

See discussions, stats, and author profiles for this publication at:
<https://www.researchgate.net/publication/229135003>

A new formalism for molecular dynamics in internal coordinates

ARTICLE *in* CHEMICAL PHYSICS · MARCH 2001

Impact Factor: 1.65 · DOI: 10.1016/S0301-0104(01)00236-1

CITATIONS

9

READS

14

3 AUTHORS, INCLUDING:



[Sang-Ho Lee](#)

University of Michigan

14 PUBLICATIONS 226 CITATIONS

SEE PROFILE



[Kim Palmo](#)

D. E. Shaw Research

31 PUBLICATIONS 1,127 CITATIONS

SEE PROFILE

A new formalism for molecular dynamics in internal coordinates

Sang-Ho Lee, Kim Palmo, Samuel Krimm *

Biophysics Research Division, Department of Physics, The University of Michigan, 930 N. University Avenue, Ann Arbor, MI 48109, USA

Received 5 September 2000

Abstract

Internal coordinate molecular dynamics (ICMD) has been used in the past in simulations for large molecules as an alternative way of increasing step size with a reduced operational dimension that is not achievable by MD in Cartesian coordinates. A new ICMD formalism for flexible molecular systems is presented, which is based on the spectroscopic **B**-matrix rather than the **A**-matrix of previous methods. The proposed formalism does not require an inversion of a large matrix as in the recursive formulations based on robot dynamics, and takes advantage of the sparsity of the **B**-matrix, ensuring computational efficiency for flexible molecules. Each molecule's external rotations about an arbitrary atom center, which may differ from its center of mass, are parameterized by the **SU**(2) Euler representation, giving singularity free parameterization. Although the formalism is based on the use of nonredundant generalized (internal and external) coordinates, an MD simulation in linearly dependent coordinates can be done by finding a transformation to a new set of independent coordinates. Based on the clear separability in the generalized coordinates between fast varying degrees of freedom and slowly varying ones, a multiple time step algorithm is introduced that avoids the previous nontrivial interaction distance classification. Also presented is a recursive method for computing nonzero **A**-matrix elements that is much easier to apply to a general molecular structure than the previous method. © 2001 Elsevier Science B.V. All rights reserved.

1. Introduction

The equation of motion of a molecular system has been described in mainly two different coordinate frames. The conventional formalism for molecular dynamics (MD) simulation [1,2] has been developed in the Cartesian coordinate frame since it provides the simplest form for the system's equation of motion, in which each atom is treated as a point mass whose position changes subject to the imposed external force. However, it has been

noted that in this formalism the step size for numerical integrations should be kept small (0.5–1 fs) in order to maintain the system's stability. This makes it almost impossible to routinely simulate in a time range longer than ns, where interesting conformational changes in biomolecules may take place. Since the instability arises mainly from rapidly varying motions like bond stretching (e.g., a typical CH stretch frequency of 3000 cm⁻¹ corresponds roughly to a period of 10 fs) and angle bending, one way of increasing step size is to remove the fast degrees of freedom by introducing suitable constraints on interatomic distances [3–9]. In the commonly used algorithms like SHAKE [3] and RATTLE [4], the system's initial states are

* Corresponding author. Fax: +1-734-764-3323.
E-mail address: skrimm@umich.edu (S. Krimm).

estimated from the unconstrained part of the equation of motion and they are corrected iteratively so as to satisfy the desired constraints to within acceptable error limits. Since the rapidly varying motions are related to bonded forces or nonbonded forces within a short distance range while nonbonded forces of long interatomic distances change slowly, another method adopts multiple time steps (MTS) [10–13] depending on the interaction distance class: a small time step for a class of fast varying forces while a long time step for a class of slowly varying forces. However, the slow force calculated at an interval of its time step may produce a resonance leading to instability [14]. In an improved algorithm, MOLLY [15], the slow forces are computed at averaged positions of the fast propagations. As a third method to increase the time step, an implicit Euler scheme is incorporated with a Langevin equation approach [16], which is introduced to effectively establish the system's thermal equilibrium. A significant improvement in this direction is made by additionally adopting a normal mode technique [17], in which in the first stage the potential energy is approximated to be harmonic, which makes the concerned Langevin equation linear, and in the next stage the analytic solution of this is further corrected by the implicit Euler scheme.

Alternatively, the system's equation of motion can be described in internal coordinates, which are defined from local atomic connectivities like bond lengths, bond angles, and proper torsions. Internal coordinates have already proven to be effective in *ab initio* geometry optimizations [18,19] and in Monte Carlo simulations [20]. Although the resulting equation of motion is far more complex and has been less used in MD studies than that in Cartesian coordinates, the internal coordinate MD (ICMD) formalism [21–31] is not only important from a theoretical point of view but also has unique and interesting features, which may also prove it to be effective in simulations for large molecules or many-molecule systems. Since internal coordinates are clearly separable from external rotations and translations, thermodynamic quantities of a system may be better determined than in Cartesian coordinates. (At a given temperature, a system's volume and pressure depend mostly on

external translations of each molecule.) In terms of internal coordinates, the fast varying degrees of freedom are clearly separable from the slowly varying ones, and a significant reduction in operational dimension can be achieved by simply neglecting fast varying degrees of freedom without introducing the constraints that are necessary to freeze such coordinates, as in SHAKE [3] or RATTLE [4]. In fact, the motions related to rapidly varying degrees of freedom are highly localized [17] and their positional displacements are closer to Gaussian type fluctuations than to significant conformational changes [32]. Thus, in the early studies of conformational energies of polypeptides, Gō and Scheraga [21] used only torsions as initial variable coordinates to find an approximate minimum energy conformation. Their idea has been further developed into MD formulations in torsion angle coordinates [22]. Mazur and Abagyan [23,24] extended this method to include bond stretches and angle bend coordinates, while Kneller and Hinsen [29] incorporated quaternion parameters and angular velocities for rotations of linked rigid body subunits. However, all these formulations require finding the inverse of a mass-matrix at each time step (or at least solving a system of linear equations), which is the costliest part in the whole process. As a result, attention has been given to recursive algorithms [26–28] that are based on multi-arm robot dynamics [33,34] and avoid the direct inversion of the large mass-matrix by using equivalent local body-level equations of motion. We refer to these previous ICMD formalisms as **A**-matrix formulations, since they are based on the mass-matrix constructed from atomic masses and the **A**-matrix that transforms internal and external coordinates into Cartesian coordinates.

