An Efficient Symplectic Integration Algorithm for Molecular Dynamics Simulations

Dušanka Janežič[†] and Franci Merzel*

National Institute of Chemistry, Hajdrihova 19, 61115 Ljubljana, Slovenia

A new explicit symplectic integration algorithm for molecular dynamics (MD) simulations is described. The method involves splitting of the total Hamiltonian of the system into the harmonic part and the remaining part in such a way that both parts can be efficiently computed. The Hamilton equations of motion are then solved using the second order generalized leap-frog integration scheme in which the high-frequency motions are treated analytically by the normal mode analysis which is carried out only once, at the beginning of the calculation. The proposed algorithm requires only one force evaluation per integration step, the computation cost per integration step is approximately the same as that of the standard leap-frog-Verlet method, and it allows an integration time step ten times larger than can be used by other methods of the same order. It was applied to MD simulations of the linear molecule of the form $H-(C\equiv C)_n-H$ and was by an order of magnitude faster than the standard leap-frog-Verlet method. The approach for MD simulations described here is general and applicable to any molecular system.

1. INTRODUCTION

Molecular dynamics (MD) simulation, in which the classical equations of motion for all particles of a system are integrated over finite period of time,[1,2] provides an important insight into the structure and function of molecules. The efficiency and, thus the scope of the MD method can be increased by using algorithms for the integration of MD equations over larger time steps without loss of stability. The need for improved algorithms has recently received greater attention since it is obvious that the time-step problem in MD cannot be overcome solely by faster computers. The problem of how to increase the time step can be overcome by use of symplectic methods.[3–8]

The Hamiltonian system

$$\frac{dp_i}{dt} = -\frac{\partial \mathcal{H}}{\partial q_i}, \quad \frac{dq_i}{dt} = \frac{\partial \mathcal{H}}{\partial p_i}, \quad i = 1...n \qquad (1)$$

where $\mathcal{H}$ is the Hamiltonian, q_i and p_i are the coordinate and momentum, respectively, and n is the number of degrees of freedom, arises in the modeling of a physical system with a finite number of degrees of freedom. Its fundamental property is, that for each fixed value of t the corresponding t-flow $\phi_{t,\mathcal{H}}$ is a symplectic or canonical mapping. The t-flow $\phi_{t,\mathcal{H}}$ is defined as $(\bar{p},\bar{q}) = \phi_{t,\mathcal{H}}(\bar{p}_0,\bar{q}_0)$ where $(\bar{p},\bar{q})$ is the value of the solution of the Hamiltonian system and takes at time $t = 0$ the value $(\bar{p}_0,\bar{q}_0)$. A mapping is said to be symplectic or canonical if it preserves the differential form $\omega = d\bar{p} \wedge d\bar{q}$ which defines the symplectic structure in the phase space.[9] In one-degree-of-freedom example symplecticness is the preservation of oriented area,[5] the property which follows from Liouville's theorem. In fact, all properties specific to Hamiltonian dynamics can be derived from preservation of oriented area, the property which holds only for Hamiltonian systems. Symplectic integration methods replace t-flow $\phi_{t,\mathcal{H}}$ in the phase space by the symplectic transformation $\psi_{t,\mathcal{H}}$,

which retains "Hamiltonian" features of $\phi_{t,\mathcal{H}}$. The feature of symplectic integration is a possibility of backward error interpretation of the numerical results: the computed solutions are solving exactly or at worst, approximately a nearby Hamiltonian problem which means that the points computed by means of symplectic integration lay either exactly or at worst approximately on the true trajectories.[5]

The approach in this paper was inspired by the work of Wisdom and Holman,[10] who used symplectic mapping method based on a separation of the Hamiltonian, for the N body problem, to compute the time evolution of the planet Pluto over a billion-year period. They split the total Hamiltonian into a Kepler part representing the low-frequency terms of the Hamiltonian and into an interaction part representing the high-frequency terms. Then they applied a second order symplectic integrator, a generalized leap-frog integration scheme. Introducing the averaging principle[9,11] to the interaction part enabled them to use a step size an order of magnitude larger than can be used by traditional numerical methods.

