Evaluation of atomic pressure in the multiple time-step integration algorithm

Yoshimichi Andoh[*], Noriyuki Yoshii[†], Atsushi Yamada[‡], Susumu Okazaki[§¶]

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Abstract

In molecular dynamics (MD) calculations, reduction in calculation time per MD loop is essential. A multiple time-step (MTS) integration algorithm, the RESPA (Tuckerman, M.E.; Berne, B.J.; *J. Chem. Phys.* **1992**, *97*, 1990-2001), enables reductions in calculation time by decreasing the frequency of time-consuming long-range interaction calculations. However, the RESPA MTS algorithm involves uncertainties in evaluating the atomic interaction-based pressure (i.e., atomic pressure) of systems with and without holonomic constraints. It is not clear which intermediate forces and constraint forces in the MTS integration procedure should be used to calculate the atomic pressure. In this article, we propose a series of equations to evaluate the atomic pressure in the RESPA MTS integration procedure on the basis of its equivalence to the Velocity-Verlet integration procedure with a single time step (STS). The equations guarantee time-reversibility even for the system with holonomic constrants. Further, we generalize the equations to both (i) arbitrary number of inner time steps and (ii) arbitrary number of force components (RESPA levels). The atomic pressure calculated by our equations with the MTS integration shows excellent agreement with the reference value with the STS, whereas pressures calculated using the conventional ad hoc equations deviated from it. Our equations can be extended straightforwardly to the MTS integration algorithm for the isothermal NVT and isothermal–isobaric NPT ensembles.

Keywords: Molecular dynamics calculation, atomic pressure, multiple time-step, RESPA, SHAKE/RATTLE

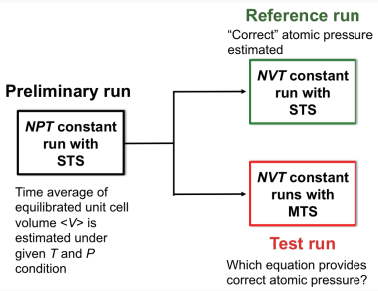
[*]Center of Computational Science, Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8603, Japan

[†]Department of Applied Chemistry, Nagoya University; Center of Computational Science, Graduate School of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8603, Japan

[‡]Department of Applied Chemistry, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464-8603, Japan

[§]Department of Applied Chemistry, Nagoya University; Center of Computational Science, Graduate School of Engineering, Furo-cho, Chikusa-ku, Nagoya 464-8603, Japan

[¶]Author to whom correspondence should be addressed. Electronic mail: okazaki@apchem.nagoya-u.ac.jp



For molecular dynamics calculations, a series of equations to evaluate the atomic pressure in the RESPA multiple time-step (MTS) integration procedure are proposed on the basis of its equivalence to the Velocity-Verlet integration procedure with a single time step (STS). The atomic pressure calculated by our equations with the MTS integration shows excellent agreement with the reference value with the STS, whereas pressures calculated using the conventional ad hoc equations deviated from it.

1 INTRODUCTION

In molecular dynamics (MD) calculations, reduction of the computation time per MD step with accuracy of the calculations unchanged has been required widely in the field. One promising approach to this is an implementation of the multiple time-step (MTS) integration algorithm to solve Newton's equations of motion numerically for each atom. The basic idea of the MTS integration is as follows[1]: Forces acting on atom j, $\boldsymbol{f}_j$, are decomposed into fast and slowly varying components, $\boldsymbol{f}_j^{\mathrm{fast}}$ and $\boldsymbol{f}_j^{\mathrm{slow}}$, respectively. Two kinds of time step, δt and Δt, are then used to solve the equation of motion, where $\delta t = \Delta t/n$ with a number of inner time steps n. $\boldsymbol{f}_j^{\mathrm{slow}}$ is evaluated only once per one MD loop, whereas $\boldsymbol{f}_j^{\mathrm{fast}}$ is evaluated n times. Therefore, the calculation time of $\boldsymbol{f}_j^{\mathrm{slow}}$, which is typically the long-range Coulombic force in the reciprocal space treated by the Ewald method[2] or that from multipole interaction in the fast multipole method (FMM)[3], can be reduced by a factor of n. When an MD code is parallelized by the Message Passing Interface (MPI), the time for MPI communications relating to the above long-range force calculation can also be saved by the MTS integration.

The most sophisticated algorithm for MTS integration is the reversible reference system propagator algorithms (RESPA).[4–7] In RESPA, the time evolution of coordinate and velocity of atom j, $\boldsymbol{r}_j(t)$ and $\boldsymbol{v}_j(t)$, respectively, are described by the time evolution operator (propagator) $\exp(iLt)$, where L is the Liouville operator and $i = \sqrt{-1}$ is the imaginary unit. For a Hamiltonian system composed of N atoms, iL can be written as:[4]

$$iL = \sum_{j=1}^{N} \boldsymbol{v}_j \cdot \frac{\partial}{\partial \boldsymbol{r}_j} + \sum_{j=1}^{N} \frac{\boldsymbol{f}_j}{m_j} \cdot \frac{\partial}{\partial \boldsymbol{v}_j}. \tag{1}$$

Let the first and the second terms in Eq. (1) be iL_1 and iL_2, then the Trotter expansion gives:

$$\exp(iL\Delta t) = \exp\left(iL_2\frac{\Delta t}{2}\right)\exp(iL_1\Delta t)\left(iL_2\frac{\Delta t}{2}\right) + \mathcal{O}(\Delta t^3), \tag{2}$$

which corresponds to the well-known velocity–Verlet integration algorithm[1] with a single time step (STS) Δt. Here, magnitude of Δt is determined by the time scale of the fastest varying component of $\boldsymbol{f}_j$.

In the MTS integration by RESPA, $\boldsymbol{f}_j$ is composed of the fast and slowly varying components, $\boldsymbol{f}_j^{\mathrm{fast}}$ and $\boldsymbol{f}_j^{\mathrm{slow}}$, respectively. Then, $iL_2 = iL_2^{\mathrm{fast}} + iL_2^{\mathrm{slow}}$, and Eq. (2) is factorized

into[4]

$$\exp(iL\Delta t) \approx \exp\left(iL_2^{\mathrm{slow}}\frac{\Delta t}{2}\right) \times \left[\exp\left(iL_2^{\mathrm{fast}}\frac{\delta t}{2}\right)\exp(iL_1\delta t)\exp\left(iL_2^{\mathrm{fast}}\frac{\delta t}{2}\right)\right]^n \exp\left(iL_2^{\mathrm{slow}}\frac{\Delta t}{2}\right). \quad (3)$$

where the propagators $\exp(iL_2^{\mathrm{fast}}\delta t/2)\exp(iL_1\delta t)\exp(iL_2^{\mathrm{fast}}\delta t/2)$ at the inner position work every step of δt, while $\exp(iL_2^{\mathrm{slow}}\Delta t/2)$s at the outermost sides work only once every n steps of δt. Thus, the cost for the calculation of $\boldsymbol{f}_j^{\mathrm{slow}}$ can be reduced by $1/n$. Δt and δt are chosen according to the time scales of $\boldsymbol{f}_j^{\mathrm{slow}}$ and $\boldsymbol{f}_j^{\mathrm{fast}}$, respectively. With an appropriate choice of n, MTSs given by Eq. (3) generates trajectories in which the Hamiltonian of the particle system is preserved at the same level as the trajectories generated by Eq. (2) with the single time step δt.

However, MTS integration algorithm involves uncertainty in evaluating the atom-based pressure (i.e., the atomic pressure) of the system. It is not clear which intermediate force that appears in the MTS procedure should be used to calculate the atomic pressure in the MD step. In this paper, we propose an analytical solution for this problem. We obtained a series of equations for the evaluation of atomic pressure which should be used in the RESPA MTS integration algorithm, on the basis of the equivalence to the velocity–Verlet method in the STS calculations. We show that MTS MD runs with holonomic constraints give proper values of the atomic pressure when they are evaluated by our equations. The new equations were generalized to the arbitrary number of inner time steps n for the calculation of the fast varying force(s) and arbitrary number of force components (RESPA levels) l_{RESPA} of $\boldsymbol{f}_j$. Our equations can be applied straightforwardly to RESPA for canonical ensembles and isothermal–isobaric ensembles.[5–7]

2 METHODOLOGY

In this sections, we derive a series of equations to calculate the atomic pressure for the RESPA MTS integration algorithm. First, in Section 2.1, the discretized equations of motion without holonomic constraints are shown to explain our basic strategy. Here, the number of inner time steps n of the fast force in Eq. (3) was set to be 2 for simplicity, and $\boldsymbol{f}_j$ is decomposed into two components, $\boldsymbol{f}_j^{\text{fast}}$ and $\boldsymbol{f}_j^{\text{slow}}$ (i.e., l_{RESPA}=2). The net force $\boldsymbol{F}$ with which the atomic virial should be calculated is obtained on the basis of the equivalence to the velocity–Verlet integration algorithm with a STS. Second, in Section 2.2, the net constraint force $\boldsymbol{G}$ is obtained to calculate atomic pressure from the holonomic constraints. In Appendices D and E in the Supporting Information, the generalized descriptions are shown for the atomic pressure produced by the net forces and net constraint forces for an arbitrary number of inner time steps n for the fast varying force(s) and for an arbitrary number of force components l_{RESPA} with different associated time scales.