We present another ICMD formalism, called a **B**-matrix formalism, which is based on the spectroscopic **B**-matrix [35–37]. As long as each molecule is considered to be entirely flexible with no rigid constraints, the spectroscopic **B**-matrix is well-defined and for each internal coordinate the corresponding **B**-matrix elements are nonzero only for a few (at most four) related atoms. This significantly reduces the required arithmetic computations. Furthermore, the **B**-matrix formalism

allows the whole process to be executed without any inversion of a large matrix as in the fast recursive algorithms [26–28]. In this respect, the proposed **B**-matrix formalism may be a very efficient method for MD simulations of large or many-molecule systems. We have also developed a singularity free formulation for external rotations that uses the Euler parameters [38], equivalent to the quaternion parameters, of an **SU**(2) representation. The explicit separation between rapidly varying degrees of freedom and slowly varying ones also enables us to effectively incorporate the MTS method [12] in ICMD, the interaction distance classification required in the Cartesian coordinate formulation not being necessary.

The imposition of rigid constraints on some internal coordinates can also be handled within the **B**-matrix formalism, as we show. This requires solving a linear equation to determine the corresponding Lagrange undetermined multipliers. Although this may be less effective in reducing operational dimensions than the **A**-matrix formalisms, the overall efficiency of this approach may be greater, although this remains to be determined. Alternatively, as an approximate way to avoid solving such a linear equation, we can effectively neglect the desired fast varying coordinates as in the **A**-matrix formalisms. This approximation of simply neglecting some fast varying coordinates without solving the linear equation might be an effective way of finding a path from an arbitrary initial system configuration to an approximate equilibrium configuration where the conformational energy of the molecule of interest is close to its minimum. Near the equilibrium configuration we can do full **B**-matrix ICMD without any rigid constraint in order to derive desired physical quantities.

From an arbitrary initial conformation of the known amino acid sequence of a protein, finding folding pathways to its observed structure or reliably predicting its stable native conformation may be one of the most interesting objectives of MD simulations. The successful accomplishment of this will ultimately depend on the full reliability of the force field [39] and on the ability to carry out extended MD simulations [40]. In combination with our general type of molecular mechanics (MM)

energy function, called a spectroscopically determined force field (SDFF) [41–43], which is developed to reproduce high level ab initio results and observed vibrational (infrared and Raman) frequencies, the **B**-matrix ICMD formalism presented in this paper may provide an optimal way to the ultimate goal.

The conventional Cartesian coordinate MD (CCMD) formalism is summarized in Section 2. In Section 3, key elements of the conventional **A**-matrix ICMD formalism are summarized and extended to general dependent coordinates. A more flexible and systematic way of calculating the non-zero **A**-matrix elements is proposed, although it is associated with a few more computational steps than the previous method [22,23]. In Section 4, the **B**-matrix ICMD formalism is introduced with the tools for computing all the required elements. The external rotations are also represented in singularity free Euler parameters of **SU**(2). In Section 5, an MTS algorithm in internal and external coordinates is introduced.

2. Dynamics in Cartesian coordinates

In a general formulation, we consider a system of N_{mol} molecules that are all flexible. Let the c th molecule contain p_c atoms and its λ th atom have atomic mass m_λ^c and position \mathbf{x}_c^λ with respect to (w.r.t.) an arbitrary laboratory-fixed frame (LFF) with $\hat{\mathbf{1}} \equiv (1, 0, 0)$, $\hat{\mathbf{2}} \equiv (0, 1, 0)$, and $\hat{\mathbf{3}} \equiv (0, 0, 1)$ being its basis. In a classical approximation, with each bond in a molecule being considered to be massless, the system's total kinetic energy T is found to be

$$2T = \sum_{c=1}^{N_{\text{mol}}} \sum_{\lambda=1}^{p_c} \sum_{k=1}^3 m_\lambda^c \dot{x}_c^{\lambda k} \dot{x}_c^{\lambda k} \quad (1)$$

where k is the index of a Cartesian coordinate component and a dot represents a derivative w.r.t. time. If the system's total potential energy V is not an explicit function of atomic velocities $\dot{x}_c^{\lambda k}$, then the motion of the λ th atom in the c th molecule is subject to Newton's equation:

$$m_\lambda^c \ddot{\mathbf{x}}_c^\lambda = \mathbf{f}_c^\lambda \quad (2)$$

with $\mathbf{f}_c^\lambda \equiv -\partial V / \partial \mathbf{x}_c^\lambda$ being the force acting on the atom at \mathbf{x}_c^λ due to V . The potential energy is usually expandable in the neighborhood of an arbitrary system configuration by

$$V = V_o + \sum_{c=1}^{N_{\text{mol}}} \sum_{\lambda=1}^{p_c} \sum_{k=1}^3 (x_c^{\lambda k} - x_{oc}^{\lambda k}) \left[\frac{\partial V}{\partial x_c^{\lambda k}} \right]_o + \frac{1}{2} \sum_{b,c=1}^{N_{\text{mol}}} \sum_{v=1}^{p_b} \sum_{\lambda=1}^{p_c} \sum_{j,k=1}^3 (x_b^{vj} - x_{ob}^{vj})(x_c^{\lambda k} - x_{oc}^{\lambda k}) \times \left[\frac{\partial^2 V}{\partial x_b^{vj} \partial x_c^{\lambda k}} \right]_o + \dots \quad (3)$$