For the purpose of MD simulation, we interpreted the separation of the Hamiltonian into Kepler and interaction parts as the division into a dynamically leading term and the remaining term of the motion. In order to generalize the gravitational N-body problem to MD, we defined, first, harmonic vibrations, governed by the harmonic terms of the total potential, as the dynamically leading term $\mathcal{H}_0$ and, second, the difference between the total potential and its harmonic terms as the remaining part $\mathcal{H}_r$ of the MD Hamiltonian as

$$\mathcal{H} = \mathcal{H}_0 + \mathcal{H}_r \qquad (2)$$

In this way the role of high- and low-frequency terms in the presentation of the Hamiltonian in eq 2 in comparison to Wisdom and Holman[10] was reversed.

In this paper, we present a new symplectic algorithm for MD simulations of large systems based on a factorization of the Liouville propagator. The algorithm is quite distinct from other approaches using the fractional-step methods[12] owing to the analytical treatment of high frequency motions.

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* Author to whom correspondence should be addressed.
† Fulbright Scholar at the National Institutes of Health on leave from National Institute of Chemistry, Ljubljana, Slovenia.

Knowing the pure harmonic Hamiltonian $\mathscr{H}_0$ which represents the main contribution of the strong chemical bonds we can treat the cumbersome high-frequency terms analytically, i.e., independent of the step size of integration. The whole integrating step combines analytical evolution of the harmonic part of the Hamiltonian with a correction arising from the remaining part. This approach represented by the partition in eq 2, was incorporated into the second order generalized leap-frog integrator. In section 2, the details of the method are given. In section 3, are presented the results of the numerical characteristics of the proposed method tested on a linear molecule of the form $H-(C\equiv C)_n-H$, using a force field consisting of a bond stretching term, Coulomb and Lennard-Jones interactions. The results were compared with those obtained by the standard leap-frog-Verlet method.[13]

The method presented here allows use of a step size at least a factor of ten larger than the standard leap-frog-Verlet method, and the computational cost per step is approximately the same for the two methods. The present method is thus an order of magnitude faster than the standard leap-frog-Verlet method. This new approach is general and applicable to force fields that also include angle bending and torsional terms and to large systems such as biological macromolecules.[14]

2. THEORY

The explicit symplectic integrator can be derived in terms of the Lie algebraic language. Hamilton eq 1 can be written[5] in the form

$$\frac{d\vec{x}}{dt} = \{\vec{x}, \mathscr{H}\} = \hat{L}_{\mathscr{H}}\vec{x} \tag{3}$$

where $\{\vec{x},\mathscr{H}\}$ denotes the Poisson bracket,[15] $\hat{L}_{\mathscr{H}}$ is the Poisson bracket operator, and $\vec{x} = (\vec{q},\vec{p})$ is a vector in phase space composed of the coordinates and momenta of all particles. The formula

$$\vec{x}|_{t_0+\Delta t} = \exp(\Delta t \hat{L}_{\mathscr{H}})\vec{x}|_{t_0} \tag{4}$$

provides a way for integrating the Hamiltonian system in terms of Lie operators. It is the formal solution of Hamilton equations or the exact time evolution of trajectories in phase space from t_0 to $t_0 + \Delta t$, and Δt is a time step. The trouble with eq 4 resides in impossibility of evaluating $\exp(\Delta t\hat{L}_{\mathscr{H}})$. Symplectic integration consists in replacing $\exp(\Delta t\hat{L}_{\mathscr{H}})$ by a product of symplectic maps which approximate $\exp(\Delta t\hat{L}_{\mathscr{H}})$ to a given order.[16]