2.1 Multiple time-step integration without holonomic constraints

The discretized equations generated by the STS propagator in Eq. (2) are given as:

$$\boldsymbol{v}_j\left(t+\frac{\Delta t}{2}\right) = \boldsymbol{v}_j(t) + \frac{\Delta t}{2}\frac{\boldsymbol{f}_j(t)}{m_j} \tag{4a}$$

$$\boldsymbol{r}_j(t+\Delta t) = \boldsymbol{r}_j(t) + \Delta t\ \boldsymbol{v}_j\left(t+\frac{\Delta t}{2}\right) \tag{4b}$$

$$\boldsymbol{v}_j(t+\Delta t) = \boldsymbol{v}_j\left(t+\frac{\Delta t}{2}\right) + \frac{\Delta t}{2}\frac{\boldsymbol{f}_j(t+\Delta t)}{m_j}, \tag{4c}$$

where we assume that there are no holonomic constraints in the system. A schematic figure of the time evolutions of $\boldsymbol{r}_j$ and $\boldsymbol{v}_j$ by eq. (4) is depicted in Fig.1A. By substituting Eq. (4a) into Eqs. (4b) and (4c), we have:

$$\boldsymbol{r}_j(\Delta t) = \boldsymbol{r}_j(0) + \Delta t\ \boldsymbol{v}_j(0) + \frac{\Delta t^2}{2}\frac{\boldsymbol{f}_j(0)}{m_j} \tag{5a}$$

$$\boldsymbol{v}_j(\Delta t) = \boldsymbol{v}_j(0) + \frac{\Delta t}{2}\frac{\boldsymbol{f}_j(0)+\boldsymbol{f}_j(\Delta t)}{m_j}, \tag{5b}$$

respectively, where the reference time t is set to be 0 just for simplicity. We named these two equations "two-step update process". We can use them to evaluate the instantaneous

atomic pressure P of the system as:

$$P(0) = \frac{1}{3V}\left[\sum_{i=1}^{N} m_j \boldsymbol{v}_j^2(0) + \sum_{i=1}^{N} \boldsymbol{r}_j(0)\cdot\boldsymbol{f}_j(0)\right], \tag{6}$$

or:

$$P(\Delta t) = \frac{1}{3V}\left[\sum_{i=1}^{N} m_j \boldsymbol{v}_j^2(\Delta t) + \sum_{i=1}^{N} \boldsymbol{r}_j(\Delta t)\cdot\boldsymbol{f}_j(\Delta t)\right]. \tag{7}$$

The first terms in the brackets in Eqs. (6) and (7) are the kinetic part of atomic pressure, and the second terms are the virial parts, which stem from interatomic interactions. Equations (6) and (7) are the same as each other except for time and used to calculate time average of P in the calculations without constraints. However, as discussed later, where constrains are involved, these two are used in different ways.

In contrast, the MTS propagator in Eq. (3) with $n = 2$ ($\Delta t = 2\delta t$), for example, gives the following discretized equations:

$$\boldsymbol{v}\left(\frac{\delta t}{2}\right) = \boldsymbol{v}(0) + \frac{\delta t}{2}\frac{\boldsymbol{f}^{\text{fast}}(0) + 2\boldsymbol{f}^{\text{slow}}(0)}{m} \tag{8a}$$

$$\boldsymbol{r}(\delta t) = \boldsymbol{r}(0) + \delta t\ \boldsymbol{v}\left(\frac{\delta t}{2}\right) \tag{8b}$$

$$\boldsymbol{v}(\delta t) = \boldsymbol{v}\left(\frac{\delta t}{2}\right) + \frac{\delta t}{2}\frac{\boldsymbol{f}^{\text{fast}}(\delta t)}{m} \tag{8c}$$

$$\boldsymbol{v}\left(\frac{3\delta t}{2}\right) = \boldsymbol{v}(\delta t) + \frac{\delta t}{2}\frac{\boldsymbol{f}^{\text{fast}}(\delta t)}{m} \tag{8d}$$

$$\boldsymbol{r}(\Delta t) = \boldsymbol{r}(2\delta t) = \boldsymbol{r}(\delta t) + \delta t\ \boldsymbol{v}\left(\frac{3\delta t}{2}\right) \tag{8e}$$

$$\boldsymbol{v}(\Delta t) = \boldsymbol{v}(2\delta t) = \boldsymbol{v}\left(\frac{3\delta t}{2}\right) + \frac{\delta t}{2}\frac{\boldsymbol{f}^{\text{fast}}(\Delta t) + 2\boldsymbol{f}^{\text{slow}}(\Delta t)}{m}, \tag{8f}$$

where, for simplicity, subscript j is not shown, and the force $\boldsymbol{f}$ is decomposed into two components $\boldsymbol{f}^{\text{fast}}$ and $\boldsymbol{f}^{\text{slow}}$ (l_{RESPA}=2). A schematic figure of the time evolutions of $\boldsymbol{r}_j$ and $\boldsymbol{v}_j$ by the discretized eq.(8) is presented in Fig.1B.

As for the STS integration in Eq. (4), there is only one choice of timing to evaluate P, that is, at $t = 0$ which is equivalent to $t = \Delta t$, since combination of $\boldsymbol{r}_j$ and $\boldsymbol{v}_j$ at an intermediate time $t = t + \frac{\Delta t}{2}$ is nonphysical. In contrast, as for the MTS integration in Eq. (8), an additional choice of timing to evaluate P at $t = \delta t$ might be possible formally. However, the trajectories at intermediate times are not based on the total atomic forces,

and thus do not reflect correct physical behavior. We should evaluate the atomic pressure at $t = 0$, equivalently $t = \Delta t$, even for the MTS integrations, too.

To obtain the proper expression for the atomic pressure in the MTS procedure, the basic strategy in the present study is (i) to generate a set of discretized equations of motion such as Eqs. (8a)–(8f) from the time evolution operator, (ii) to derive equations for a two-step update process with Δt in the same way as that in Eq. (5), and (iii) to obtain an instantaneous atomic pressure for the system as will be shown later in Eq. (11).

An example for the case of n=2 is as follows. First, in the same way as the case of Eq. (4) and (5), Eq. (8) can be simplified by the substitution and can be reduced to

$$\boldsymbol{r}(\Delta t) = \boldsymbol{r}(0) + \Delta t \boldsymbol{v}(0) + \frac{\Delta t^2}{2}\frac{\boldsymbol{F}(0)}{m} \tag{9a}$$

$$\boldsymbol{v}(\Delta t) = \boldsymbol{v}(0) + \frac{\Delta t}{2}\frac{\boldsymbol{F}(0) + \boldsymbol{F}(\Delta t)}{m}, \tag{9b}$$

where we define the "net forces" $\boldsymbol{F}(0)$ and $\boldsymbol{F}(\Delta t)$ at $t = 0$ and Δt, respectively, to be

$$\boldsymbol{F}(0) = \frac{\boldsymbol{f}^{\mathrm{fast}}(0) + \boldsymbol{f}^{\mathrm{fast}}(\delta t)}{2} + \boldsymbol{f}^{\mathrm{slow}}(0) \tag{10a}$$

$$\boldsymbol{F}(\Delta t) = \frac{\boldsymbol{f}^{\mathrm{fast}}(\delta t) + \boldsymbol{f}^{\mathrm{fast}}(\Delta t)}{2} + \boldsymbol{f}^{\mathrm{slow}}(\Delta t), \tag{10b}$$

respectively. $\boldsymbol{F}(0)$ and $\boldsymbol{F}(\Delta t)$ are composed of $\boldsymbol{f}^{\mathrm{fast}}$ and $\boldsymbol{f}^{\mathrm{slow}}$ at various intermediate times.

It should be noted that the update of $\boldsymbol{r}(0)$ and $\boldsymbol{v}(0)$ by these $\boldsymbol{F}(0)$ and $\boldsymbol{F}(\Delta t)$ formally using the STS equation for Δt given by Eq. (9) presents the same trajectory as the update following Eqs. (8). Therefore, one reasonable choice for the description of the instantaneous atomic pressure of the system should be

$$P(0) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(0) + \sum \boldsymbol{r}(0)\cdot\boldsymbol{F}(0)\right] \tag{11a}$$

$$P(\Delta t) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(\Delta t) + \sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{F}(\Delta t)\right]. \tag{11b}$$

in accordance with Eqs.(6) and (7).

Eqs. (11) can be obtained in a different way by decomposing propagator for the isothermal–isobaric ensemble with a MTS proposed by Tuckerman et al.[6] as is discussed in Appendix A in the Supporting Information.

Furthermore, equation (11) is essentially different from the conventional ad hoc estimation of $P(0)$ and $P(\Delta t)$, where the pressures are calculated as

$$P^{\mathrm{adhoc1}}(0) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(0) + \sum \boldsymbol{r}(0)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(0) + 2\boldsymbol{f}^{\mathrm{slow}}(0)\}\right] \tag{12a}$$

$$P^{\mathrm{adhoc1}}(\Delta t) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(\Delta t) + \sum \boldsymbol{r}(\Delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\Delta t) + 2\boldsymbol{f}^{\mathrm{slow}}(\Delta t)\}\right], \tag{12b}$$

respectively. The prefactors 2 of $\boldsymbol{f}^{\mathrm{slow}}(0)$ and $\boldsymbol{f}^{\mathrm{slow}}(\Delta t)$ may result from the force expressions in Eqs.(8a) and (8f). $P^{\mathrm{adhoc1}}(0)$ and $P^{\mathrm{adhoc1}}(\Delta t)$ are evaluated only from the information of $\boldsymbol{v}$, $\boldsymbol{r}$, and $\boldsymbol{f}$ at $t = 0$ and Δt, respectively.