where the $[\partial^2 V / \partial x_b^{vj} \partial x_c^{\lambda k}]_o$ define the system's Hessian matrix. In the cases of MM or MD simulations, the total potential energy is usually separable into two parts:

$$V = V^r + V^S \quad (4)$$

where V^r is due to nonbonded (van der Waals or electrostatic) interactions and V^S represents bonded interaction terms. Typically, V^S is expressed by each molecule's internal coordinates S_c^γ , while V^r can be put in the form of

$$V^r = \frac{1}{2} \sum_{a \neq b} \sum_{\mu=1}^{p_a} \sum_{v=1}^{p_b} V_{ab}^{\mu v}(r_{ab}^{\mu v}) + \frac{1}{2} \sum_{b=1}^{N_{\text{mol}}} \sum_{\mu \neq v}^{p_b} V_{bb}^{\mu v}(r_{bb}^{\mu v}) \quad (5)$$

where $V_{ab}^{\mu v} (= V_{ba}^{\nu \mu})$ and $V_{bb}^{\mu v}$ represent the inter- and intra-molecular nonbonded interaction potentials between atom μ in the a th molecule and atom v in the b th molecule, respectively. Since $V_{ab}^{\mu v}$ is a function of the distance $r_{ab}^{\mu v}$ defined by

$$r_{ab}^{\mu v} \equiv |\mathbf{x}_{ab}^{\mu v}| \equiv |\mathbf{x}_b^v - \mathbf{x}_a^\mu| \quad (6)$$

where $\mathbf{x}_{ab}^{\mu v}$ is the vector from atom μ to atom v , the derivatives of V^r w.r.t. $x_c^{\lambda k}$ are found to be

$$\begin{aligned} \frac{\partial V^r}{\partial x_c^{\lambda k}} &= \sum_{a \neq c} \sum_{\mu=1}^{p_a} \frac{\partial V_{ac}^{\mu \lambda}}{\partial x_{ac}^{\mu \lambda}} + \sum_{\mu \neq \lambda}^{p_c} \frac{\partial V_{cc}^{\mu \lambda}}{\partial x_{cc}^{\mu \lambda}} \\ &= \sum_{a \neq c} \sum_{\mu=1}^{p_a} \frac{\partial V_{ac}^{\mu \lambda}}{\partial r_{ac}^{\mu \lambda}} e^{\mu \lambda k} + \sum_{\mu \neq \lambda}^{p_c} \frac{\partial V_{cc}^{\mu \lambda}}{\partial r_{cc}^{\mu \lambda}} e^{\mu \lambda k}, \end{aligned} \quad (7)$$

$$\begin{aligned} \frac{\partial^2 V^r}{\partial x_b^{vj} \partial x_c^{\lambda k}} &\equiv \frac{\partial}{\partial x_b^{vj}} \left(\frac{\partial V^r}{\partial x_c^{\lambda k}} \right) \\ &= \sum_{a \neq c} \sum_{\mu=1}^{p_a} \frac{\partial}{\partial x_{ac}^{\mu \lambda}} \left(\frac{\partial V_{ac}^{\mu \lambda}}{\partial r_{ac}^{\mu \lambda}} e^{\mu \lambda k} \right) (\delta_c^b \delta_v^\lambda - \delta_a^b \delta_v^\mu) \\ &\quad + \sum_{\mu \neq \lambda}^{p_c} \frac{\partial}{\partial x_{cc}^{\mu \lambda}} \left(\frac{\partial V_{cc}^{\mu \lambda}}{\partial r_{cc}^{\mu \lambda}} e^{\mu \lambda k} \right) (\delta_v^\lambda - \delta_v^\mu) \delta_c^b \end{aligned} \quad (8)$$

where $e_{ac}^{\mu \lambda} \equiv \mathbf{x}_{ac}^{\mu \lambda} / r_{ac}^{\mu \lambda}$ and $\delta_c^b = 0$ for $b \neq c$ and $\delta_c^b = 1$ for $b = c$. In the neighborhood of an arbitrary expansion center \mathbf{x}_{oc}^λ , the γ th internal coordinate S_c^γ can be expanded by

$$\begin{aligned} S_c^\gamma &= S_{oc}^\gamma + \sum_{\lambda=1}^{p_c} \sum_{k=1}^3 B_{c\lambda^k}^\gamma (x_c^{\lambda k} - x_{oc}^{\lambda k}) \\ &\quad + \frac{1}{2} \sum_{v,\lambda=1}^{p_c} \sum_{j,k=1}^3 [\mathbf{B}_{2,v\lambda^k}^c]^\gamma (x_c^{vj} - x_{oc}^{vj})(x_c^{\lambda k} - x_{oc}^{\lambda k}) + \dots \end{aligned} \quad (9)$$

where the coefficients $B_{c\lambda^k}^\gamma$ and $[\mathbf{B}_{2,v\lambda^k}^c]^\gamma$ are called the first- and the second-order \mathbf{B} -matrix elements, respectively. It is implicitly assumed in the expression of Eq. (9) that changes in S_c^γ are due only to changes in atomic coordinates in the c th molecule. When there are strong intermolecular (e.g., hydrogen bond) interactions and some internal coordinates must be defined based on atomic coordinates that belong to different molecules, we should consider the group of related molecules as a super-molecule that is formed by virtual bonds between the related molecules. The derivatives of V^S w.r.t. $x_c^{\lambda k}$ are found to be

$$\frac{\partial V^S}{\partial x_c^{\lambda k}} = \sum_{b=1}^{N_{\text{mol}}} \sum_{\beta} \frac{\partial V^S}{\partial S_b^\beta} \frac{\partial S_b^\beta}{\partial x_c^{\lambda k}} = \sum_{\beta} \frac{\partial V^S}{\partial S_c^\beta} B_{c\lambda^k}^\beta, \quad (10)$$

$$\begin{aligned} \frac{\partial^2 V^S}{\partial x_b^{vj} \partial x_c^{\lambda k}} &= \left(\sum_{\beta, \gamma} \frac{\partial^2 V^S}{\partial S_c^\beta \partial S_c^\gamma} B_{cv^j}^\beta B_{c\lambda^k}^\gamma \right. \\ &\quad \left. + \sum_{\beta} \frac{\partial V^S}{\partial S_c^\beta} [\mathbf{B}_{2,v\lambda^k}^c]^\beta \right) \delta_{bc}. \end{aligned} \quad (11)$$