The construction of an efficient mapping for any problem rests on the ability to separate the Hamiltonian into parts which are themselves not only integrable but efficiently computable.[10] Suppose that the Hamiltonian $\mathscr{H}$ is split into two parts as suggested by eq 2. Both parts can be solved exactly as independent Hamiltonians. Since $\hat{L}_{\mathscr{H}} = \hat{L}_{\mathscr{H}_0} + \hat{L}_{\mathscr{H}_r}$, we can use the following approximation for the propagation operator in eq 4

$$\exp(\Delta t\hat{L}_{\mathscr{H}}) \approx \exp\left(\frac{\Delta t}{2}\hat{L}_{\mathscr{H}_0}\right)\exp(\Delta t\hat{L}_{\mathscr{H}_r})\exp\left(\frac{\Delta t}{2}\hat{L}_{\mathscr{H}_0}\right) \tag{5}$$

Using the Baker—Campbell—Hausdorff formula for combining the exponents of two Lie group elements[5]

$$\exp(Z) = \exp(X)\exp(Y)$$

$$Z = X + Y + \frac{1}{2}[X,Y] + \frac{1}{12}([X,[X,Y]] + [Y,[Y,X]]) + \ldots \tag{6}$$

where $[X,Y] = XY - YX$ denotes the commutator, we express the right hand side of eq 5 as

$$\exp\left(\frac{\Delta t}{2}\hat{L}_{\mathscr{H}_0}\right)\exp(\Delta t\hat{L}_{\mathscr{H}_r})\exp\left(\frac{\Delta t}{2}\hat{L}_{\mathscr{H}_0}\right) = \exp\left(\Delta t\left(\frac{\hat{L}_{\mathscr{H}_0}}{2} + \hat{L}_{\mathscr{H}_r}\right) + \frac{\Delta t^2}{4}[\hat{L}_{\mathscr{H}_0},\hat{L}_{\mathscr{H}_r}] + \mathcal{O}(\Delta t^3)\right)\exp\left(\frac{\Delta t}{2}\hat{L}_{\mathscr{H}_0}\right) =$$

$$\exp\left(\Delta t\hat{L}_{\mathscr{H}} + \frac{\Delta t^2}{4}([\hat{L}_{\mathscr{H}_0},\hat{L}_{\mathscr{H}_r}] + [\hat{L}_{\mathscr{H}_r},\hat{L}_{\mathscr{H}_0}]) + \mathcal{O}(\Delta t^3)\right) =$$

$$\exp(\Delta t\hat{L}_{\mathscr{H}} + \mathcal{O}(\Delta t^3)) \tag{7}$$

It follows that the approximation in eq 5 is quadratic. Inserting eq 5 into eq 4 gives

$$\vec{x}|_{t_0+\Delta t} \approx \exp\left(\frac{\Delta t}{2}\hat{L}_{\mathscr{H}_0}\right)\exp(\Delta t\hat{L}_{\mathscr{H}_r})\exp\left(\frac{\Delta t}{2}\hat{L}_{\mathscr{H}_0}\right)\vec{x}|_{t_0} \tag{8}$$

which is the new explicit second order symplectic integration algorithm. It prescribes how to propagate from one point in phase space to another as follows: the system is propagated a half step evolution with $\mathscr{H}_0$, then a whole step with $\mathscr{H}_r$, and finally another half step with $\mathscr{H}_0$. This scheme is called the generalized leap-frog.[10,17] Because it is a product of symplectic mappings, it is also symplectic.[5]

