The constants k_i are the force constants which typically take values of a few hundred $\mathrm{kcal\,mol}^{-1}\,\text{Å}^{-2}$ for the bond-stretching potentials and a few tens up to a hundred $\mathrm{kcal\,mol}^{-1}\,\mathrm{deg}^{-2}$ for the bond-bending potentials.

Denoting the remaining entries in the potential function by $V(q)$ and using matrix notation, the Hamiltonian function of a molecular system can be written as

$$H(q,p) \;=\; \frac{p^T M^{-1} p}{2} + V(q) + \frac{g(q)^T K g(q)}{2}, \tag{9}$$

where g is the column vector of all the g_i's and K is a diagonal matrix with diagonal entries $K_{ii} = k_i$.

The corresponding equations of motion are then given by

$$\begin{aligned} \frac{d}{dt} q &= M^{-1} p, \\ \frac{d}{dt} p &= -\nabla_q V(q) - g_q(q)^T K g(q). \end{aligned} \tag{10}$$

The impediment to taking longer time steps is the high frequency components of the motion due to the potential (8).

The idea of multiple timesteps (MTS) is to evaluate different force terms at different interval lengths; positions and velocities are updated in principle every time any force is evaluated. For example, for the interactions represented above by V and for those represented by $V^{\text{hard}} = \frac{1}{2} g(q)^T K g(q)$ the time scales are considerably different, and it would be natural to use different timesteps for V than for V^{hard}. We might try the following time-splitting integration method:

$\Delta t/2$, V
Δt, $T + V^{\text{hard}}$ numerically—N steps of Verlet with stepsize $\Delta t/N$
$\Delta t/2$, V

Such *symplectic* multiple time stepping methods were discovered independently at Illinois [6, 15] and Columbia [43]. Nonsymplectic MTS methods go back over 25 years in the astrophysics literature [18] and 16 years in the MD literature [42]. Typical nonsymplectic MTS methods will exhibit poor behavior on long enough time intervals. On the other hand, it seems that there may be serious accuracy and stability problems with symplectic MTS methods. For example, the possibility of resonance is reported in [15, 6]. And there are other concerns that do not appear in the literature. Unless these can be cleared up, it seems more prudent to use the better nonsymplectic MTS methods proposed in [15, 6, 37].

The use of MTS with a timestep fixed for each bonded interaction is appropriate and probably optimal, but it is inadequate for nonbonded interactions because softness or hardness can vary greatly depending on the interparticle distance r. It is highly desirable to vary the stepsize for such an interaction depending on the distance between two atoms.

Variable stepsize is possible in a way that still employs the machinery of MTS: For each nonbonded interaction $U(r)$ we introduce an artificial splitting

$$U(r) = U^{\mathrm{hard}}(r) + U^{\mathrm{soft}}(r)$$

such that $U^{\mathrm{hard}}(r)$ vanishes for $r \geq r_{\mathrm{cut}}$ and $U^{\mathrm{soft}}(r)$ is soft for all r. So $U^{\mathrm{soft}}(r)$ never requires a small timestep. The effect of this is to permit a large timestep whenever r exceeds the cutoff.

For example with $U(r) = 1/r$ we suggest

$$U^{\mathrm{soft}}(r) = \begin{cases} \frac{3}{2} r_{\mathrm{cut}}^{-1} - \frac{1}{2} r_{\mathrm{cut}}^{-3} r^2, & r \leq r_{\mathrm{cut}}, \\ r^{-1}, & r \geq r_{\mathrm{cut}}, \end{cases}$$

and $U^{\mathrm{hard}} = U - U^{\mathrm{soft}}$. Preliminary experiments with this method appear in [40].

6 Constrained dynamics

A traditional approach to taking larger timesteps has been to freeze the bonded motions, thus reducing the stability restriction. This leads to constrained equations of motion which can be discretized, e.g., by the well-known SHAKE/RATTLE method. In this section we wish to discuss various recent results on the numerical and analytical aspects of constrained dynamics. In the following subsection, we introduce the concept of the *smoothed dynamics* [31] of a molecule and show that, for example, constraining the bond-lengths to their equilibrium value leads to a first approximation of the corresponding smoothed dynamics. The second subsection is devoted to numerical aspects of constrained dynamics. In particular, we discuss new efficient techiques for solving the nonlinear equations at each SHAKE/RATTLE step. Finally, in the last subsection, we come back to the concept of the smoothed dynamics of a molecule and derive a better approximation. This will lead us to a new type of constraints which we call *soft* or *flexible constraints* [8],[31]. It seems possible that the introduction of soft constraints will allow one to constrain bond-angles as well as bond-lengths and thus to effectively reduce the motion of a molecule to its torsion dynamics. (It has been shown in [44] that constraining the bond-angles by "hard" constraints to their equilibrium value leads to qualitatively incorrect results.)