Once \mathbf{f}_c^λ is computed from Eqs. (7) and (10) at some instant t , which is the costliest part in CCMD, the new positions and velocities after a time step Δt in the trajectory (following the ve-

locity Verlet propagation scheme) are determined by

$$\mathbf{x}_c^\lambda(t + \Delta t) = \mathbf{x}_c^\lambda(t) + \Delta t \dot{\mathbf{x}}_c^\lambda(t) + \frac{\Delta t^2}{2m_c^\lambda} \mathbf{f}_c^\lambda(t), \quad (12)$$

$$\dot{\mathbf{x}}_c^\lambda(t + \Delta t) = \dot{\mathbf{x}}_c^\lambda(t) + \frac{\Delta t}{2m_c^\lambda} \{\mathbf{f}_c^\lambda(t) + \mathbf{f}_c^\lambda(t + \Delta t)\}. \quad (13)$$

3. Internal coordinate dynamics with A-matrix

3.1. Basic formulation

A molecule's internal coordinates S^γ can be constructed from arbitrary functions of the primitive internals ξ^λ , which are bond lengths, bond angles, or proper torsion angles based on the atomic connectivity in the molecule. (Since the entire system's equations of motion can be determined from that of each molecule, we concentrate on a specific molecule, viz., the c th molecule, and drop the molecular index if it causes no confusion.) The number, n , of all the primitive internals may exceed the molecule's internal degrees of freedom f , in which case some of them are connected through $n-f$ redundancy (linear or nonlinear) relations. The changes in internal coordinates due to infinitesimal displacements in the primitive internals can be expressed by

$$\Delta S^\gamma = \sum_{\lambda=1}^n U_{\lambda}^{\gamma} \Delta \xi^\lambda + \frac{1}{2} \sum_{v,\lambda=1}^n U_{v\lambda}^{\gamma} \Delta \xi^v \Delta \xi^\lambda + \cdots \quad (14)$$

with $U_{v\lambda}^{\gamma} \equiv \partial^2 S^\gamma / \partial \xi^v \partial \xi^\lambda$. Although there are many ways of defining a molecule's internal coordinates, we consider only such internal coordinates that give a nonsingular inverse relation of Eq. (14) as

$$\Delta \xi^\lambda = \sum_{\gamma=1}^n V_{\gamma}^{\lambda} \Delta S^\gamma + \frac{1}{2} \sum_{v,\gamma=1}^n V_{v\gamma}^{\lambda} \Delta S^v \Delta S^\gamma + \cdots \quad (15)$$

This enables us to calculate values in the primitive internals ξ^λ from the specified values in internal coordinates S^γ , which may involve iterative processes if we only use terms to the first order. The atomic coordinates in an arbitrary coordinate system fixed to the molecule can be obtained from

the primitive internals by constructing a \mathbf{Z} -matrix, which is commonly used in setting up ab initio geometry optimization in internal coordinates [18,19]. Not all the primitive internals are necessary to construct a \mathbf{Z} -matrix but only a suitable set of f independent primitive internals are required in order to define all atomic coordinates in a molecule-fixed frame (MFF). We refer to the primitive internals in this independent subset as \mathbf{Z} -coordinates R^λ , which are orthogonal to each other. For convenience, we put the primitive internals in the order of

$$\xi^\lambda = \begin{cases} R^\lambda, & \text{for } 1 \leq \lambda \leq f, \\ \zeta^\lambda, & \text{for } f < \lambda \leq n. \end{cases} \quad (16)$$

In order to determine atomic coordinates in an MFF, we consider an arbitrary molecule (which may be constructed from some virtual atoms or virtual bonds) as in Fig. 1, where each atom is indexed according to the order of the step in constructing a desired \mathbf{Z} -matrix. Since a molecule's center of mass is obtained only after determining its atomic coordinates, instead of using the center of mass frame (Appendix B), we select the atom $\zeta (= 1)$ as the origin (or base) of the MFF with its basis being $\{\hat{\mathbf{1}}_m, \hat{\mathbf{2}}_m, \hat{\mathbf{3}}_m\}$, which is arbitrarily defined by

$$\hat{\mathbf{1}}_m \equiv \mathbf{e}_{12m} = -\mathbf{e}_{21m}, \quad (17)$$

$$\begin{aligned} \hat{\mathbf{3}}_m &\equiv -\mathbf{u}_{13m} \equiv -(\mathbf{e}_{21m} \times \mathbf{e}_{23m}) / \sin \theta_{13} \\ &= (\mathbf{e}_{12m} \times \mathbf{e}_{23m}) / \sin \theta_{13} = \mathbf{u}_{31m}, \end{aligned} \quad (18)$$

$$\hat{\mathbf{2}}_m \equiv \hat{\mathbf{3}}_m \times \hat{\mathbf{1}}_m = \mathbf{e}_{12m} \times \mathbf{u}_{13m}. \quad (19)$$

The first three atomic coordinates in $\{\hat{\mathbf{1}}_m, \hat{\mathbf{2}}_m, \hat{\mathbf{3}}_m\}$ are easily found to be

$$\mathbf{z}_{1m} = (0, 0, 0)_m, \quad (20)$$

$$\mathbf{z}_{2m} = r_{12} \mathbf{e}_{12m} = (r_{12}, 0, 0)_m, \quad (21)$$

$$\mathbf{z}_{3m} = \mathbf{z}_{2m} - r_{23} \cos \theta_{13} \mathbf{e}_{12m} + r_{23} \sin \theta_{13} \mathbf{e}_{12m} \times \mathbf{u}_{13m}. \quad (22)$$