Another conventional ad hoc method is a simple averaging of instantaneous atomic pressures at every intermediate time in the MTS procedure[8,9]. If the number of inner time steps for the fast varying force n is two, then ad hoc equations for the pressures are

$$\begin{aligned} P^{\mathrm{adhoc2}}(0) = \frac{1}{3V}\Bigg[&\frac{1}{2}\left(\sum m\boldsymbol{v}^2(0) + \sum m\boldsymbol{v}^2(\delta t)\right) \\ &+ \frac{1}{2}\left(\sum \boldsymbol{r}(0)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(0) + \boldsymbol{f}^{\mathrm{slow}}(0)\} + \sum \boldsymbol{r}(\delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\delta t) + \boldsymbol{f}^{\mathrm{slow}}(0)\}\right)\Bigg] \end{aligned} \tag{13a}$$

$$\begin{aligned} P^{\mathrm{adhoc2}}(\Delta t) = \frac{1}{3V}\Bigg[&\frac{1}{2}\left(\sum m\boldsymbol{v}^2(\delta t) + \sum m\boldsymbol{v}^2(\Delta t)\right) \\ &+ \frac{1}{2}\left(\sum \boldsymbol{r}(\delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\delta t) + \boldsymbol{f}^{\mathrm{slow}}(0)\} + \sum \boldsymbol{r}(\Delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\Delta t) + \boldsymbol{f}^{\mathrm{slow}}(\Delta t)\}\right)\Bigg]. \end{aligned} \tag{13b}$$

Note that $\boldsymbol{f}^{\mathrm{slow}}(\Delta t)$ is yet not calculated at $t = \delta t$. Thus, $\boldsymbol{r}(\delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\delta t)+\boldsymbol{f}^{\mathrm{slow}}(0)\}$ appears. When $n = 2$ in the Eq. (3), these equations are almost the same as Eqs. (11) together with Eqs. (10).

It is also interesting to note that Eqs.(11) together with Eqs.(10) present time-reversibility for the trajectories. That is, when t=0 and Δt are interchanged, these equations remain unchanged, whereas Eqs.(13) do not.

A practical implementation of Eq. (11) for the two-body interatomic potential is shown in Appendix B in the Supporting Information.

2.2 Multiple time-step integration with holonomic constraints

We assume that the system includes K holonomic constraints described by

$$g_k = (\boldsymbol{r}_l - \boldsymbol{r}_m)^2 - d_{lm}^2 = 0, k = 1, ..., K, \tag{14}$$

where d_{lm} is an interatomic distance to be constrained between the two atoms l and m. The STS velocity–Verlet integration algorithm with the SHAKE[10] and RATTLE[11] methods gives:

$$\boldsymbol{v}\left(\frac{\Delta t}{2}\right) = \boldsymbol{v}(0) + \frac{\Delta t}{2}\frac{\boldsymbol{f}(0) + \boldsymbol{g}^{\mathrm{SHAKE}}(0)}{m} \tag{15a}$$

$$\boldsymbol{r}(\Delta t) = \boldsymbol{r}(0) + \Delta t\ \boldsymbol{v}\left(\frac{\Delta t}{2}\right) \tag{15b}$$

$$\boldsymbol{v}(\Delta t) = \boldsymbol{v}\left(\frac{\Delta t}{2}\right) + \frac{\Delta t}{2}\frac{\boldsymbol{f}(\Delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\Delta t)}{m}, \tag{15c}$$

or equivalently:

$$\boldsymbol{r}(\Delta t) = \boldsymbol{r}(0) + \Delta t\ \boldsymbol{v}(0) + \frac{\Delta t^2}{2}\frac{\boldsymbol{f}(0) + \boldsymbol{g}^{\mathrm{SHAKE}}(0)}{m} \tag{16a}$$

$$\boldsymbol{v}(\Delta t) = \boldsymbol{v}(0) + \frac{\Delta t}{2}\left[\frac{\boldsymbol{f}(0) + \boldsymbol{g}^{\mathrm{SHAKE}}(0)}{m} + \frac{\boldsymbol{f}(\Delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\Delta t)}{m}\right], \tag{16b}$$

where $\boldsymbol{g}^{\mathrm{SHAKE}}(0)$ and $\boldsymbol{g}^{\mathrm{RATTLE}}(\Delta t)$ are the constraint forces at $t = 0$ for the SHAKE and at $t = \Delta t$ for the RATTLE. According to Eqs. (6) and (7), an instantaneous atomic pressure of the system with holonomic constraints is:

$$P(0) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(0) + \sum \boldsymbol{r}(0) \cdot \{\boldsymbol{f}(0) + \boldsymbol{g}^{\mathrm{SHAKE}}(0)\}\right], \tag{17a}$$

$$P(\Delta t) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(\Delta t) + \sum \boldsymbol{r}(\Delta t) \cdot \{\boldsymbol{f}(\Delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\Delta t)\}\right]. \tag{17b}$$

In contrast, with the holonomic constraints, the propagator Eq. (3) with $n = 2$ (i.e.,

$\Delta t = 2\delta t$), for example, generates the discretized equations of motion as follows

$$\boldsymbol{v}\left(\frac{\delta t}{2}\right) = \boldsymbol{v}(0) + \frac{\delta t}{2}\frac{\boldsymbol{f}^{\mathrm{fast}}(0) + 2\boldsymbol{f}^{\mathrm{slow}}(0) + \boldsymbol{g}^{\mathrm{SHAKE}}(0)}{m} \tag{18a}$$

$$\boldsymbol{r}(\delta t) = \boldsymbol{r}(0) + \delta t\ \boldsymbol{v}\left(\frac{\delta t}{2}\right) \tag{18b}$$

$$\boldsymbol{v}(\delta t) = \boldsymbol{v}\left(\frac{\delta t}{2}\right) + \frac{\delta t}{2}\frac{\boldsymbol{f}^{\mathrm{fast}}(\delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\delta t)}{m} \tag{18c}$$

$$\boldsymbol{v}\left(\frac{3\delta t}{2}\right) = \boldsymbol{v}(\delta t) + \frac{\delta t}{2}\frac{\boldsymbol{f}^{\mathrm{fast}}(\delta t) + \boldsymbol{g}^{\mathrm{SHAKE}}(\delta t)}{m} \tag{18d}$$

$$\boldsymbol{r}(\Delta t) = \boldsymbol{r}(\delta t) + \delta t\ \boldsymbol{v}\left(\frac{3\delta t}{2}\right) \tag{18e}$$

$$\boldsymbol{v}(\Delta t) = \boldsymbol{v}\left(\frac{3\delta t}{2}\right) + \frac{\delta t}{2}\frac{\boldsymbol{f}^{\mathrm{fast}}(\Delta t) + 2\boldsymbol{f}^{\mathrm{slow}}(\Delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\Delta t)}{m}. \tag{18f}$$

In Eq. (18), the SHAKE and RATTLE procedures are performed according to the XI-RESPA expansion of the time evolution operator, taking into account their applicability to the NPT ensemble[5].

Similar to Eq. (15), Eq. (18) can also be simplified by the substitution and can be rewritten as

$$\boldsymbol{r}(\Delta t) = \boldsymbol{r}(0) + \Delta t\boldsymbol{v}(0) + \frac{\Delta t^2}{2}\frac{\boldsymbol{F}(0) + \boldsymbol{G}^{\mathrm{SHAKE}}(0)}{m} \tag{19a}$$

$$\boldsymbol{v}(\Delta t) = \boldsymbol{v}(0) + \frac{\Delta t}{2}\left[\frac{\boldsymbol{F}(0) + \boldsymbol{G}^{\mathrm{SHAKE}}(0)}{m} + \frac{\boldsymbol{F}(\Delta t) + \boldsymbol{G}^{\mathrm{RATTLE}}(\Delta t)}{m}\right], \tag{19b}$$

where the net constraint forces $\boldsymbol{G}^{\mathrm{SHAKE}}(0)$ and $\boldsymbol{G}^{\mathrm{RATTLE}}(\Delta t)$ at $t = 0$ for the SHAKE and at $t = \Delta t$ for the RATTLE are defined by:

$$\boldsymbol{G}^{\mathrm{SHAKE}}(0) = \frac{\boldsymbol{g}^{\mathrm{SHAKE}}(0)}{2} + \frac{\boldsymbol{g}^{\mathrm{SHAKE}}(\delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\delta t)}{4} \tag{20a}$$

$$\boldsymbol{G}^{\mathrm{RATTLE}}(\Delta t) = \frac{\boldsymbol{g}^{\mathrm{SHAKE}}(\delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\delta t)}{4} + \frac{\boldsymbol{g}^{\mathrm{RATTLE}}(\Delta t)}{2}, \tag{20b}$$

respectively. Equation (19) indicates that the STS update of $\boldsymbol{r}(0)$ and $\boldsymbol{v}(0)$ by $\boldsymbol{F}(0) + \boldsymbol{G}^{\mathrm{SHAKE}}(0)$ and $\boldsymbol{F}(\Delta t)+\boldsymbol{G}^{\mathrm{RATTLE}}(\Delta t)$, respectively, is formally equivalent to the MTS update of $\boldsymbol{r}(0)$ and $\boldsymbol{v}(0)$ by Eq. (18). Thus, one promising choice for the instantaneous atomic pressure of the system should be

$$P(0) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(0) + \sum \boldsymbol{r}(0)\cdot\{\boldsymbol{F}(0) + \boldsymbol{G}^{\mathrm{SHAKE}}(0)\}\right] \tag{21a}$$

$$P(\Delta t) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(\Delta t) + \sum \boldsymbol{r}(\Delta t)\cdot\{\boldsymbol{F}(\Delta t) + \boldsymbol{G}^{\mathrm{RATTLE}}(\Delta t)\}\right]. \tag{21b}$$

Eqs. (21) can be also obtain in a different way by decomposing the propagator for the isothermal–isobaric (NPT) ensemble with a MTS in the same manner as in the Appendix A in the Supporting Information.