In this integration scheme the partitioned part of the MD Hamiltonian $\mathscr{H}_0$ describes the vibrational motion of the system.[18] It represents the dynamically leading contribution whose potential depends only on constant parameters of the simulation. This separation allows us to calculate normal modes only once, at the beginning of the calculation. In this term are included all bonding interactions within the harmonic approximation. The motion governed by $\mathscr{H}_0$ is resolved by means of normal coordinates that rotate in phase space with the corresponding vibrational frequencies which are obtained by solving the secular equation[19] at the outset of the calculation.
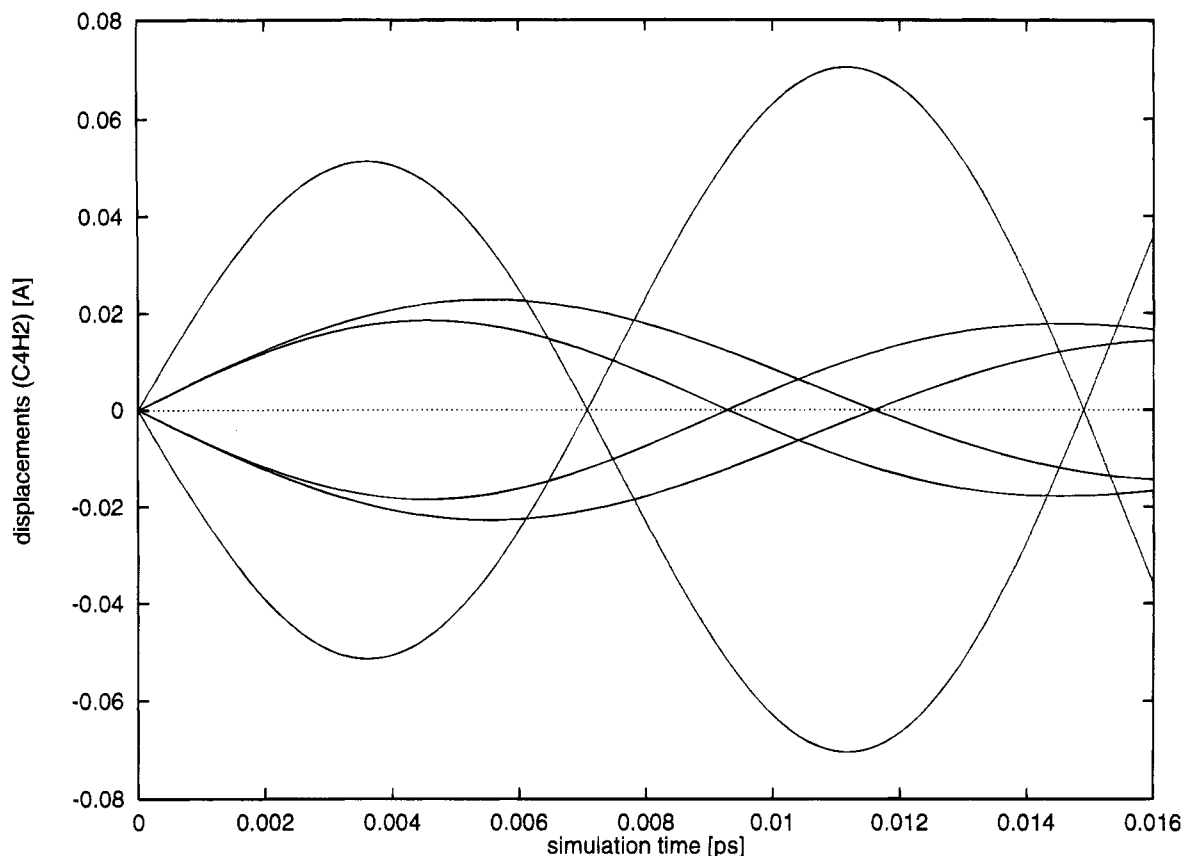
For a typical MD Hamiltonian

$$\mathscr{H} = \sum_i \frac{\mathbf{p}_i^2}{2m_i} + \sum_{bonds} k_b(b - b_0)^2 + \sum_{angles} k_\varphi(\varphi - \varphi_0)^2 + \sum_{dihed} k_\vartheta(1 + \cos(n\vartheta - \delta)) + \sum_{i>j} \frac{e_i e_j}{r_{ij}} + \sum_{i>j} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^6\right] \tag{9}$$

where i and j run over all atoms, e_i denotes the charge on the i atom, and r_{ij} is the distance between atoms i and j, we can define

$$\mathscr{H}_0 = \mathscr{H}^{harm}(m_i,b_0,\varphi_0,\delta,k_b,k_\varphi,k_\vartheta)$$

$$\mathscr{H}_r = \mathscr{H} - \mathscr{H}^{harm}(m_i,b_0,\varphi_0,\delta,k_b,k_\varphi,k_\vartheta) \tag{10}$$

where $\mathscr{H}^{harm}$ denotes the harmonic approximation; m_i is the mass of the i atom, b_0, φ_0, and δ are reference values for bond lengths, angles, and dihedral angles, respectively, and k_b, k_φ, and k_ϑ are corresponding force constants.