Thus, the coordinates of atom δ , which can be defined from the \mathbf{Z} -matrix input representation of

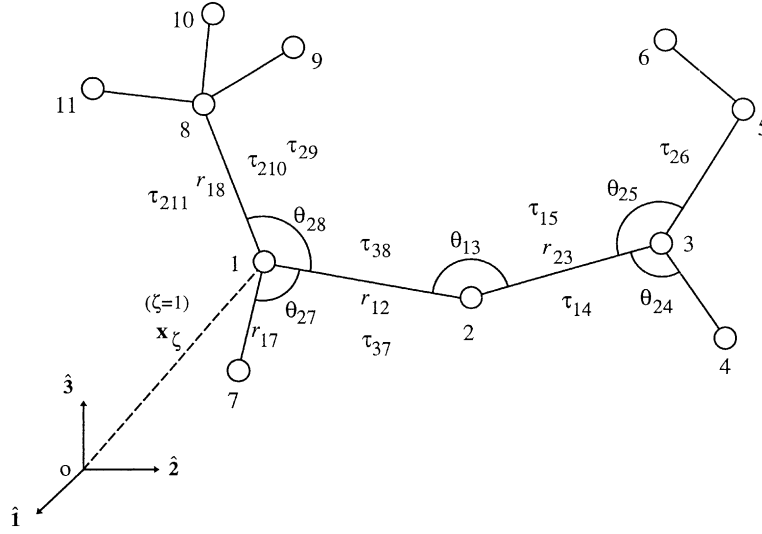


Fig. 1. Orientation of an arbitrary molecule with respect to a laboratory-fixed coordinate frame.

δ , λ , $r_{\lambda\delta}$, v , $\theta_{v\delta}$, μ , and $\tau_{\mu\delta}$, are to be obtained by the trigonometric relation

$$\mathbf{z}_{\delta m} = \mathbf{z}_{\lambda m} - r_{\lambda\delta} \cos \theta_{v\delta} \mathbf{e}_{v\lambda m} + r_{\lambda\delta} \sin \theta_{v\delta} \times (\cos \tau_{\mu\delta} \mathbf{e}_{v\lambda m} \times \mathbf{u}_{\mu\lambda m} - \sin \tau_{\mu\delta} \mathbf{u}_{\mu\lambda m}), \quad (23)$$

where $\mathbf{e}_{v\lambda m}$, $\mathbf{u}_{\mu\lambda m}$, and $\mathbf{e}_{v\lambda m} \times \mathbf{u}_{\mu\lambda m}$ can be computed from the already determined $\mathbf{z}_{\mu m}$, $\mathbf{z}_{v m}$, and $\mathbf{z}_{\lambda m}$ in the previous steps. In this way, all atomic coordinates in the MFF can be obtained recursively from the ones determined in the previous steps. Since the position of the ζ th atom is taken as the origin of the MFF, it is evident that the position vector of atom ζ in $\{\hat{\mathbf{1}}, \hat{\mathbf{2}}, \hat{\mathbf{3}}\}$ itself is the translation vector from the LFF to the MFF. Therefore, the atomic coordinates, \mathbf{x}_λ , in $\{\hat{\mathbf{1}}, \hat{\mathbf{2}}, \hat{\mathbf{3}}\}$ can be determined from $\mathbf{z}_{\lambda m}$ by

$$\mathbf{x}_\lambda = \mathbf{x}_\zeta + \Xi \mathbf{z}_{\lambda m} \quad (24)$$

where Ξ is the relative rotation matrix between the two frames. Just for convenience, we take the external rotation matrix Ξ to be parameterized as [44]

$$\begin{aligned} \Xi(\vec{\phi}) &\equiv \Xi(\phi^1, \phi^2, \phi^3) \\ &\equiv \exp(\phi^3 \mathbf{D}_3) \exp(\phi^2 \mathbf{D}_2) \exp(\phi^1 \mathbf{D}_1) \end{aligned} \quad (25)$$

with

$$\begin{aligned} \mathbf{D}_1 &\equiv \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & -1 \\ 0 & 1 & 0 \end{pmatrix}, \\ \mathbf{D}_2 &\equiv \begin{pmatrix} 0 & 0 & 1 \\ 0 & 0 & 0 \\ -1 & 0 & 0 \end{pmatrix}, \\ \mathbf{D}_3 &\equiv \begin{pmatrix} 0 & -1 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}. \end{aligned} \quad (26)$$

Thus, the matrix $\Xi(\mathbf{0})$ of zero rotational parameters is just an identity matrix, which implies that the MFF is related to the LFF by translations only. The coordinate vector \mathbf{x}_δ in $\{\hat{\mathbf{1}}, \hat{\mathbf{2}}, \hat{\mathbf{3}}\}$, which is equivalent to Eq. (23), is found to be

$$\begin{aligned} \mathbf{x}_\delta &= \mathbf{x}_\lambda - r_{\lambda\delta} \cos \theta_{v\delta} \mathbf{e}_{v\lambda} \\ &\quad + r_{\lambda\delta} \sin \theta_{v\delta} (\cos \tau_{\mu\delta} \mathbf{e}_{v\lambda} \times \mathbf{u}_{\mu\lambda} - \sin \tau_{\mu\delta} \mathbf{u}_{\mu\lambda}). \end{aligned} \quad (27)$$

Eqs. (24)–(27) enable us to naturally derive a relation that is complementary to Eq. (9),

$$\begin{aligned} x_\lambda^k &= x_{o\lambda}^k + \sum_\gamma A_\gamma^{\lambda k} (S_\gamma^\gamma - S_o^\gamma) \\ &\quad + \frac{1}{2} \sum_{\beta, \gamma} [A_2]_{\beta\gamma}^{\lambda k} (S_\beta^\beta - S_o^\beta) (S_\gamma^\gamma - S_o^\gamma) + \cdots, \end{aligned} \quad (28)$$

where the coefficients $A_{\gamma}^{\lambda k}$ and $[\mathbf{A}_2]_{\beta\gamma}^{\lambda k}$ are called the first- and the second-order \mathbf{A} -matrix elements, respectively. The nonzero \mathbf{A} -matrix elements for internal coordinates can be computed from the direct derivatives of Eq. (27) w.r.t. the \mathbf{Z} -coordinates, or from simple relations related to vector rotations [22,23], which will be further investigated in this section. It should be noted that Eq. (28) is well-defined also for the external rotations and translations, with related \mathbf{A} -matrix elements being computed from the direct derivatives of Eq. (24). When S^{γ} represent not only the internal coordinates but also the molecule's external rotations and translations, we will designate the S^{γ} as generalized coordinates.