These two equations are essentially different from the conventional ad hoc equations to calculate the atomic pressure using $\boldsymbol{v}$, $\boldsymbol{r}$, $\boldsymbol{f}$, and $\boldsymbol{g}$ at $t = 0$ and Δt

$$P^{\mathrm{adhoc1}}(0) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(0) + \sum \boldsymbol{r}(0)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(0) + 2\boldsymbol{f}^{\mathrm{slow}}(0) + \boldsymbol{g}^{\mathrm{SHAKE}}(0)\}\right] \tag{22a}$$

$$P^{\mathrm{adhoc1}}(\Delta t) = \frac{1}{3V}\left[\sum m\boldsymbol{v}^2(\Delta t) + \sum \boldsymbol{r}(\Delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\Delta t) + 2\boldsymbol{f}^{\mathrm{slow}}(\Delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\Delta t)\}\right], \tag{22b}$$

and from the ad hoc simple average of instantaneous atomic pressures at every intermediate time in the MTS procedure[8,9]

$$\begin{aligned} P^{\mathrm{adhoc2}}(0) &= \frac{1}{3V}\left[\frac{1}{2}\left(\sum m\boldsymbol{v}^2(0) + \sum m\boldsymbol{v}^2(\delta t)\right)\right. \\ &+ \frac{1}{2}\left(\sum \boldsymbol{r}(0)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(0) + \boldsymbol{f}^{\mathrm{slow}}(0) + \boldsymbol{g}^{\mathrm{SHAKE}}(0)\}\right. \\ &+ \left.\left.\sum \boldsymbol{r}(\delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\delta t) + \boldsymbol{f}^{\mathrm{slow}}(0) + \boldsymbol{g}^{\mathrm{SHAKE}}(\delta t)\}\right)\right] \end{aligned} \tag{23}$$

for the SHAKE and

$$\begin{aligned} P^{\mathrm{adhoc2}}(\Delta t) &= \frac{1}{3V}\left[\frac{1}{2}\left(\sum m\boldsymbol{v}^2(\delta t) + \sum m\boldsymbol{v}^2(\Delta t)\right)\right. \\ &+ \frac{1}{2}\left(\sum \boldsymbol{r}(\delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\delta t) + \boldsymbol{f}^{\mathrm{slow}}(0) + \boldsymbol{g}^{\mathrm{RATTLE}}(\delta t)\}\right. \\ &+ \left.\left.\sum \boldsymbol{r}(\Delta t)\cdot\{\boldsymbol{f}^{\mathrm{fast}}(\Delta t) + \boldsymbol{f}^{\mathrm{slow}}(\Delta t) + \boldsymbol{g}^{\mathrm{RATTLE}}(\Delta t)\right)\right] \end{aligned} \tag{24}$$

for the RATTLE.

Again, it is interesting to note that Eqs.(21) together with Eqs.(10) and (20) are time-reversible in time. It is shown that the velocity-Velret algorithm combined with the SHAKE and RATTLE methods is symplectic and time-reversible if the iteration is carried to convergence[12]. As numerically shown later in Table 3 and 4, the constraint forces by the SHAKE and RATTLE are symmetric in time, too. Thus, when t=0 and Δt are interchanged, these equations remain unchanged. In contrast, Eqs.(23) and (24) does not have such time-reversible symmetric nature.

As shown later in Table 1, difference between Eq. (21) and Eqs. (23) and (24) causes a difference in the time-averaged atomic pressure. Difference between Eq. (21) and Eq. (22) causes larger difference in the time-averaged atomic pressure. An example of Fortran coding of Eq. (21) is shown in Appendix C in the Supporting Information.

Furthermore, we also derived the generalized equations for the net forces and the net constraint forces for an arbitrary number of inner time steps n and an arbitrary number of force components l_{RESPA} for the total force $\boldsymbol{f}_j$ chosen. Consequently, the generalized net forces:

$$\boldsymbol{F}(0) = \frac{1}{n^2}\left[\sum_{k=0}^{n-1}\sum_{j=0}^{k}\boldsymbol{f}^{\mathrm{fast}}(j\delta t) + \sum_{k=1}^{n-1}\sum_{j=1}^{k}\boldsymbol{f}^{\mathrm{fast}}(j\delta t)\right] + \boldsymbol{f}^{\mathrm{slow}}(0) \tag{25a}$$

$$\boldsymbol{F}(\Delta t) = \frac{1}{n}\left[\sum_{j=0}^{n-1}\boldsymbol{f}^{\mathrm{fast}}(j\delta t) + \sum_{j=1}^{n}\boldsymbol{f}^{\mathrm{fast}}(j\delta t)\right] + \boldsymbol{f}^{\mathrm{slow}}(0) + \boldsymbol{f}^{\mathrm{slow}}(\Delta t) - \boldsymbol{F}(0) \tag{25b}$$

and, the generalized net constraint forces:

$$\boldsymbol{G}^{\mathrm{SHAKE}}(0) = \frac{1}{n^2}\left[\sum_{k=0}^{n-1}\sum_{j=0}^{k}\boldsymbol{g}^{\mathrm{SHAKE}}(j\delta t) + \sum_{k=1}^{n-1}\sum_{j=1}^{k}\boldsymbol{g}^{\mathrm{RATTLE}}(j\delta t)\right] \tag{26a}$$

$$\boldsymbol{G}^{\mathrm{RATTLE}}(\Delta t) = \frac{1}{n}\left[\sum_{j=0}^{n-1}\boldsymbol{g}^{\mathrm{SHAKE}}(j\delta t) + \sum_{j=1}^{n}\boldsymbol{g}^{\mathrm{RATTLE}}(j\delta t)\right] - \boldsymbol{G}^{\mathrm{SHAKE}}(0) \tag{26b}$$

can be obtained as a function of n (see appendix D and E in the Supporting Information). On the other hand, the net forces and net constraint forces generalized to l_{RESPA} are obtained by introducing intermediate generalized net forces hierarchically. An example for the case of $l_{\mathrm{RESPA}} = 3$ is described in Appendix D in the Supporting Information.

3 CALCULATIONS

We have carried out a series of MD calculations to demonstrate that the expressions for the atomic pressures given in the present study based on the net forces and net constraint forces is proper for the system with holonomic constraints for the cases $l_{\mathrm{RESPA}} = 2$ with $n = 2$, and $l_{\mathrm{RESPA}} = 3$ with $n_1 = 4$ and $n_2 = 2$.

We performed two kinds of MD runs in the canonical ensemble, reference runs and test runs. For the reference runs, the STS integration scheme was adopted to update atomic

coordinates and velocities using the total forces, which gives the correct time-averaged atomic pressure for the system. For the test runs, the MTS integration scheme was adopted for the multistage update of atomic coordinates and velocities based on the decomposed forces. The resultant pressures were compared with the reference ones.

3.1 System

Three different systems were prepared in a cubic cell with three-dimensional periodic boundary condition. The first one contains water molecules only (WAT), while the second one contains ethanol molecules only (ETH). The third one contains protein self-assembly poliovirus capsid, lipid, ions, and water molecules (PV), identical to our previous work[13].

In the system WAT, three distance constraints (O–H, O–H, and H–H) were imposed on the water molecules to form a rigid body. In the system ETH, C–H and O–H distances were constrained, whereas other intramolecular degrees of freedom, stretchings, bendings, and dihedral rotations, were flexible. In the system PV, the water molecules were treated as rigid body in the same manner as the system WAT, and the distances of all chemical bonds relevant to hydrogen atom were constrained, keeping other intramolecular degrees of freedom flexible. The system WAT consists of 6510 water molecules and the system ETH has 1331 ethanol molecules. In the system PV, the capsid is composed of 240 viral proteins (60 each of VP1, VP2, VP3, and VP4) and 60 sphingosine lipid pocket factors, while an electrolyte solution contains 10652 ions and 1884218 water molecules. Thus, total number of atoms N was 19530 for the system WAT, 11979 for the system ETH, and about 6.5 million for the system PV.

To distinguish between the reference and demonstration runs, subscripts were added to the system notation. For example, $\mathrm{WAT}_{\mathrm{ref}}$, and $\mathrm{ETH}_{\mathrm{mts}}$ represent the reference run for the system WAT with a STS and the demonstration runs for the system ETH with MTS, respectively.

3.2 MD calculations

The modified TIP3P (mTIP3P[14,15]) model commonly used in the CHARMM was adopted for water. For ethanol, the all-atom CHARMM potential was adopted, where all parameters were taken from the standard CHARMM topology and parameter files registered as RESI ETOH. For proteins and electrolytes, the CHARMM22[16] with CMAP[17] and ion parameters in the standard CHARMM files was used, while the CHARMM27[18] was used for sphingosine. The Lennard-Jones (LJ) interaction was cut off at 1.2 nm without the long-range correction for potential energy and pressure. The Coulomb interaction was calculated by the particle-mesh Ewald (PME) method[19] with the damping parameter $\alpha = 3.20$ nm^{-1} for WAT and ETH. The space grid for the FFT was made $64\times64\times64$. For system PV, it was calculated by the FMM[3] with the spherical harmonic expansion up to the fourth order, and the interaction with the multipole moments of the entire MD simulation cell in the periodic boundary condition was calculated using the Ewald method for multipoles[20]. We emphasize that our conclusions do not depend on molecular species, choice of the potential model, calculation method for the Coulomb interaction used in the test calculations, or whether the LJ long-range correction is taken into account or not.