6.1 Analytical aspects I

In this section we introduce the notion of the *smoothed dynamics* [31] of a Hamiltonian system (10). By this we mean the following:

With a suitable scaled Hamiltonian H, the shortest period in the motion of (10) due to the potential $V(q)$ is of order $O(1)$. In contrast to this, the potential $g(q)^T K g(q)/2$ contributes high-frequency terms with period of order $O(1/\sqrt{||K||})$. To separate these high frequency components from the slowly varying parts, we introduce the smoothing operator

$$\langle w\rangle_\alpha(t) \;:=\; \frac{1}{\alpha}\int_{-\infty}^{+\infty} \rho(\frac{t-t'}{\alpha})\, w(t')\, dt', \tag{11}$$

with $0<\alpha<1$ and $w:\mathbf{R}\to\mathbf{R}$. Here $\rho:\mathbf{R}\to\mathbf{R}$ is an appropriate weight function such that for any smooth function w we have

$$\langle w\rangle_\alpha(t) - w(t) \;=\; O(\alpha^s), \tag{12}$$

and for any (bounded) continuous function w we have

$$\langle\langle w\rangle_\alpha\rangle_\alpha(t) - \langle w\rangle_\alpha(t) \;=\; O(\alpha^s), \tag{13}$$

where s is a fixed integer with $s \gg 1$. One could, for example, chose for ρ the Meyer scaling function [12]. From now on we will always assume that the terms of order $O(\alpha^s)$ are sufficiently small and can be neglected.

We call a function $w(t)$ *smooth w.r.t. the time scale* α, if $\langle w\rangle_\alpha(t)\approx w(t)$. The idea is now to replace the rapidly varying solutions $q(t)$ of (10) by $\langle q\rangle_\alpha(t)$ with

$$\sqrt{||K^{-1}||} \;<\; \alpha \;<\; 1,$$

and then to seek numerical approximations to the smooth $\langle q\rangle_\alpha$ rather then to the rapidly varying $q(t)$. We call the functions $\langle q\rangle_\alpha(t)$, corresponding to solutions $q(t)$ of (10), the *smoothed dynamics* of (10) [31].

For a given scaling of the Hamiltonian H, k_BT, k_B the Boltzmann constant and T the temperature, becomes a quantity which we call δ and which we assume to satisfy

$$||K^{-1}|| \;\le\; \delta \;<\; 1.$$

For example, in a molecular dynamics simulation where the potential V contains the torsion, Lennard-Jones, and electrostatic potentials, the corresponding scaling of the Hamiltonian by ≈ 5 kcal/mol yields at room-temperature $\delta\approx 0.1$. Let us also introduce the quantity ϵ by

$$\epsilon \;:=\; ||K^{-1}||.$$

We typically have $\epsilon \approx 0.1$ for the bond stretching and bond-angle bending potentials.

In the sequel, we will show how the application of the smoothing operator (11) to (10) leads to constrained equations of motion that approximate the smoothed dynamics of (10). By such an approximation we mean a differential equation in the variables Q and P such that the corresponding solutions $(Q(t), P(t))$ satisfy

$$\langle q \rangle_\alpha (t) - Q(t) \;=\; O(\delta^k \epsilon^l),$$

and

$$\langle p \rangle_\alpha (t) - P(t) \;=\; O(\delta^k \epsilon^l),$$

over bounded intervals of time with appropriate integers $k \geq 0$ and $l > 0$. Here $(q(t), p(t))$ is a solution of (10) and $(Q(0), P(0))$ is chosen such that $\langle q \rangle_\alpha (0) - Q(0) = O(\delta^k \epsilon^l)$ and $\langle p \rangle_\alpha (0) - P(0) = O(\delta^k \epsilon^l)$.