From Eq. (28) the velocity of the λ th atom is found to be

$$\dot{\mathbf{x}}_{\lambda}^k = \sum_{\gamma} A_{\gamma}^{\lambda k} \dot{S}^{\gamma}. \quad (29)$$

Substituting this into Eq. (1), we have for the system's kinetic energy

$$2T = \sum_{c=1}^{N_{\text{mol}}} \sum_{\beta,\gamma} g_{c\beta\gamma} \dot{S}_c^{\beta} \dot{S}_c^{\gamma} = \sum_{c=1}^{N_{\text{mol}}} \dot{\mathbf{S}}_c^T \mathbf{g}_c \dot{\mathbf{S}}_c \quad (30)$$

with

$$g_{c\beta\gamma} \equiv \sum_{\lambda=1}^p \sum_{k=1}^3 m_{\lambda}^c A_{c\beta}^{\lambda k} A_{c\gamma}^{\lambda k} = [\mathbf{A}_c^T \mathbf{u}_c^{-1} \mathbf{A}_c]_{\beta\gamma}, \quad (31)$$

where \mathbf{u}_c is a diagonal matrix containing triads of the inverse atomic masses and \mathbf{A}_c^T is the transpose matrix of \mathbf{A}_c . The system's Euler–Lagrange equation of motion w.r.t. the generalized coordinates S_c^{γ} leads to

$$\sum_{\gamma} g_{c\beta\gamma} \ddot{S}_c^{\gamma} + \sum_{\gamma,\delta} \eta_{\beta\gamma\delta}^c \dot{S}_c^{\gamma} \dot{S}_c^{\delta} = - \frac{\partial V}{\partial S_c^{\beta}} \quad (32)$$

with

$$\begin{aligned} \eta_{\beta\gamma\delta}^c &\equiv \frac{1}{2} \left(\frac{\partial g_{c\beta\delta}}{\partial S_c^{\gamma}} + \frac{\partial g_{c\beta\gamma}}{\partial S_c^{\delta}} - \frac{\partial g_{c\gamma\delta}}{\partial S_c^{\beta}} \right) \\ &= \frac{1}{2} \sum_{\lambda=1}^p \sum_{k=1}^3 m_{\lambda}^c \left\{ A_{c\beta}^{\lambda k} [\mathbf{A}_2]_{+\gamma\delta}^{\lambda k} + A_{c\gamma}^{\lambda k} [\mathbf{A}_2]_{-\delta\beta}^{\lambda k} \right. \\ &\quad \left. + A_{c\delta}^{\lambda k} [\mathbf{A}_2]_{-\gamma\beta}^{\lambda k} \right\}, \end{aligned} \quad (33)$$

where

$$\begin{aligned} [\mathbf{A}_2]_{+\gamma\delta}^{\lambda k} &\equiv [\mathbf{A}_2]_{\gamma\delta}^{\lambda k} + [\mathbf{A}_2]_{\delta\gamma}^{\lambda k} \quad \text{and} \\ [\mathbf{A}_2]_{-\gamma\delta}^{\lambda k} &\equiv [\mathbf{A}_2]_{\gamma\delta}^{\lambda k} - [\mathbf{A}_2]_{\delta\gamma}^{\lambda k}. \end{aligned}$$

Note that the values of $[\mathbf{A}_2]_{-\gamma\delta}^{\lambda k}$ are zero for all internal coordinates but are nonzero for external rotations due to the noncommutativity of external rotations. The derivative of V w.r.t. S_c^{β} is found to be

$$\begin{aligned} \frac{\partial V}{\partial S_c^{\beta}} &= \sum_{a \neq c}^{N_{\text{mol}}} \sum_{\mu=1}^{p_a} \sum_{\nu=1}^{p_c} \sum_{j=1}^3 \frac{\partial V_{ac}^{\mu\nu}}{\partial x_{ac}^{\mu\nu j}} A_{c\beta}^{\nu j} \\ &\quad + \sum_{\mu \neq \nu}^{p_c} \sum_{j=1}^3 \frac{\partial V_{cc}^{\mu\nu}}{\partial x_{cc}^{\mu\nu j}} A_{c\beta}^{\nu j} + \frac{\partial V^S}{\partial S_c^{\beta}}. \end{aligned} \quad (34)$$

A usual way of solving Eq. (32) requires inverting the matrix \mathbf{g}_c , which is also called a mass-matrix since the conjugate momentum of S_c^{γ} is given by

$$J_{c\gamma} \equiv \frac{\partial T}{\partial \dot{S}_c^{\gamma}} = \sum_{\delta} g_{c\gamma\delta} \dot{S}_c^{\delta}. \quad (35)$$