The equations of motion were solved using STS RESPA for the reference runs, and with MTSs for the test runs. In the test runs, the total atomic forces $\boldsymbol{f}_j$ were decomposed into fast forces $\boldsymbol{f}_j^{\mathrm{fast}}$, intermediate forces $\boldsymbol{f}_j^{\mathrm{intermed}}$, and slow forces $\boldsymbol{f}_j^{\mathrm{slow}}$. The $\boldsymbol{f}_j^{\mathrm{fast}}$ is from intramolecular interactions. For system WAT, these interactions were not taken into account. The $\boldsymbol{f}_j^{\mathrm{intermed}}$ is from the LJ and Coulomb interactions in the real space within the cutoff radius for the PME method and in the pairwize additive part for the FMM. The $\boldsymbol{f}_j^{\mathrm{slow}}$ is from the Coulomb interaction in the reciprocal space for the PME method and that by multipoles for the FMM.

The distance constraints were imposed using the SHAKE/RATTLE methods[10,11] with tolerance of 10^{-8}. The P-SHAKE and P-RATTLE algorithms[21], which give the same calculation accuracy as the standard SHAKE and RATTLE methods were adopted. All calculations were performed using the MODYLAS,[22] in which subroutines to calculate the atomic pressure of the system at $t = \Delta t$ given by Eq. (21b) are implemented.

First, for the system WAT and ETH, the preliminary STS MD runs were carried out for 10 ns under the constant NPT condition with P = 1.0 atm and T = 298.15 K to estimate a thermally equilibrated volume of the system $\langle V_{\rm MD}\rangle$. The time step, Δt, was 2 fs for WAT and 0.5 fs for ETH, according to the time scale of fastest varying force component in the system under consideration, $\boldsymbol{f}_j^{\rm intermed}$ for WAT and $\boldsymbol{f}_j^{\rm fast}$ for ETH. For the system PV, $\langle V_{\rm MD}\rangle$ was obtained from the result of our previous study[13]: Thermally equilibrated system was obtained by 200 ns MD calculation under constant NPT calculation with P=1 atm and T = 310.15 K, where $\langle V_{\rm MD}\rangle$ was obtained over the last 100 ns run. In the MD run[13], multiple time steps of ΔT=4 fs with $l_{\rm RESPA}$=3, n_1=4, and n_2=2 (i.e. δt=0.5 fs and Δt=2.0 fs) in Eq. (A31) in the Appendix D was adopted. Because it is computationally too expensive to calculate $\langle V_{\rm MD}\rangle$ based on the constant NPT MD calculation with a STS of 0.5 fs for a 6.5 million atoms system, $\langle V_{\rm MD}\rangle$ obtained by the MTS NPT run was used in the following discussion. P and T were controlled by the Andersen barostat[23] and the Nosé–Hoover chain thermostat[24–26] to their target values. The time constants of the thermostat and barostat were 0.5 ps and 1.0 ps, respectively.

Next, for the system WAT and ETH, the reference MD runs with a STS and test runs with MTSs were carried out for 20 ns under the constant NVT condition with $V = \langle V_{\rm MD}\rangle$ and T = 298.15 K. For the system PV, calculation time length was over 5 ns with $V = \langle V_{\rm MD}\rangle$ and T=310.15 K. In these runs, T was controlled by the Nosé–Hoover chain thermostat with the time constant 0.5 ps. The propagators of the thermostat were located at the outermost position in accordance with the XO-RESPA.[5] We chose NVT ensemble instead of NVE ensemble because we found that the initial velocities strongly influence the accuracy of the calculated atomic pressure $\langle P_{\rm MD}\rangle$, in the NVE ensemble.

In the reference MD runs, the STS Δt was 2 fs for $\rm WAT_{ref}$ and 0.5 fs for $\rm ETH_{ref}$ and $\rm PV_{ref}$. In the test MD runs, the MTSs were as follows. For $\rm WAT_{mts}$ with $l_{\rm RESPA}$=2 and n=2, δt and Δt were 2 fs, and 4 fs, respectively. For $\rm ETH_{mts}$ and $\rm PV_{mts}$ with $l_{\rm RESPA}$=3, n_1=4, and n_2=2 in Eq. (A31) in the Appendix D, δt, Δt, and ΔT were 0.5 fs, 2 fs, and 4 fs, respectively.

4 RESULTS

The value of $\langle V_{\mathrm{MD}} \rangle^{1/3}$ averaged over the 10 ns preliminary NPT runs was 5.7792 ± 0.0001 nm for the system WAT, 5.0503 ± 0.0005 nm for ETH, and that averaged over the 100 ns run was 39.996 ± 0.001 nm for the system PV. Errors are defined as the standard deviation of block average over each 2 ns interval. The density of the system $\langle \rho_{\mathrm{MD}} \rangle$ was 1.0090 ± 0.0001 g cm^{-3} for WAT, which corresponds well with that obtained in a previous MD study with the mTIP3P water model[15] (1.009 g cm^{-3}) under the same thermodynamic and calculation conditions.

Figure 2 shows block average of pressures $\langle P_{\mathrm{MD}} \rangle_i$ for the reference and test runs in the NVT ensemble. The averaged atomic pressure $\langle P_{\mathrm{MD}} \rangle$ over the entire simulation time (20 ns for WAT and ETH, 5 ns for PV) in the thermal equilibrium are listed in Table 1.

Agreement of the resultant pressures in the test runs with those in the reference runs depends much on the equations adopted for the pressure calculation. As clearly shown in Table 1, our equations showed excellent agreement with the reference values for the system WAT and ETH. The calculated $\langle P_{\mathrm{MD}} \rangle$ based on our equation (21) was 1 ± 1 atm for $\mathrm{WAT}_{\mathrm{mts}}$, and 1 ± 3 atm for $\mathrm{ETH}_{\mathrm{mts}}$, which agree well with 1 ± 1 atm for $\mathrm{WAT}_{\mathrm{ref}}$ and 0 ± 2 atm for $\mathrm{ETH}_{\mathrm{ref}}$, respectively. It was -0.4 ± 0.3 for $\mathrm{PV}_{\mathrm{mts}}$, which a little deviated from -4.6 ± 0.4 for $\mathrm{PV}_{\mathrm{ref}}$. This small deviation might stem from a shortage of average time length of 5 ns with a STS. However, it should be noted that difference in $\langle P_{\mathrm{MD}} \rangle$ between $\mathrm{PV}_{\mathrm{mts}}$ and $\mathrm{PV}_{\mathrm{ref}}$ is much smaller than that calculated by the ad hoc equations.

The ad hoc simple average equation (24) tends to overestimate the atomic pressure. For $\mathrm{WAT}_{\mathrm{mts}}$ with $n = 2$ and $l_{\mathrm{RESPA}} = 2$, $\langle P_{\mathrm{MD}}^{\mathrm{adhoc2}} \rangle = 3 \pm 2$ atm. Agreement is worse for $\mathrm{ETH}_{\mathrm{mts}}$ and $\mathrm{PV}_{\mathrm{mts}}$ with $n_1 = 4$, $n_2 = 2$ and $l_{\mathrm{RESPA}} = 3$; that is, $\langle P_{\mathrm{MD}}^{\mathrm{adhoc2}} \rangle = 6 \pm 2$ atm for the former and 10.5 ± 0.2 atm for the latter, respectively.

Further, the pressure based on the ad hoc equation (22) greatly underestimated the pressure regardless of the choice of n and l_{RESPA}; $\langle P_{\mathrm{MD}}^{\mathrm{adhoc1}} \rangle = -29 \pm 1$ atm for $\mathrm{WAT}_{\mathrm{mts}}$, -5830 ± 9 atm for $\mathrm{ETH}_{\mathrm{mts}}$, and -159 ± 2 atm for $\mathrm{PV}_{\mathrm{mts}}$. These large deviations indicate that the ad hoc equations (24) and (22) are not appropriate to evaluate the atomic pressure of the system.

5 DISCUSSION

In order to investigate the mechanism that the equations (21) only provides the atomic pressures corresponding well to their reference values, we decomposed the averaged atomic pressure into contributions from each terms. The decompositions were done for the systems $\mathrm{WAT}_{\mathrm{ref}}$ and $\mathrm{ETH}_{\mathrm{ref}}$.

First, Table 2 lists decomposed contributions of each terms in the equations (6) and (7) to $\langle P_{\mathrm{MD}}(0)\rangle$ and $\langle P_{\mathrm{MD}}(\Delta t)\rangle$ with a STS. In these cases, large positive values of kinetic terms $\langle\frac{\sum m\boldsymbol{v}^2(j\Delta t)}{3V}\rangle$ and virial terms from interatomic potential functions $\langle\frac{\sum \boldsymbol{r}(j\Delta t)\cdot\boldsymbol{f}(j\Delta t)}{3V}\rangle$ are cancelled by the virial terms from constraint forces $\langle\frac{\sum \boldsymbol{r}(j\Delta t)\cdot\boldsymbol{f}^{\mathrm{SHAKE}}(j\Delta t)}{3V}\rangle$ and $\langle\frac{\sum \boldsymbol{r}(j\Delta t)\cdot\boldsymbol{f}^{\mathrm{RATTLE}}(j\Delta t)}{3V}\rangle$ with large negative values, which results in $\langle P_{\mathrm{MD}}(0)\rangle$=$\langle P_{\mathrm{MD}}(\Delta t)\rangle$=1 atm.