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Figure 1. Cartesian displacements of each atom for butadiyne, H$-$(C$\equiv$C)$-$(C$\equiv$C)$-$H. Higher frequencies correspond to hydrogen atoms and lower frequencies to carbon atoms.

Following the procedure defined by eq 8, the new symplectic algorithm for MD simulations is written explicitly as follows:

Step 0: Perform normal mode calculation for the harmonic part ($\mathcal{H}_0$) of the Hamiltonian to get frequencies and normal modes of vibration. Normal modes are represented by normal coordinates, hereafter denoted P and Q, obtained by means of the transformational matrix $\mathbf{V}$. The columns of matrix $\mathbf{V}$ are the normal mode vectors.

Step 1: Propagate by $\mathcal{H}_0$ for the time $\Delta t/2$. This corresponds to the rotation of normal coordinates, P_i^0 and Q_i^0, in the phase space by the corresponding vibrational frequency ω_i

$$\begin{bmatrix} P'_i \\ Q'_i \end{bmatrix} = \begin{bmatrix} \cos\left(\omega_i\dfrac{\Delta t}{2}\right) & -\omega_i\sin\left(\omega_i\dfrac{\Delta t}{2}\right) \\ (1/\omega_i)\sin\left(\omega_i\dfrac{\Delta t}{2}\right) & \cos\left(\omega_i\dfrac{\Delta t}{2}\right) \end{bmatrix}\begin{bmatrix} P_i^0 \\ Q_i^0 \end{bmatrix} \quad (11)$$

Step 2: Intermediate step in preparation for step 3. Transformation from normal coordinates P'_k and Q'_k to Cartesian displacement coordinates p'_k and q'_k

$$p'_i = \sqrt{m_i}\sum_k \mathbf{V}_{ik}P'_k$$

$$q'_i = \frac{1}{\sqrt{m_i}}\sum_k \mathbf{V}_{ik}Q'_k \quad (12)$$

Step 3: Evolve with $\mathcal{H}_r$ by means of numerical integration

$$p''_i = p'_i - \Delta t\left(\frac{\partial\mathcal{H}_r}{\partial q_i}\right)_{q_i=q'_i}$$

$$q''_i = q'_i + \Delta t\left(\frac{\partial\mathcal{H}_r}{\partial p_i}\right)_{p_i=p'_i} \quad (13)$$

Since $\mathcal{H}_r = \mathcal{H}_r(q)$, $[(\partial\mathcal{H}_r/\partial p_i)_{p_i=p'_i} = 0]$, only the momentum changes at this step.

Step 4: Intermediate step in the preparation for step 5. Back transformation from Cartesian displacement coordinates p''_k and q''_k to normal coordinates P''_k and Q''_k

$$P''_i = \sum_k \frac{1}{\sqrt{m_k}}\mathbf{V}_{ik}^T p''_k$$

$$Q''_i = \sum_k \sqrt{m_k}\mathbf{V}_{ik}^T q''_k \quad (14)$$

Step 5: Again the rotation of normal coordinates in the phase space

$$\begin{bmatrix} P_i \\ Q_i \end{bmatrix} = \begin{bmatrix} \cos\left(\omega_i\dfrac{\Delta t}{2}\right) & -\omega_i\sin\left(\omega_i\dfrac{\Delta t}{2}\right) \\ (1/\omega_i)\sin\left(\omega_i\dfrac{\Delta t}{2}\right) & \cos\left(\omega_i\dfrac{\Delta t}{2}\right) \end{bmatrix}\begin{bmatrix} P''_i \\ Q''_i \end{bmatrix} \quad (15)$$

This concludes one whole integration step. At this point, the transformation from normal coordinates to Cartesian displacement coordinates has to be performed whether the physical properties of the system, e.g., energy and displacements, are to be derived.

Step 6: Return to step 1 ($P_i \rightarrow P_i^0$, $Q_i \rightarrow Q_i^0$) and continue for the desired number of time steps.