Although \mathbf{g}_c is positive definite for linearly independent generalized coordinates, it is singular when there is a redundancy relation in S_c^{γ} , which requires a special treatment to solve Eq. (32). Since $\mathbf{g}_c \equiv \mathbf{A}_c^T \mathbf{u}_c^{-1} \mathbf{A}_c$ is symmetric, there is an orthogonal matrix $\mathbf{P}_c^T \equiv (\mathbf{K}_c^T \quad \mathbf{L}_c^T)$ such that

$$\begin{aligned} \mathbf{P}_c \mathbf{g}_c \mathbf{P}_c^T &\equiv \begin{pmatrix} \mathbf{K}_c \\ \mathbf{L}_c \end{pmatrix} (\mathbf{A}_c^T \mathbf{u}_c^{-1} \mathbf{A}_c) \begin{pmatrix} \mathbf{K}_c^T & \mathbf{L}_c^T \end{pmatrix} \\ &= \begin{pmatrix} \mathbf{\Gamma}_c & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{pmatrix}, \end{aligned} \quad (36)$$

where $\mathbf{\Gamma}_c$ is a nonsingular diagonal matrix of order $3p_c$. The corresponding generalized (Moore–Penrose) inverse of \mathbf{g}_c is defined so that

$$\mathbf{P}_c \mathbf{g}_c^{-} \mathbf{P}_c^T \equiv \mathbf{P}_c (\mathbf{A}_c^T \mathbf{u}_c^{-1} \mathbf{A}_c)^{-} \mathbf{P}_c^T = \begin{pmatrix} \mathbf{\Gamma}_c^{-1} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} \end{pmatrix}. \quad (37)$$

In fact, it is of no use to apply \mathbf{g}_c^{-} directly to the left-hand side of Eq. (32). Note that $\mathbf{L}_c \mathbf{S}_c$ defines a set of redundant coordinates that remain constant under an infinitesimal displacement in the molecule, while $\mathbf{K}_c \mathbf{S}_c$ defines a set of nonredundant coordinates. If we define $\underline{\mathbf{S}}_c \equiv \mathbf{K}_c \mathbf{S}_c$, $\underline{\mathbf{A}}_c \equiv \mathbf{A}_c \mathbf{K}_c^T$,

$\underline{\mathbf{g}}_c \equiv \underline{\mathbf{A}}_c^T \underline{\mathbf{u}}_c^{-1} \underline{\mathbf{A}}_c (= \mathbf{K}_c \mathbf{g}_c \mathbf{K}_c^T)$, and $\underline{\mathbf{g}}_c^- \equiv \mathbf{K}_c \mathbf{g}_c^- \mathbf{K}_c^T$, then from Eqs. (36) and (37) we have

$$\underline{\mathbf{g}}_c^- \underline{\mathbf{g}}_c = \mathbf{1}_{3p_c \times 3p_c} = \underline{\mathbf{g}}_c \underline{\mathbf{g}}_c^- \quad (38)$$

This shows that $\underline{\mathbf{g}}_c^-$ is the inverse matrix of $\underline{\mathbf{g}}_c$, and we denote its elements by $\underline{g}_c^{\beta\gamma}$ with raised indices. With the consideration of

$$\mathbf{g}_c \ddot{\mathbf{S}} = \mathbf{P}_c^T \mathbf{P}_c \mathbf{g}_c \mathbf{P}_c^T \mathbf{P}_c \ddot{\mathbf{S}} = \mathbf{K}_c^T \underline{\mathbf{g}}_c \ddot{\mathbf{S}}, \quad (39)$$

if we apply $\underline{\mathbf{g}}_c^{-1} \mathbf{K}_c$ to the left-hand side of Eq. (32) and define $\underline{\dot{\mathbf{S}}}_c \equiv \mathbf{K}_c \dot{\mathbf{S}}_c$, $\underline{\ddot{\mathbf{S}}}_c \equiv \mathbf{K}_c \ddot{\mathbf{S}}_c$, and $\underline{\mathbf{A}}_c^c \equiv \mathbf{K}_c \mathbf{A}_2^c \mathbf{K}_c^T$, then the system's equation of motion reduces to

$$\ddot{\underline{\mathbf{S}}}_c^\alpha + \sum_{\gamma, \delta=1}^{3p_c} \underline{\eta}_{c\gamma\delta}^\alpha \dot{\underline{\mathbf{S}}}_c^\gamma \dot{\underline{\mathbf{S}}}_c^\delta = \underline{f}_c^\alpha \quad (40)$$

with

$$\underline{\eta}_{c\gamma\delta}^\alpha \equiv \sum_{\beta=1}^{3p_c} \underline{g}_c^{\alpha\beta} \underline{\eta}_{\beta\gamma\delta}^c, \quad (41)$$

$$\underline{f}_c^\alpha \equiv - \sum_{\beta=1}^{3p_c} \left[\underline{\mathbf{g}}_c^{-1} \mathbf{K}_c \right]^{\alpha\beta} \frac{\partial V}{\partial S_c^\beta} = - \sum_{\beta=1}^{3p_c} \underline{g}_c^{\alpha\beta} \frac{\partial V}{\partial \underline{S}_c^\beta}. \quad (42)$$

Thus, the equivalent to Eqs. (12) and (13) can be formulated as

$$\underline{S}_c^\alpha(t + \Delta t) = \underline{S}_c^\alpha(t) + \Delta t \underline{\dot{S}}_c^\alpha(t) + \frac{\Delta t^2}{2} \underline{\ddot{S}}_c^\alpha(t), \quad (43)$$

$$\underline{\dot{S}}_c^\alpha(t + \Delta t) = \underline{\dot{S}}_c^\alpha(t) + \frac{\Delta t}{2} \left\{ \underline{\ddot{S}}_c^\alpha(t) + \underline{\ddot{S}}_c^\alpha(t + \Delta t) \right\}. \quad (44)$$

At each time step, once new values of all $\underline{\mathbf{S}}_c$, $\underline{\dot{\mathbf{S}}}_c$, and $\underline{\ddot{\mathbf{S}}}_c$ are determined, values in redundant coordinates are obtained by $\mathbf{S}_c = \mathbf{K}_c^T \underline{\mathbf{S}}_c$, $\dot{\mathbf{S}}_c = \mathbf{K}_c^T \underline{\dot{\mathbf{S}}}_c$, and $\ddot{\mathbf{S}}_c = \mathbf{K}_c^T \underline{\ddot{\mathbf{S}}}_c$.