Let us introduce now the new variable λ by

$$\lambda \;:=\; K g(q).$$

Then the equations of motion (10) can be rewritten as

$$\begin{aligned} \frac{d}{dt} q &= M^{-1} p, \\ \frac{d}{dt} p &= -\nabla_q V(q) - g_q(q)^T \lambda, \\ K^{-1} \lambda &= g(q). \end{aligned} \tag{14}$$

In a naive approach, one would now look for the smooth solutions of (14) hoping that this yields an order $O(\epsilon)$ approximation to the smoothed dynamics of (10). Since a smooth $p(t)$ implies that $(dp/dt)(t) = O(1)$, λ has to remain bounded as $\epsilon \rightarrow 0$. Thus

$$g(q) \;=\; O(\epsilon).$$

In the limit $\epsilon \rightarrow 0$, this suggests replacing the last equation in (14) by the holonomic constraint $g(q) = 0$ and we obtain the constrained equations of motion

$$\begin{aligned} \frac{d}{dt} Q &= M^{-1} P, \\ \frac{d}{dt} P &= -\nabla_q V(Q) - g_q(Q)^T \Lambda, \\ 0 &= g(Q). \end{aligned} \tag{15}$$

Note that the new variable Λ is implicitly defined by twice differentiating the constraint $g(Q) = 0$ with respect to time. As a result we obtain

$$\Lambda \;=\; [g_q\, M^{-1} g_q^T]^{-1}\, [g_{qq}\, (M^{-1}P)(M^{-1}P) - g_q\, M^{-1} \nabla_q V],$$

where, for notational convenience, we suppressed the variable Q in $V(Q)$, $g_q(Q)$, and the second derivative $g_{qq}(Q)$. The equations (15) constitute a constrained Hamiltonian system with Hamiltonian

$$H(Q,P) \;=\; \frac{P^T M^{-1} P}{2} + V(Q) + g(Q)^T \Lambda,$$

and constraints $g(Q) = 0$. The flow of (15) can be shown to be symplectic [23]. The solutions of (15) are also time-reversible.

The approximation (15) has been used in MD simulations to remove the bond stretching/bond-angle bending modes [34], [44]. Since $g(Q) = 0$ constrains the bond-lengths/bond-angles to their equilibrium values r_0, ϕ_0 respectively, we call $g(Q) = 0$ *hard constraints.*

We will discuss in Subsection 3 how well the constrained equations (15) reflect the correct smoothed dynamics of the original system (10). In particular, we will see that the equations (15) are appropriate for constraining the bond-lengths, but are doomed to fail when applied to the bond-angle bending.

6.2 Numerical aspects

Ryckaert, Ciccotti, Berendsen (1977) proposed an algorithm SHAKE [34] for the constrained equations (15), which can be formulated as

$$\begin{aligned} Q_{n+1} &= Q_n + \Delta t\, M^{-1} P_{n+1/2}, \\ P_{n+1/2} &= P_{n-1/2} - \Delta t\, [\nabla_q V(Q_n) + g_q(Q_n)^T \Lambda_n], \\ 0 &= g(Q_{n+1}). \end{aligned} \tag{16}$$

Together with the starting procedure

$$P_{1/2} = P_0 - \frac{1}{2} \Delta t\, [\nabla_q V(Q_0) + g_q(Q_0)^T \Lambda_0],$$

this can be viewed as a constrained variant of leap-frog. Strictly speaking, the scheme is implicit since nonlinear equations must be solved at each time-step, but it is partially explicit in the sense that only one $\nabla_q V$-evaluation is needed per time step. The equations can be reduced to nonlinear equations for Λ_n only:

$$0 = F(\Lambda) := g(\bar{Q}_{n+1} - \Delta t^2 M^{-1} g_q(Q_n)^T \Lambda_n), \tag{17}$$

where $\bar{Q}_{n+1}$ is the *unconstrained step* based on Verlet approximation. Thus the dimension of the nonlinear system is the number of constraints.

An alternative scheme, RATTLE, was proposed by Anderson in 1983. RATTLE is a modification of SHAKE such that P_{n+1} also satisfies the "hidden constraint" $g_q(Q)M^{-1}P = 0$. However, both methods lead to identical results in terms of the Q variable [22].

It has been shown [22] that (16) is a second-order, time-reversible, symplectic discretization of (15). In addition, the method preserves angular momentum [48] and can be viewed as the exact solution of a perturbed constrained Hamiltonian system [32].

But SHAKE requires an efficient technique for solving the nonlinear equations at each step. In fact, the original paper [34] describing the SHAKE discretization presented an iterative solver for the nonlinear equations, and the term SHAKE typically is used to refer to the overall procedure consisting of discretization by (16) together with the iterative solver used in satisfying the constraints (*coordinate resetting*). For clarity, we will refer to the iterative solver as *SHAKE iteration* and the discretization scheme as *SHAKE discretization*.