In Contrast, Table 3 and 4 list decomposed contributions of each terms in the equation (21b) to $\langle P_{\mathrm{MD}}(\Delta t)\rangle$ with a MTS. Note that superscript $^{\mathrm{fast}}$ in $\boldsymbol{f}^{\mathrm{fast}}$ in Eqs.(10b), (22b) and (24) are replaced by superscript $^{\mathrm{intermed}}$ in the following discussion for $\mathrm{WAT}_{\mathrm{mts}}$. The results for $\langle P_{\mathrm{MD}}(0)\rangle$ are shown in Table S1 and S2 in the Supporting Information. In these tables, we also listed weight factors of the weighted-average of $\langle P_{\mathrm{MD}}(\Delta t)\rangle$ for each term, $w^{\mathrm{kinetic}}(j)$, $w^{\mathrm{fast}}(j)$, $w^{\mathrm{intermed}}(j)$, $w^{\mathrm{slow}}(j)$, $w^{\mathrm{SHAKE}}(j)$ and $w^{\mathrm{RATTLE}}(j)$. That is,

$$
\begin{aligned}
\langle P_{\mathrm{MD}}(\Delta t)\rangle &= \sum_j w^{\mathrm{kinetic}}(j)\left\langle\frac{\sum m\boldsymbol{v}^2(j\delta t)}{3V}\right\rangle \\
&+ \sum_j w^{\mathrm{fast}}(j)\left\langle\frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{fast}}(j\delta t)}{3V}\right\rangle + \sum_j w^{\mathrm{intermed}}(j)\left\langle\frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{intermed}}(j\delta t)}{3V}\right\rangle \\
&+ \sum_j w^{\mathrm{slow}}(j)\left\langle\frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{slow}}(j\delta t)}{3V}\right\rangle \\
&+ \sum_j \left(w^{\mathrm{SHAKE}}(j)\left\langle\frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{g}^{\mathrm{SHAKE}}(j\delta t)}{3V}\right\rangle + w^{\mathrm{RATTLE}}(j)\left\langle\frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{g}^{\mathrm{RATTLE}}(j\delta t)}{3V}\right\rangle\right)
\end{aligned}
\tag{27}
$$

The values of $w(j)$ for $\mathrm{WAT}_{\mathrm{mts}}$ are determined by the equation (21b) together with the eqs.(10b) and (20b). Those for $\mathrm{ETH}_{\mathrm{mts}}$ are determined by factorizing eqs.(A38b) and (A39b) in the Appendix D with given n_1 and n_2. Note that a summation of $w(j)$ over j is 1 for each term, and that $\sum_j(w^{\mathrm{SHAKE}}(j)+w^{\mathrm{RATTLE}}(j))=1$ for constraint force terms.

The weighted-averages of $\langle P_{\mathrm{MD}}(\Delta t)\rangle$ with these $w(j)$ correspond well to their reference values with a STS as shown in Table 1. The same conclusion is obtained for $\langle P_{\mathrm{MD}}(0)\rangle$ (see

Table S1 and S2 in the Supporting Information).

On the other hand, weight factors for the ad hoc equations are shown in Table 5. For the ad hoc simple average based on eq.(24), all weight factors have a value of 0.5. Then, the weighted-averaged values of the slowly varying force term and constraint force term are coincidentally equivalent to those based on the eq. (21b). However, the weighted-averaged values of the kinetic term and fast varying force term are slightly but evidently different from those based on eq. (21b). These differences result in deviation of the estimated pressure from its reference value with a STS.

Phenomenologically, it might be better to change weight factors for these terms to $\frac{1}{2}, 0$, and $\frac{1}{2}$ for $j = 0, 1$, and 2, respectively, to obtain an agreement of the weighted-averaged pressure value with its reference value. However, in general, such adjustments can not be made in advance. For example, in the case of $\mathrm{ETH}_{\mathrm{mts}}$ shown in table 4 with $l_{\mathrm{RESPA}} = 3$, $n_1 = 4$, and $n_2 = 2$, it is almost impossible to find proper $w(j)$ for each term beforehand.

For the case of the ad hoc average based on eq.(22b), weight factors has a value of 1 except for slowly varying force term. Large negative deviation of the estimated pressure from its reference value results from the factor 2 of the slowly varying force term. However, it is also impossible to adjust these weight factors, because the average based on eq.(22b) is ad hoc.

Therefore, our equation (21) with the generalized net forces and the net constraint forces present excellent evaluation for the atomic pressure when Newton's equations of motion are numerically solved by the RESPA integration method with MTSs.

Further, it is interesting to note that Eqs. (21) with net forces, $\boldsymbol{F}(0)$ and $\boldsymbol{F}(\Delta t)$, and net constraint forces, $\boldsymbol{G}^{\mathrm{SHAKE}}(0)$ and $\boldsymbol{G}^{\mathrm{RATTLE}}(\Delta t)$, have time-reversibile symmetric nature. As is shown in Table 3 and Table S1 for the case of n=2 and $l_{\mathrm{RESPA}} = 2$, and in Table 4 and Table S2 for the case of n_1=4, n_2=2 and $l_{\mathrm{RESPA}} = 3$, time averages and weight factors are symmetric in time. Functional form of $\boldsymbol{F}(0)$ and $\boldsymbol{F}(\Delta t)$, together with $\boldsymbol{G}^{\mathrm{SHAKE}}(0)$ and $\boldsymbol{G}^{\mathrm{RATTLE}}(\Delta t)$, are unchanged when the direction of time evolution is reversed for any n and l_{RESPA}. This time-reversible symmetric structure of the equations might be important for the agreement of the calculated atomic pressure values with MTSs with their reference values.

It should be noted that, when NVT and NVE ensembles are adopted for the MD calcula-

tions, trajectories generated by RESPA with MTSs are the same irrespective of the pressure calculation . That is, the physical properties remain unchanged except for the pressure even when the ad hoc estimations are used. However, the MD calculations are usually carried out in the NPT ensemble. In this case, the correct calculation for the pressure is essential in the reliability of the MD calculations.

6 CONCLUSIONS

We proposed a series of equations for the calculation of atomic pressures on the basis of the net forces and net constraint forces when the RESPA MTS integration algorithm is used in the MD calculations. Further, we have generalized the formulas of these net forces and net constraint forces for the arbitrary number of inner time steps n and force components l_{RESPA}. We examined the validity of our descriptions by carrying out a series of MD calculations for water, ethanol, and protein assembly in electrolyte solution. The averaged atomic pressures based on our equations agreed well with the value obtained from the reference MD runs with the STS, although the pressures based on ad hoc equations showed systematic deviation from the reference values.

In recent large-scale MD calculations handling more than, for example, 10^6 atoms, the RESPA MTS integration becomes essential in order to reduce the calculation time of the long-range forces and MPI communications related to the long-range force calculations when MD codes are parallelized by the MPI. Then, the present description can be a basis of the pressure calculation in those large-scale MD calculations.

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References

1. Allen, M.P.; Tildesley, D.J. Computer Simulation of Liquids, Oxford Univ. Press: Claredon, 1987.

2. Ewald, P. Die Berechnung optischer und elektrostatischer Gitterpotentiale. *Ann. Phys.* **1921**, *64*, 253-287.

3. Greengard, J.F. The Rapid Evaluation of Potential Fields in Particle Systems. MIT Press: Cambridge, 1988.

4. Tuckerman, M.E.; Berne, B. J. Reversible multiple time scale molecular dynamics. *J. Chem. Phys.* **1992**, *97*, 1990-2001.

5. Martyna, G.J.; Tuckerman, M.E.; Tobias, D.J.; Klein, M.L. Explicit reversible integrators for extended systems dynamics. *Mol. Phys.* **1996**, *87*, 1117-1157.

6. Tuckerman, M.E.; Alejandre, J.; Lopez-Rendon, R.; Jochim, A.L.; Martyna, G.J. A Liouville-operator derived measure-preserving integrator for molecular dynamics simulations in the isothermal-isobaric ensemble. *J. Phys. A: Math. Gen.* **2006**, *39*, 5629-5651.

7. Yu, T.Q.; Alejandre, J.; Lopez-Rendon, R.; Martyna, G.J.; Tuckerman, M.E. Measure-preserving integrators for molecular dynamics in the isothermal-isobaric ensemble derived from the Liouville operator. *Chem. Phys.* **2010**, *370*, 294-305.

8. Qian, X.; Schlick, T. Efficient multiple-time-step integrators with distance-based force splitting for particle-mesh-Ewald molecular dynamics simulations. *J. Chem. Phys.* **2002**, *116*, 5971-5983.

9. Barash, D.; Yang, L.; Qian, X.; Schlick, T. Inherent Speedup limitations in multiple time step/particle mesh Ewald algorithms. *J. Comput. Chem.* **2002**, *24*, 77-88.

10. Ryckaert, J.P.; Ciccotti, G.; Berendsen, H.J.C. Numerical integration of the cartesian equation of motion of a system with constraints: molecular dynamics of n-alkanes. *J. Comput. Phys.* **1977**, *23*, 327-341.

11. Andersen, H.C. Rattle: A "velocity" version of the Shake algoritm for molecular dynamics calculations. *J. Comput. Phys.* **1983**, *52*, 24-34.

12. Leimkuhler, B. J.; Skeel, R. D. Symplectic numerical integrators in constrained Hamiltonian systems. *J. Comput. Phys.* **1994**, *112*, 117-125.

13. Andoh, Y.; Yoshii, N.; Yamada, A.; Fujimoto, K.; Kojima, H.; Mizutani, K.; Nakagawa, A.; Nomoto, A.; Okazaki, S. All-atom molecular dynamics calculation study of entire poliovirus empty capsids in solution. *J. Chem. Phys.* **2014**, *141*, 165101.

14. Durell, S. R., Brooks, B. R.; Ben-Naim, A. Solvent-Induced Forces between Two Hydrophilic Groups. *J. Phys. Chem.* **1994**, *98*, 2198-2202.

15. Price D.J.; Brooks III, C.L. A modified TIP3P water potential for simulation with Ewald summation. *J. Chem. Phys.* **2004**, *121*, 10096-10103.