But, if no physical properties of the system are desired at the end of a step, then step 5 of the current step can be merged with step 1 of the next step into a single rotation by $\omega_i\Delta t$ radians.
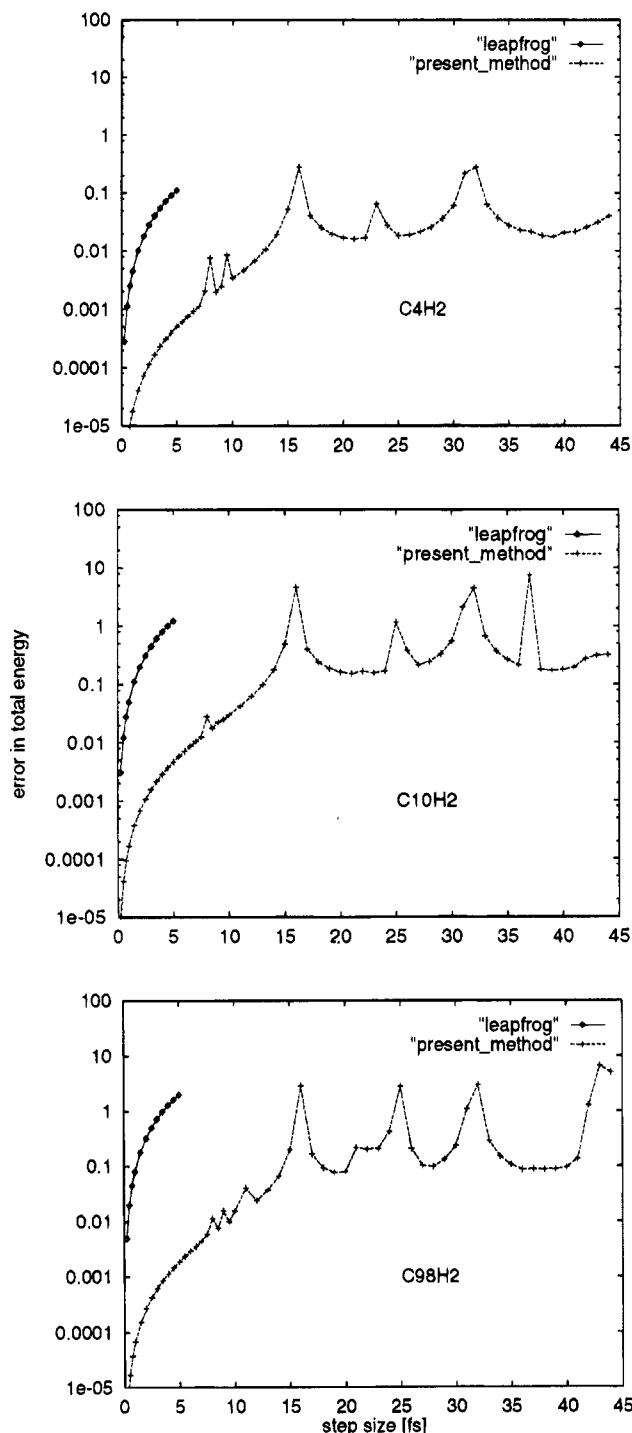
Figure 2. Error in total energy for leap-frog-Verlet algorithm and the present method of H−(C≡C)$_n$−H for n = 2, 5, and 49. Results are plotted for two different algorithms (− ◊ −, leap-frog-Verlet algorithm, − + −, present method).

The treatment of high frequency terms in the Hamiltonian permits the new simplectic algorithm proposed in eqs 11−15 to use a much larger integration step size Δt than the standard methods.