In SHAKE iteration, we cycle through the constraints one by one, adjusting one multiplier at each step. Let g_i be the ith component of g, and let G_i represent the ith row of g_q, then the iteration proceeds as follows: First, we initialize $Q = \bar{Q}_{n+1} = Q_n + \Delta t\, M^{-1}[P_{n-1/2} - \Delta t\, \nabla_q V(Q_n)]$ which corresponds to the initial guess $\Lambda_n = 0$. Next, we compute the correction of the ith component $\Delta\Lambda^i$ needed to satisfy the ith linearized constraint equation:

$$\Delta\Lambda^i \leftarrow \frac{g_i(Q)}{G_i(Q)M^{-1}G_i(Q_n)},$$

and update Q by

$$Q \leftarrow Q - \Delta t^2 M^{-1} G_i(Q_n)^T \Delta\Lambda_i.$$

This cycle should be repeated until all constraint residuals $g_i(Q)$ are below a prescribed tolerance.

As shown in [4], SHAKE can be viewed as a 1-step nonlinear Gauss-Seidel-Newton iteration in the framework developed by Ortega and Rheinboldt [26]. Local convergence is guaranteed precisely when standard Gauss-Seidel iteration converges for the linear system of equations

$$A_n x = b,$$

where $A_n = g_q(Q_{n+1})M^{-1}g_q(Q_n)$. For unconstrained approximations $\bar{Q}_{n+1}$ sufficiently close to Q_{n+1} (i.e., for sufficiently small timestep Δt), SHAKE iteration converges with asymptotic rate of convergence approximately

$$\rho((D+L)^{-1}U),$$

where $A_n = L + D + U$ is the splitting of A_n into strictly lower triangular, diagonal, and strictly upper triangular parts.

The matrix $B_n = g_q(Q_n)M^{-1}g_q(Q_n) = A_n + O(h)$ has a very special structure which can be easily analyzed. In the current setting where g consists only of bond length constraints, it can be shown that the matrix is nearly constant along solutions, so also the matrix A_n is nearly constant along solutions. Thus SHAKE iteration will converge with a similar rate at each timestep. It can also be seen that SHAKE iteration will converge very slowly for chainlike structures unless successive bonds are nearly perpendicular, and degraded convergence would be anticipated for molecules with high connectivity.

A natural improvement to Gauss-Seidel iteration is based on the use of overrelaxation. In this method, we update the iterate at each step by forming a weighted combination of the previous iterate and the G-S step: in essence, we exaggerate each G-S correction by a *relaxation parameter* ω, changing the update of Λ from

$$\Lambda^i \leftarrow \Lambda^i + \Delta\Lambda^i$$

to

$$\Lambda^i \leftarrow \Lambda^i + \omega\Delta\Lambda^i.$$

The parameter ω can be a fixed value obtained through some preliminary experiment, or it can be obtained automatically during the integration by a simple adaptive algorithm [4].

This adjustment is essentially free of cost. And it can mean substantial speedups in coordinate resetting. Since the method is just an alternative nonlinear equation solver to SHAKE iteration, the converged numerical solution will be identical (up to rounding error) to that computed by SHAKE iteration.

A second alternative to SHAKE iteration was also considered in [4]: we could use a Newton iteration, or variant thereof, to compute successive updates to the vector Λ_n. In particular, we could apply a true Newton iteration to the original nonlinear equations and use *sparse matrix techniques* to solve the resulting linear equations. This turns out to be somewhat expensive for most problems because the factorization of a matrix—even a sparse matrix—is relatively costly. A better alternative is to use an adaptive Newton iteration based on a factorization of the symmetric matrix B_n which is close to A_n and changes little from step to step.

These methods iteratively improve the whole vector of multipliers:

$$\Delta\Lambda \leftarrow R^{-1}F(\Lambda),$$

where for the true Newton iteration (NIP) we have $R = g_q(Q)M^{-1}g_q(Q_n)^T$ with Q the latest approximation to Q_{n+1}. For the symmetric, adaptive iteration we have $R = GM^{-1}G^T$, with $G = g_q(Q_k)$ for some previous step k (G is updated as needed for convergence). The Newton-based techniques are robust as long as the initial data lie on or very near the constraint manifold; in practice, SHAKE (or SOR) should probably be used at the first timestep to insure that the initial iterate is very close to the constraint manifold.

The techniques have been integrated into the CHARMM software package and successfully applied to several examples: C_{60}, a box of water, Myoglobin, BPTI; detailed results are reported in [4]. A MATLAB "toolbox" has been developed by Barth for studying the algorithms [3].