16. MacKerell Jr. A.D.; Bashford, D.; Bellott, M.; Dunbrack Jr, R.L.; Evanseck, J.D.; Field, M.J.; Fischer, S.; Gao, J.; Guo, H.; Ha, S.; Joseph-MacCarthy, D.; Kuchnir, L.; Kuczera, K.; Lau, F.T.K.; Mattos, C.; Michnick, S.; Ngo, T.; Nguyen, D.T.; Prodhom, B.; Reiher, W.E.; Roux, B.; Schlenkrich, M.; Smith, J.C.; Stote, R.; Straub, J.; Watanabe, M.; Wiórkiewicz-Kuczera, J.; Yin, D.; Karplus, M. All-atom empirical potential for molecular modeling and dynamics studies of proteins. *J. Phys. Chem. B* **1998**, *102*, 3586—3616.

17. Mackerrell Jr., A.D.; Feig, M.; Brooks III, C.L. Extending the treatment of backbone energetics in protein force fields: limitations of gas-phase quantum mechanics in reproducing protein conformational distributions in molecular dynamics simulations. *J. Comput. Chem.* **2004**, *25*, 1400—1415

18. Hyvönen, M.T.; Kovanen, P.T. Molecular dynamics simulation of sphingomyeline bilayer. *J. Phys. Chem. B* **2003**, *107*, 9102-9108.

19. Essmann, U.; Perera, L.; Berkowitz, M.L.; Darden, T.; Lee, H.; Pedersen, L.G. A smooth particle mesh Ewald method. *J. Chem. Phys. 1995*, *103*, 8577-8593.

20. Figueirido, F.; Levy, R.M.; Zhou, R.; Berne, B.J. Large scale simulation of macromolecules in solution: Combining the periodic fast multiple method with multiple time step integrators. *J. Chem. Phys.* **1997**, *106*, 9835-9849.

21. Gonnet, P. P-SHAKE: A quadratically convergent SHAKE in $O(n^2)$. *J. Comput. Phys.* **2007**, *220*, 740-750.

22. Andoh, Y.; Yoshii, N.; Fujimoto, K.; Mizutani, K.; Kojima, H.; Yamada, A.; Okazaki, S.; Kawaguchi, K.; Nagao, H.; Iwahashi, K.; Mizutani, F; Minami, K.; Ichikawa, S.; Komatsu, H.; Ishizuki, S.; Takeda, Y.; Fukushima, M. MODYLAS: a highly parallelized general-purpose molecular dynamics simulation program for large-scale systems with long-range forces calculated by fast multipole method (FMM) and highly scalable fine-grained new parallel processing algorithms. *J. Chem. Theory Compt.* **2013**, *9*, 3201-3209.

23. Andersen, H.C. Molecular dynamics simulations at constant pressure and/or temperature. *J. Chem. Phys.* **1980**, *72*, 2384-2393.

24. Nosé, S. A molecular dynamics method for simulations in the canonical ensemble. *Mol. Phys.* **1984**, *52*, 255-268.

25. Hoover, W.G. Canonical dynamics: Equilibrium phase-space distribution. *Phys. Rev. A* **1985**, *31*, 1695-1697.

26. Martyna, G.J.; Tuckerman, M.E.; Klein, M.L. Nosé–Hoover chains: The canonical ensemble via continuous dynamics. *J. Chem. Phys.* **1992**, *97*, 2635-2643.

Figure 1: A schematic figure for the time evolutions of $\boldsymbol{r}_j$ and $\boldsymbol{v}_j$ following eq.(4) (panel A), and eq.(8) (panel B).

Figure 2: Block average of pressure $\langle P_{\rm MD} \rangle_i$ over 2 ns long interval for system WAT (panel A) and ETH (panel B), and that over 1 ns long interval for system PV (panel C). Open circles: reference run with a STS; closed diamonds: test run for equation (21) with MTSs; cross marks: test run for the ad hoc equation (24) with MTSs; and open triangles: test run for the ad hoc equation (22) with MTSs. In every panel, the dotted line shows 1 atm as a guide.

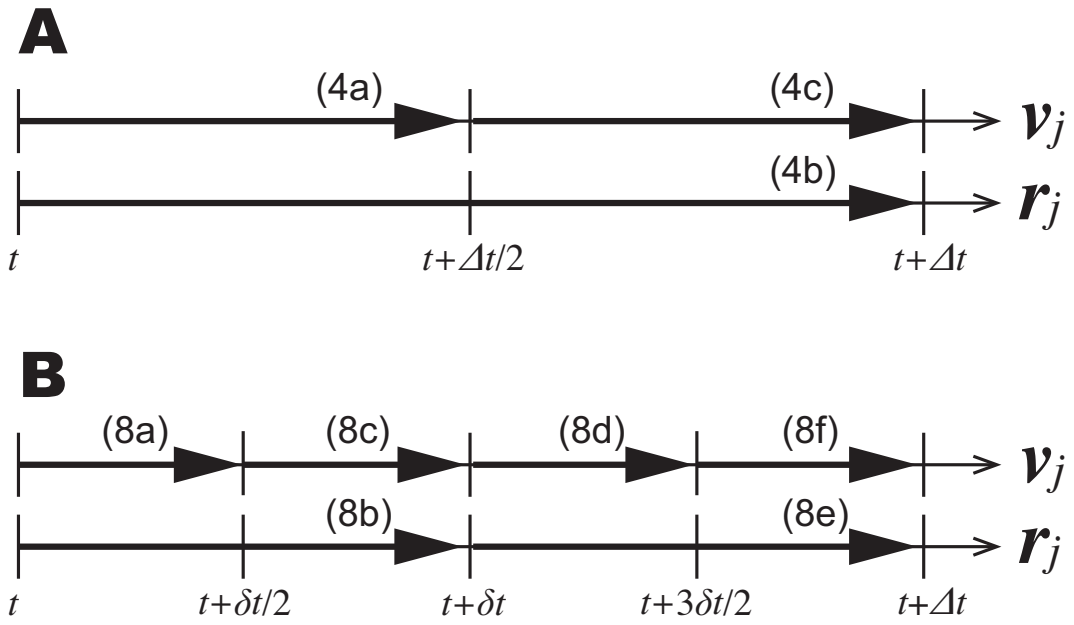

Figure 1
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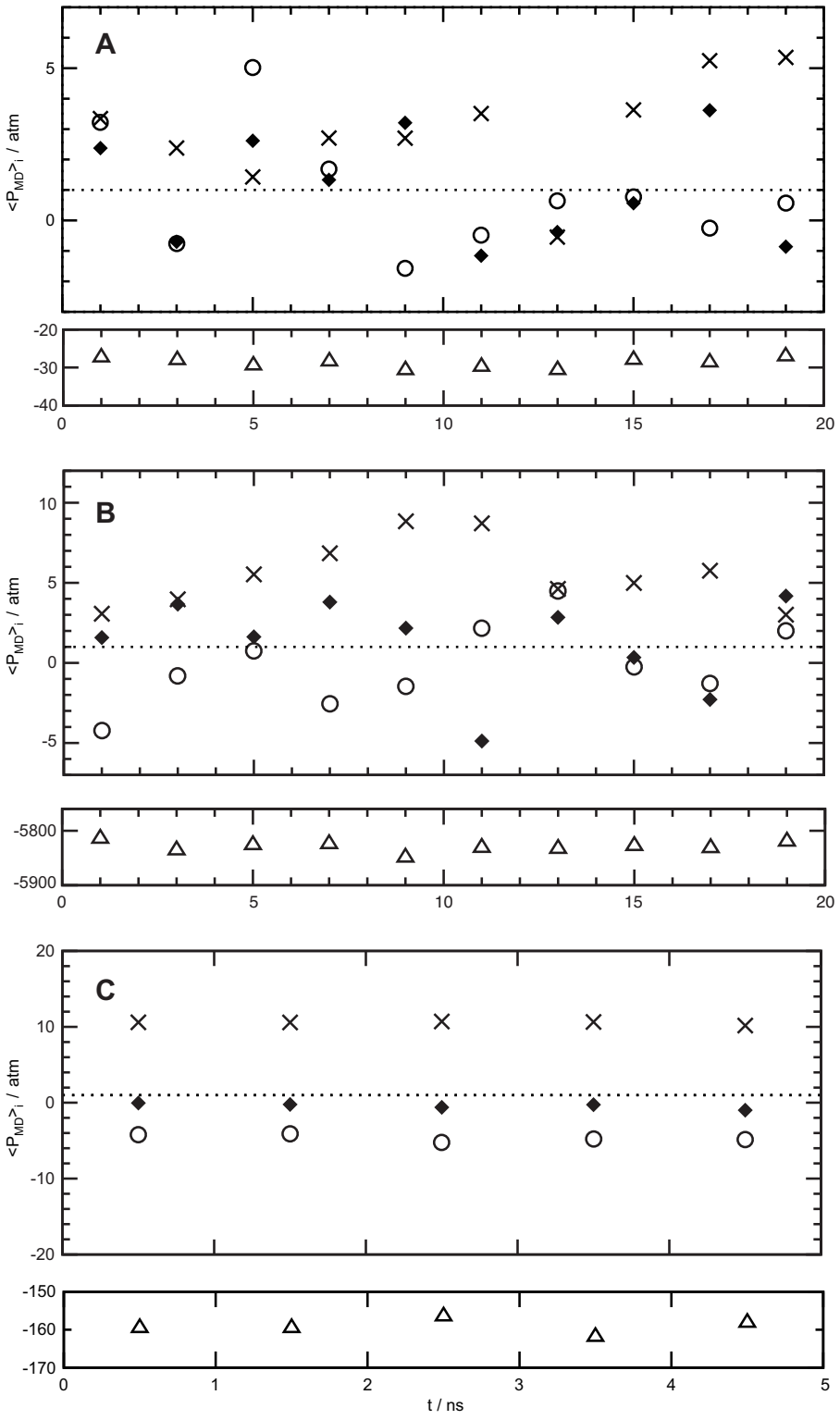

Figure 2
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Table 1: The calculated pressure $\langle P_{\mathrm{MD}} \rangle$ from the 20 ns reference runs and test runs in NVT ensemble. A STS of $\Delta t = 2.0$ fs was used for $\mathrm{WAT}_{\mathrm{ref}}$, and $\Delta t = 0.5$ fs for $\mathrm{ETH}_{\mathrm{ref}}$ and $\mathrm{PV}_{\mathrm{ref}}$. MTSs of $\delta t = 2.0$ fs and $\Delta t = 4.0$ fs were used for $\mathrm{WAT}_{\mathrm{mts}}$, and the values $\delta t = 0.5$ fs, $\Delta t = 2.0$ fs, and $\Delta T = 4.0$ fs for $\mathrm{ETH}_{\mathrm{mts}}$ and $\mathrm{PV}_{\mathrm{mts}}$. The errors represent the standard deviation among ten 2 ns long block averages for the system WAT and ETH, and five 1 ns interval averages for the system PV.