3. RESULTS

To test the efficiency of the new method, we compared it to the standard leap-frog-Verlet method for the simulation of linear molecules H−(C≡C)$_n$−H for n = 2, 5, and 49. For n = 2 this is butadiyne, H−(C≡C)−(C≡C)−H, a six atom molecule. These molecules were chosen as a bench-

Table 1. CPU Time [s] for 200 MD Steps of H−(C≡C)$_n$−H Using the Leap-Frog-Verlet and the Present Method for Equal Time Steps Computed on an HP 715/75 Workstation

no. of atoms	leap-frog-Verlet	present method
12	0.37	0.16
100	5.41	4.47
200	16.89	17.81
400	58.66	70.89
800	217.73	279.23

Table 2. Comparison of the Values of the Atomic Displacements [Å] for H−(C≡C)$_2$−H After 1.1 ps of Simulation Using the Leap-Frog-Verlet Method with Time Steps of 0.1 and 1 fs and the Present Method with Time Steps of 0.1 and 11 fs

atom no.	step size (fs)			
	leap-frog-Verlet		present method	
	0.1	1	0.1	11
1	8.258×10^{-2}	-7.033×10^{-2}	8.231×10^{-2}	8.361×10^{-2}
2	-9.537×10^{-3}	-1.142×10^{-3}	-9.466×10^{-3}	-1.023×10^{-2}
3	-2.570×10^{-2}	-1.835×10^{-2}	-2.577×10^{-2}	-2.601×10^{-2}
4	2.570×10^{-2}	1.835×10^{-2}	2.577×10^{-2}	2.601×10^{-2}
5	9.537×10^{-3}	1.142×10^{-3}	9.466×10^{-3}	1.023×10^{-2}
6	-8.258×10^{-2}	7.033×10^{-2}	-8.231×10^{-2}	-8.361×10^{-2}

mark system because the primary restriction on time step usually in macromolecule simulations arises form the presence of strong chemical bonds.[20]

Assuming that bond stretching satisfactorily describes all vibrational motions for linear molecules, the partitioned parts of Hamiltonian are

$$\mathcal{H}_0 = \sum_i \frac{\mathbf{p}_i^2}{2m_i} + \sum_{bonds} k_b(b - b_0)^2$$

$$\mathcal{H}_r = \sum_{i>j} \frac{e_i e_j}{r_{ij}} + \sum_{i>j} 4\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}}\right)^6\right] \quad (16)$$

The initial atomic positions for these molecules were taken at the equilibrium, and thus all the displacements were equal to zero. The initial velocities were defined at T = 300 K by the equipartition theorem. Bond lengths and stretching constants were taken from van Gunsteren et al.,[21] and Lennard-Jones parameters were taken from Allen et al.[2] Atomic charges were calculated by fitting the point charges to the *ab initio* molecular electrostatic potential rather than Mulliken charges.[22]

Figure 1 displays the displacements of each atom for the butadiyne molecule. The displacements are mutually symmetric because the initial momenta were symmetric. The two curves with higher frequencies correspond to hydrogen atoms and those with lower frequencies to carbon atoms. The figure demonstrates the physical behavior of the system during a 0.016 ps time interval.

In order to compare the efficiency of the present method with the standard leap-frog-Verlet method, we compared computational performance for the same level of accuracy. We monitored the error in total energy, ΔE, defined as

$$\Delta E = \frac{1}{M}\sum_{i=1}^{M}\left|\frac{E_0 - E_i}{E_0}\right| \quad (17)$$

where E_i is the total energy at step i, E_0 is the initial energy, and M is the total number of time steps.

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Table 3. Time Reversibility of the Present Method for $H-(C\equiv C)_2-H^a$