Roughly speaking, we can summarize the results as follows: (1) the use of an SOR parameter can improve SHAKE iteration convergence by a factor of two to three in protein dynamics simulations for no additional cost or loss of robustness, (2) the adaptive scheme for determining optimal ω in [4], though not robust, does demonstrate the feasibility of computing the SOR parameter, and (3) the symmetric adaptive Newton method may show improvement over SHAKE iteration at large step size Δt for problems with high bond connectivity, e.g. the *buckminsterfullerene* C_{60}.

Some higher-order extensions of SHAKE/RATTLE have been proposed by Reich [32] and independently by Jay [20]. However, competitive practical implementations for molecular dynamics applications have not been demonstrated.

6.3 Analytical aspects II

Let us see now how well the constrained equations (15) reflect the correct smoothed dynamics of the original system (10). To do so, we introduce (for theoretical purposes) local coordinates (q_1, q_2) by

$$\begin{aligned} q_1 &= g(q), \\ q_2 &= b(q), \end{aligned}$$

where $b(q)$ is a vector valued function such that $g_q(q)M^{-1}b_q(q)^T = 0$ and the composed matrix $[g_q(q)^T\, b_q(q)^T]$ is invertible. The existence of such a coordinate system follows, at least locally, from the Frobenius theorem [7].

To obtain a transformed system that remains Hamiltonian, we define *conjugate momenta* [23] by

$$[g_q(q)^T\, b_q(q)^T] \begin{bmatrix} p_1 \\ p_2 \end{bmatrix} = p,$$

which results in the Hamiltonian

$$H = \frac{p_1^T g_q\, M^{-1} g_q^T p_1}{2} + \frac{p_2^T b_q\, M^{-1} b_q^T p_2}{2} + V + \frac{q_1^T K q_1}{2}. \qquad (18)$$

The equations of motion are now given by

$$\begin{aligned} \frac{d}{dt}q_1 &= g_q\, M^{-1} g_q^T p_1, \\ \frac{d}{dt}p_1 &= -\nabla_{q_1} V - K q_1 - \nabla_{q_1} \frac{p_1^T g_q\, M^{-1} g_q^T p_1 + p_2^T b_q\, M^{-1} b_q^T p_2}{2} \end{aligned} \tag{19}$$

and

$$\begin{aligned} \frac{d}{dt}q_2 &= b_q\, M^{-1} b_q^T p_2, \\ \frac{d}{dt}p_2 &= -\nabla_{q_2} V - \nabla_{q_2} \frac{p_1^T g_q\, M^{-1} g_q^T p_1 + p_2^T b_q\, M^{-1} b_q^T p_2}{2}, \end{aligned}$$

where, for notational convenience, we suppressed the arguments in the mappings $V(q_1, q_2)$, $g_q(q_1, q_2)$, and $b_q(q_1, q_2)$.

The constrained equations (15) are obtained by replacing the first set of equations by $Q_1 = P_1 = 0$. In terms of the variables (Q_2, P_2), this results in

$$\begin{aligned} \frac{d}{dt}Q_2 &= b_q(Q_2)\, M^{-1} b_q(Q_2)^T P_2, \\ \frac{d}{dt}P_2 &= -\nabla_{q_2} V(Q_2) - \nabla_{q_2} \frac{P_2^T b_q(Q_2)\, M^{-1} b_q(Q_2)^T P_2}{2}. \end{aligned}$$

By applying the smoothing operator (11) to the second equation in (19), we obtain

$$\begin{aligned} \langle \frac{d}{dt}p_1 \rangle_\alpha &= -\langle \nabla_{q_1} V \rangle_\alpha - K \langle q_1 \rangle_\alpha - \\ &\qquad \langle \nabla_{q_1} \frac{p_1^T g_q M^{-1} g_q^T p_1 + p_2^T b_q M^{-1} b_q^T p_2}{2} \rangle_\alpha, \end{aligned} \tag{20}$$

since each term in (20) has to remain bounded as $\epsilon \to 0$ [31], it follows that

$$\langle q_1 \rangle_\alpha \;=\; O(\epsilon).$$

Furthermore, equipartition of energy [27] implies [31]

$$\langle q_1^T q_1 \rangle_\alpha \;=\; O(\delta\, \epsilon).$$

Now, by Taylor expansion of V about $\langle q_1 \rangle_\alpha$ and applying the smoothing operator (11) to this expansion, one can show [31] that

$$\langle V(q_1, q_2) \rangle_\alpha \;=\; V(\langle q_1 \rangle_\alpha, q_2) + O(\langle q_1^T q_1 \rangle_\alpha).$$