	Ref.	present work	ad hoc (24)	ad hoc (22b)
WAT	1 ± 1	1 ± 1	3 ± 2	-29 ± 1
ETH	1 ± 2	1 ± 3	6 ± 2	-5830 ± 9
PV	-4.6 ± 0.4	-0.4 ± 0.3	10.5 ± 0.2	-159 ± 2

Table 2: Contributions of each terms in the equations (6) and (7) to $\langle P_{\mathrm{MD}}(0)\rangle$ and $\langle P_{\mathrm{MD}}(\Delta t)\rangle$ with a STS, where $\boldsymbol{f} = \boldsymbol{f}^{\mathrm{fast}} + \boldsymbol{f}^{\mathrm{intermed}} + \boldsymbol{f}^{\mathrm{slow}}$. Contributions from three types of forces are separately shown. Each value has an unit of atm. Long hyphens in the table indicate that the value can not be logically calculated.

	WAT		ETH	
j	0	1	0	1
$\left\langle \frac{\sum m\boldsymbol{v}^2(j\Delta t)}{3V} \right\rangle$	2740.2	2740.2	2938.0	2938.0
$\left\langle \frac{\sum \boldsymbol{r}(j\Delta t)\cdot\boldsymbol{f}^{\mathrm{fast}}(j\Delta t)}{3V} \right\rangle$	–	–	400.2	400.2
$\left\langle \frac{\sum \boldsymbol{r}(j\Delta t)\cdot\boldsymbol{f}^{\mathrm{intermed}}(j\Delta t)}{3V} \right\rangle$	19832.9	19832.9	2599.5	2599.5
$\left\langle \frac{\sum \boldsymbol{r}(j\Delta t)\cdot\boldsymbol{f}^{\mathrm{slow}}(j\Delta t)}{3V} \right\rangle$	-132.2	-132.2	-269.1	-269.1
$\left\langle \frac{\sum \boldsymbol{r}(j\Delta t)\cdot\boldsymbol{g}^{\mathrm{SHAKE}}(j\Delta t)}{3V} \right\rangle$	-22440.2	–	-5667.4	–
$\left\langle \frac{\sum \boldsymbol{r}(j\Delta t)\cdot\boldsymbol{g}^{\mathrm{RATTLE}}(j\Delta t)}{3V} \right\rangle$	–	-22440.2	–	-5667.4

Table 3: Contributions of each term in the equation (21b) to $\langle P_{\mathrm{MD}}(\Delta t)\rangle$ for $\mathrm{WAT}_{\mathrm{mts}}$. Each value has an unit of atm. Long hyphens in the table indicate that the value can not be logically calculated in the MTS procedure.

j	0	1	2
$\left\langle \frac{\sum m\boldsymbol{v}^2(j\delta t)}{3V} \right\rangle$	2740.3	2743.5	2740.3
$w^{\mathrm{kinetic}}(j)$	0	0	1
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{intermed}}(j\delta t)}{3V} \right\rangle$	19830.2	19827.8	19830.2
$w^{\mathrm{intermed}}(j)$	0	$\frac{1}{2}$	$\frac{1}{2}$
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{slow}}(j\delta t)}{3V} \right\rangle$	-132.5	–	-132.5
$w^{\mathrm{slow}}(j)$	0	0	1
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{g}^{\mathrm{SHAKE}}(j\delta t)}{3V} \right\rangle$	-22333.7	-22537.8	–
$w^{\mathrm{SHAKE}}(j)$	0	$\frac{1}{4}$	0
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{g}^{\mathrm{RATTLE}}(j\delta t)}{3V} \right\rangle$	–	-22537.8	-22333.7
w^{RATTLE}	0	$\frac{1}{4}$	$\frac{1}{2}$

Table 4: Contributions of each terms to $\langle P_{\mathrm{MD}}(\Delta t)\rangle$ for $\mathrm{ETH}_{\mathrm{mts}}$. Each value has an unit of atm. Long hyphens in the table indicate that the value can not be logically calculated in the MTS procedure.

j	0	1	2	3	4	5	6	7	8
$\left\langle \frac{\sum m\boldsymbol{v}^2(j\delta t)}{3V} \right\rangle$	2938.3	2944.4	2944.7	2944.6	2939.3	2944.6	2944.7	2944.4	2938.3
$w^{\mathrm{kinetic}}(j)$	0	0	0	0	0	0	0	0	1
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{fast}}(j\delta t)}{3V} \right\rangle$	388.7	396.2	400.5	401.7	399.8	401.7	400.5	396.2	388.7
$w^{\mathrm{fast}}(j)$	0	$\frac{1}{32}$	$\frac{1}{16}$	$\frac{3}{32}$	$\frac{1}{8}$	$\frac{5}{32}$	$\frac{3}{16}$	$\frac{7}{32}$	$\frac{1}{8}$
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{intermed}}(j\delta t)}{3V} \right\rangle$	2598.7	–	–	–	2598.7	–	–	–	2598.7
$w^{\mathrm{intermed}}(j)$	0	0	0	0	$\frac{1}{2}$	0	0	0	$\frac{1}{2}$
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{slow}}(j\delta t)}{3V} \right\rangle$	-269.3	–	–	–	–	–	–	–	-269.3
$w^{\mathrm{slow}}(j)$	0	0	0	0	0	0	0	0	1
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{g}^{\mathrm{SHAKE}}(j\delta t)}{3V} \right\rangle$	-17400.7	-1668.7	-1668.3	-1668.3	-17906.7	-1668.7	-1668.3	-1668.2	–
$w^{\mathrm{SHAKE}}(j)$	0	$\frac{1}{64}$	$\frac{1}{32}$	$\frac{3}{64}$	$\frac{1}{16}$	$\frac{5}{64}$	$\frac{3}{32}$	$\frac{7}{64}$	0
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{g}^{\mathrm{RATTLE}}(j\delta t)}{3V} \right\rangle$	–	-1668.2	-1668.2	-1668.7	-17906.6	-1668.3	-1668.3	-1668.7	-17400.7
$w^{\mathrm{RATLTLE}}(j)$	0	$\frac{1}{64}$	$\frac{1}{32}$	$\frac{3}{64}$	$\frac{1}{16}$	$\frac{5}{64}$	$\frac{3}{32}$	$\frac{7}{64}$	$\frac{1}{8}$

Table 5: Weight factors according to the ad hoc equations (22b) and (24) to calculate $P(\Delta t)$ for $\mathrm{WAT}_{\mathrm{mts}}$. Long hyphens in the table indicate that the term is not considered in averaging procedure.

j	0	1	2
$\left\langle \frac{\sum m\boldsymbol{v}^2(j\delta t)}{3V} \right\rangle$			
$w^{\mathrm{kinetic}}_{\mathrm{adhoc(24)}}(j)$	–	$\frac{1}{2}$	$\frac{1}{2}$
$w^{\mathrm{kinetic}}_{\mathrm{adhoc(22b)}}(j)$	–	–	1
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{intermed}}(j\delta t)}{3V} \right\rangle$			
$w^{\mathrm{intermed}}_{\mathrm{adhoc(24)}}(j)$	–	$\frac{1}{2}$	$\frac{1}{2}$
$w^{\mathrm{intermed}}_{\mathrm{adhoc(22b)}}(j)$	–	–	1
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{f}^{\mathrm{slow}}(j\delta t)}{3V} \right\rangle$			
$w^{\mathrm{slow}}_{\mathrm{adhoc(24)}}(j)$	$\frac{1}{2}$	–	$\frac{1}{2}$
$w^{\mathrm{slow}}_{\mathrm{adhoc(22b)}}(j)$	–	–	2
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{g}^{\mathrm{SHAKE}}(j\delta t)}{3V} \right\rangle$			
$w^{\mathrm{SHAKE}}_{\mathrm{adhoc(24)}}(j)$	–	–	–
$w^{\mathrm{SHAKE}}_{\mathrm{adhoc(22b)}}(j)$	–	–	–
$\left\langle \frac{\sum \boldsymbol{r}(\Delta t)\cdot\boldsymbol{g}^{\mathrm{RATTLE}}(j\delta t)}{3V} \right\rangle$			
$w^{\mathrm{RATTLE}}_{\mathrm{adhoc(24)}}(j)$	–	$\frac{1}{2}$	$\frac{1}{2}$
$w^{\mathrm{RATTLE}}_{\mathrm{adhoc(22b)}}(j)$	–	–	1