integration time (ps)	step size (ps)					
	0.001	0.002	0.005	0.010	0.025	0.050
0.000	12.892 45	12.892 45	12.892 45	12.892 45	12.892 45	12.892 45
0.050	12.892 04	12.890 78	12.879 97	12.872 79	13.392 98	14.094 04
0.100	12.892 06	12.890 87	12.880 56	12.878 83	13.449 86	14.572 09
0.150	12.892 48	12.892 56	12.893 29	12.899 55	13.005 57	13.568 02
0.200	12.892 72	12.893 54	12.898 96	12.990 50	12.556 01	12.387 42
0.250	12.892 72	12.893 53	12.899 06	12.995 16	12.480 09	12.512 30
0.300	12.892 46	12.892 49	12.892 51	12.895 19	12.833 46	13.604 84
0.350	12.892 05	12.890 81	12.880 24	12.864 31	13.328 47	14.228 58
0.400	12.892 05	12.890 82	12.880 21	12.882 30	13.427 51	14.069 74
0.450	12.892 48	12.892 58	12.893 50	12.906 67	13.093 51	13.486 84
0.450	12.892 48	12.892 58	12.893 50	12.906 67	13.093 51	13.486 84
0.400	12.892 05	12.890 82	12.880 21	12.882 30	13.427 51	14.069 74
0.350	12.892 05	12.890 81	12.880 24	12.864 31	13.328 47	14.228 58
0.300	12.892 46	12.892 49	12.892 51	12.895 19	12.833 46	13.604 84
0.250	12.892 72	12.893 53	12.899 06	12.995 16	12.480 09	12.512 30
0.200	12.892 72	12.893 54	12.898 96	12.990 50	12.556 01	12.387 42
0.150	12.892 48	12.892 56	12.893 29	12.899 55	13.005 57	13.568 02
0.100	12.892 06	12.890 87	12.880 56	12.878 83	13.449 86	14.572 09
0.050	12.892 04	12.890 78	12.879 97	12.872 79	13.392 98	14.094 04
0.000	12.892 45	12.892 45	12.892 45	12.892 45	12.892 45	12.892 45

^{a} Values of total energy (kcal/mol) are shown for different step sizes (ps) and integration steps (ps).

Figure 2 shows the error in total energy for test molecules $H-(C\equiv C)_n-H$ with $n = 2$, 5, and 49. The solid line represents the leap-frog-Verlet method, and the dashed line represents the present method. It is obvious that for the same level of accuracy, the time step in the present method can be ten times or more larger as in the leap-frog-Verlet method. Furthermore, the leap-frog-Verlet method is stable for only very short time steps, up to 5 fs, while the present method is stable even up to a time step 200 fs. Although it should be noted that such large step sizes no longer represent physical reality and are identified with linear molecules which have no bending or torsional intramolecular interactions. There are anomalous variations in total energy (the "spikes" on the curve) which might be due to the so called "step size resonance",[20] and a detailed analysis of this phenomenon will be reported in the following paper.[14]

In Table 1 the CPU times required by the two methods for 200 integration steps computed on an HP 715/75 workstation are compared for various model systems (12, 100, 200, 600, and 800 atoms). The computation cost per integration step is approximately the same for both methods, so that the speedup of the present method over the leap-frog-Verlet is determined mainly by the difference in step size which is significant.

Table 2 shows atomic displacements for butadiyne after 1.1 ps of simulation for both methods, using different step sizes. The third column, calculated with the present method and a time step of 0.1 fs, displays the most precise displacements and should be compared with the values of displacements in other columns, obtained with different methods and/or step sizes. For the present method, displacements are in a very good agreement with the exact values even for a step size of 11 fs, while the displacements obtained with the leap-frog-Verlet algorithm already have lost their deterministic character at a step size of less than 1 fs.

Symplectic integrators tend to confuse with time-reversible integrators. Symplectic integration methods which are also symmetric are time reversible.[5] Since the present method is symplectic and symmetric, it must be time-reversible. To test this fact we calculated the trajectories for the butadiyne

molecule also for negative time. Table 3 presents total energy for the butadiyne molecule for different step sizes and integration times. The data demonstrate the time reversibility of the present method.

5. CONCLUSIONS

The present work is a first attempt to design and analyze a new symplectic integration algorithm for molecular dynamics simulations which uses an analytical treatment of high frequency motions within a generalized leap-frog scheme. This algorithm is an order of magnitude faster than the commonly used leap-frog-Verlet method. The main restriction on step size in the general MD simulations, which stems from the high-frequency motion, is, to a large extent overcome in this approach.

Much work remains in the development of this approach: the method will be extended to the force fields that include angle bending and torsional terms, and large systems such as biological macromolecules will be treated. Further improvements in efficiency could be achieved by implementing the method on computers with highly parallel architecture.[23-25] Although we have not yet tested these alternative strategies in the present paper, we believe that the proposed symplectic algorithm will become the choice for MD simulations.

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