(Here we used facts like $\langle q_2 \rangle_\alpha \approx q_2$, $\langle V(\langle q_1 \rangle_\alpha, q_2) \rangle_\alpha \approx V(\langle q_1 \rangle_\alpha, q_2)$, $\langle \Delta q_1 \rangle_\alpha := \langle q_1 - \langle q_1 \rangle_\alpha \rangle_\alpha \approx 0$, and $\langle \Delta q_1^T \Delta q_1 \rangle_\alpha = \langle q_1^T q_1 \rangle_\alpha + O(\epsilon^2)$.) Now, per degree of freedom, we have $\langle \phi^2 \rangle_\alpha \approx 0.01\,\mathrm{deg}^2$ for the bond-angle bending and $\langle r^2 \rangle_\alpha \approx 0.001 \mathring{A}$ for the bond stretching. Thus

$$\langle V(q_1, q_2) \rangle_\alpha \approx \;\; V(\langle q_1 \rangle_\alpha, q_2),$$

and

$$\langle \nabla_{q_2} V(q_1, q_2) \rangle_\alpha \quad \to \quad \nabla_{q_2} V(0, q_2),$$

as $\epsilon \to 0$, and a similar result holds for the term

$$\langle \nabla_{q_2} \frac{p_2^T b_q M^{-1} b_q^T p_2}{2} \rangle_\alpha .$$

However, by equipartition of energy, we have [31]

$$\langle \frac{p_1^T g_q \, M^{-1} g_q^T p_1}{2} \rangle_\alpha \quad \approx \quad \frac{m}{2} \, \delta,$$

where m is the number of constraints. Thus the force term

$$\langle \nabla_{q_2} \frac{p_1^T g_q \, M^{-1} g_q^T p_1}{2} \rangle_\alpha$$

is not necessarily small even in the limit $\epsilon \to 0$. It has been pointed out before [14] that the appropriate correction to the constrained dynamics (15) is given by the Fixman potential

$$V_F \quad = \quad \frac{\delta}{2} \ln \det g_q \, M^{-1} g_q^T . \tag{21}$$

Thus an $O(\epsilon)$ approximation to the correct smoothed dynamics of (10) is given by the modified constrained equations

$$\begin{aligned} \frac{d}{dt} Q &= M^{-1} P, \\ \frac{d}{dt} P &= -\nabla_q V(Q) - \nabla_q V_F(Q) - g_q(Q)^T \Lambda, \\ 0 &= g(Q). \end{aligned} \tag{22}$$

The variable Λ satisfies now

$$\Lambda \quad = \quad [g_q M^{-1} g_q^T]^{-1} \, [g_{qq}(M^{-1}p)(M^{-1}p) - g_q M^{-1} [\nabla_q V + \nabla_q V_F]]. \tag{23}$$

For large systems, the computation of the Fixman potential (21) becomes rather time-consuming. However, a few simplifications seem possible: (i) In case that we constrain only the bond-lengths, the matrix $g_q \, M^{-1} g_q^T$ can be shown to be a function of the bond-angles ϕ and the bond-lengths r which we keep constant. Since the corresponding force $\nabla V_F(\phi)$ amounts to a few $k_B T \deg^{-1}$ [45] and is thus small compared to the contributions stemming from the bond-angle bending potentials, the Fixman potential can safely be ignored in this situation. (ii) The situation differs if we include bond-angle constraints. In this case the matrix $g_q \, M^{-1} g_q^T$ depends on the torsion angles

ψ (and, of course, on the bond-lengths and the bond-angles which, however, we keep constant). The Fixman potential $V_F(\psi)$ can now no longer assumed to be small compared to the torsion potentials [45].

To keep the computational costs low, we suggest [33] to approximate the Fixman potential by

$$V_F(\psi) \quad \approx \quad \sum_j V_F^j(\psi_j),$$

where $V_F^j(\psi_j)$ stands for the Fixman potential due to the three bond-length and two bond-angle constraints defining the torsion angle ψ_j. (In this case, each matrix $g_q\,M^{-1}g_q^T$ becomes a 5×5 matrix that depends only on ψ_j.). This approximation is justified by the fact that

$$\frac{\partial^2}{\partial\psi_i\,\partial\psi_j}\,V_F(\psi) \quad \approx \quad 0,$$

for all $i \neq j$ [33].

Remark. The Fixman potential can easily be derived in the following way [31]: Let $Q(q)$ be an orthogonal matrix such that $Q^T g_q\,M^{-1}g_q^T Q$ is a diagonal matrix $D(q)$ with entries $d_{ii}(q)$. Let π_i denote the ith entry in the m dimensional vector $Q(q)^T\,p_1$. Then

$$\langle\,\nabla_{q_2}\frac{p_1^T g_q\,M^{-1}g_q^T p_1}{2}\,\rangle_\alpha \quad \approx \quad \sum_i \frac{\langle\pi_i^2\rangle_\alpha}{2}\,\nabla_{q_2}\langle d_{ii}\rangle_\alpha,$$

and, by equipartition of energy,

$$\langle\pi_i^2\rangle_\alpha \quad \approx \quad \frac{\delta}{\langle d_{ii}\rangle_\alpha}.$$

Thus we obtain

$$\sum_i \frac{\langle\pi_i^2\rangle_\alpha}{2}\,\nabla_{q_2} d_{ii}(Q) \quad \approx \quad \frac{\delta}{2}\,\nabla_{q_2}\ln\,\det\,D(Q),$$

which, in terms of the original matrix $g_q\,M^{-1}g_q^T$, leads to the potential (21).

The constrained equations (22) yield correct results only in the limit $\epsilon \to 0$. While this condition is approximately satisfied for the force constants corresponding to bond stretching, one has to take finite size effects of ϵ into account when looking at bond-angle bending [44]. In other words, the estimate

$$\langle q_1\rangle_\alpha \quad = \quad 0$$

has to be replaced by a more accurate one. As suggested in [8],[31], this can be achieved by using (20) together with $\langle dp_1/dt\rangle_\alpha = O(\epsilon)$ (which follows from the fact that $\langle q_1\rangle_\alpha = O(\epsilon)$ and $\langle p_1\rangle_\alpha = O(\epsilon)$) to derive

$$\langle q_1\rangle_\alpha \quad = \quad -K^{-1}\nabla_{q_1} V(\langle q_1\rangle_\alpha, q_2) + O(\delta\,\epsilon).$$

Here we also used that

$$\nabla_{q_1} \frac{p_1^T g_q M^{-1} g_q^T p_1 + p_2^T b_q M^{-1} b_q^T p_2}{2} \quad = \quad O(\delta),$$

by equipartition of energy [31] and that $\epsilon^2 \leq \delta\,\epsilon$.

The corresponding constrained equations of motion are now given by

$$\begin{aligned} \frac{d}{dt}Q &= M^{-1}P, \\ \frac{d}{dt}P &= -\nabla_q V(Q) - \nabla_q V_F(Q) - g_q(Q)^T\tilde{\Lambda}, \\ 0 &= g(Q) + K^{-1}\,[g_q(Q)M^{-1}g_q(Q)^T]^{-1}\,g_q(Q)M^{-1}\nabla_q V(Q). \end{aligned} \tag{24}$$

One can show that this formulation provides an $O(\delta\epsilon)$ approximation [31].

In contrast to the formulation (15), the system (24) can no longer be derived from a Hamiltonian principle. However, the solutions of (24) are still time-reversible. For a Hamiltonian reformulation of (24) see [31].

As opposed to the *hard constraint* $g(Q) = 0$, we call the constraint $\tilde{g}(Q) = 0$ with

$$\tilde{g}(Q) \quad := \quad g(Q) + K^{-1}\,[g_q(Q)M^{-1}g_q(Q)^T]^{-1}\,g_q(Q)M^{-1}\nabla_q V(Q),$$

a *soft constraint.*

Finally a few words on the discretization of (24). Any constrained Hamiltonian system of the form (15) can efficiently be discretized by (16). The same scheme can also be applied to the constrained system (24) with soft constraints. This time we obtain

$$\begin{aligned} Q_{k+1} &= Q_k + \Delta t\, M^{-1}P_{k+1/2}, \\ P_{k+1/2} &= P_{k-1/2} - \Delta t\,[\nabla_q V(Q_k) + \nabla_q V_F(Q_k) + g_q(Q_k)^T\tilde{\Lambda}_k], \\ 0 &= \tilde{g}(Q_{k+1}). \end{aligned} \tag{25}$$

The method is time-reversible but not symplectic.

The scheme (25) is computationally expensive. If the nonlinear system of equations in $\tilde{\Lambda}_k$ is solved by Newton's method, it requires the computation of $\nabla_q V(q)$ in each Newton iteration. To avoid this, one can use [8] the following modification

$$\begin{aligned} \bar{Q}_{k+1} &= \bar{Q}_k + \Delta t\, M^{-1} P_{k+1/2}, \\ P_{k+1/2} &= P_{k-1/2} - \Delta t\, [\nabla_q V(Q_k) + \nabla_q V_F(Q_k) + g_q(\bar{Q}_k)^T \tilde{\Lambda}_k^1], \\ 0 &= g(\bar{Q}_{k+1}), \end{aligned} \tag{26}$$

and

$$\begin{aligned} Q_k &= \bar{Q}_k + M^{-1} g_q(\bar{Q}_k)^T \tilde{\Lambda}_k^2, \\ 0 &= g(Q_k) + K^{-1}[g_q(\bar{Q}_k) M^{-1} g_q(\bar{Q}_k)^T]^{-1} g_q(\bar{Q}_k) M^{-1} \nabla_q V(\bar{Q}_k). \end{aligned} \tag{27}$$

This scheme is time-reversible and differs from the method (25) by a term of order $O(\epsilon^2)$ [8]. Now the force field $\nabla_q V(q)$ has to be computed only twice per integration step. Both nonlinear systems in $\tilde{\Lambda}_k^1$ and $\tilde{\Lambda}_k^2$ can be solved by the same methods as proposed for (16) in Section 6.2.

A further simplification seems possible [8]: If we split the potential into $V = V^{\text{hard}} + V^{\text{soft}}$, one can replace the constraint function $\tilde{g}$ by

$$\tilde{g}(Q) \;\approx\; g(Q) + [g_q(Q) M^{-1} g_q(Q)^T]^{-1}\, g_q(Q)\, M^{-1} \nabla_q V^{\text{hard}}(Q),$$

where V^{hard} would include perhaps only the Lennard-Jones and the torsion potentials.

Example In this example we consider a four-bead-three-bond structure [28] where the structure is restricted to move in a finite volume by the potential

$$V_r(q) \;=\; \sum_i K_r \left(\frac{r_i}{\sigma}\right)^6 .$$

Here r_i denotes the distance of each of the four beads to the origin, $\sigma = 2$, and $K_r = 0.1$. We set the mass of all four beads equal to $m = 1$ and choose $r_0 = 1$ as the equilibrium bond-length and $\phi_0 = 90^o$ as the equilibrium bond-angle. For simplicity, we included no torsion potential. The force constant for the harmonic bond-angle bending potentials was $K_a = 60\,\text{deg}^{-2}$ and $K_b = 600$ for the corresponding bond stretching potentials. Note that these values correspond to force constants typically found in molecular dynamics simulations for a scaling of the Hamiltonian by approximately 1.0kacl/mol [44].

We started the structure from its equilibrium position with the initial velocities in x-direction equal to $p_x = 1.0$. The impact of the structure clashing with the potential-wall V_r can be seen in Fig. 2. We computed

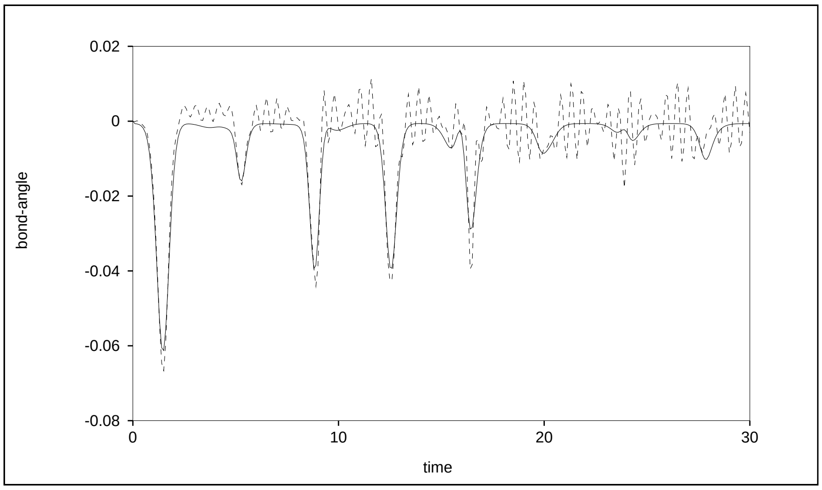

Figure 2: Trajectory of one of the bond-angles for the unconstrained formulation (dotted line) compared to the one for the formulation with hard constraints on the bond-lengths and flexible constraints on the bond-angles (solid line).

the trajectory of one bond-angle (plotted as $\cos(\phi)$) for the unconstrained formulation and compared this trajectory with the one obtained by constraining the bond-lengths by hard constraints and the bond-angles by flexible constraints.

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