For nonredundant coordinates, the inverse matrix of \mathbf{g}_c is well-defined and the transformation to a new set of nonredundant coordinates is not necessary, and we can simply remove the underlines in Eqs. (40)–(42). We assume the generalized coordinates S_c^γ to be nonredundant if not otherwise noted. In order to advance S_c^γ along the time tra-

jectory by Eq. (40), however, it is necessary at each time step to compute not only $\partial V / \partial S_c^\beta$ and $\eta_{\beta\gamma\delta}^c$, which involve computations of the first- and the second-order \mathbf{A} -matrices, but also \mathbf{g}_c^- , which is known to be the costliest part. The whole process is so complex and time consuming that ICMD, compared to CCMD, has rarely been used thus far and the attention that has been given to it has been devoted to developing fast algorithms to compute \mathbf{A} -matrices and \mathbf{g}_c^- . Although a significant achievement was made in this direction by adopting, instead of the direct matrix inversion of \mathbf{g}_c , the recursive formulation [26–28], it will not be pursued here.

One of the big advantages obtainable from an ICMD simulation is the fact that we can significantly reduce the operational dimension of each molecule by simply neglecting stiff and rapidly varying degrees of freedom such as valence bond length and bond angle coordinates in Eqs. (29) and (32), without introducing any constraint equation as is necessary in the equivalent treatments like SHAKE [3] or RATTLE [4] in a CCMD formulation. In real molecular systems, valence bond length and bond angle coordinates of each molecule do not deviate much from their average values during a finite time, which may be much longer than the time step, while torsion angles may undergo significant changes [21]. Therefore, the early formulation of ICMD to find the minimum energy conformations of macromolecules was developed by taking only torsional degrees of freedom into consideration with other degrees of freedom being kept rigid [22,25], which simplifies the calculations of \mathbf{A} , \mathbf{A}_2 , and \mathbf{g}_c^- .

3.2. Computation of \mathbf{A} -matrix elements for internal coordinates

The method of computing \mathbf{A} -matrix elements in the previous ICMD formalisms is based on the observation that (for a specific illustration see Fig. 1) the changes in \mathbf{x}_6 due to infinitesimal changes in θ_{25} and τ_{15} can be viewed as infinitesimal rotations of \mathbf{x}_{36} about \mathbf{u}_{25} and \mathbf{e}_{23} , respectively [22,23]:

$$\frac{\partial \mathbf{x}_6}{\partial \theta_{25}} = \mathbf{u}_{25} \times (\mathbf{x}_6 - \mathbf{x}_3), \quad (45)$$

$$\frac{\partial \mathbf{x}_6}{\partial \tau_{15}} = \mathbf{e}_{23} \times (\mathbf{x}_6 - \mathbf{x}_3), \quad (46)$$

and the derivative of \mathbf{x}_6 w.r.t. r_{23} can be obtained from

$$\frac{\partial \mathbf{x}_6}{\partial r_{23}} = \frac{\partial}{\partial r_{23}} (\mathbf{x}_2 + \mathbf{x}_{23} + \mathbf{x}_{35} + \mathbf{x}_{56}) = \mathbf{e}_{23}. \quad (47)$$

Values of \mathbf{x}_{36} , \mathbf{u}_{25} , and \mathbf{e}_{23} are easily computable from the defined atomic coordinates up to the stage for atom 6. Similarly, with R^y involving all \mathbf{Z} -coordinates corresponding to stages from atom 6 to atom 1 (the base), values of $\partial \mathbf{x}_6 / \partial R^y$ can be determined. Otherwise, $\partial \mathbf{x}_6 / \partial R^y$ are all zero. (The derivatives of \mathbf{x}_6 w.r.t. the primitive internals not yet defined to stage 6 or belonging to different branches from the base are all zero.) In this way all the nonzero first- and second-order \mathbf{A} -matrix elements in \mathbf{Z} -coordinates can be computed once a suitable atomic numeration of the molecular tree topology is done. But great care, especially in the case of a molecule containing an internal ring structure, should be taken in the atomic ordering for constructing a proper \mathbf{Z} -matrix in order to keep relations like Eqs. (45)–(47) valid [24]. (Note that in this formulation even the atomic ordering given in Fig. 1 cannot be used but should be modified by setting the base to one of the end atoms, e.g., atom 6.)

An alternative way of recursively computing \mathbf{A} -matrix elements in \mathbf{Z} -coordinates can be found from Eq. (27). Direct differentiations of this equation w.r.t. the newly specified \mathbf{Z} -coordinates, $r_{\lambda\delta}$, $\theta_{v\delta}$, and $\tau_{\mu\delta}$, respectively, give

$$\begin{aligned} \frac{\partial \mathbf{x}_\delta}{\partial r_{\lambda\delta}} &= -\cos \theta_{v\delta} \mathbf{e}_{v\lambda} \\ &+ \sin \theta_{v\delta} (\cos \tau_{\mu\delta} \mathbf{e}_{v\lambda} \times \mathbf{u}_{\mu\lambda} - \sin \tau_{\mu\delta} \mathbf{u}_{\mu\lambda}), \end{aligned} \quad (48)$$

$$\begin{aligned} \frac{\partial \mathbf{x}_\delta}{\partial \theta_{v\delta}} &= r_{\lambda\delta} \sin \theta_{v\delta} \mathbf{e}_{v\lambda} \\ &+ r_{\lambda\delta} \cos \theta_{v\delta} (\cos \tau_{\mu\delta} \mathbf{e}_{v\lambda} \times \mathbf{u}_{\mu\lambda} - \sin \tau_{\mu\delta} \mathbf{u}_{\mu\lambda}), \end{aligned} \quad (49)$$

$$\frac{\partial \mathbf{x}_\delta}{\partial \tau_{\mu\delta}} = -r_{\lambda\delta} \sin \theta_{v\delta} (\sin \tau_{\mu\delta} \mathbf{e}_{v\lambda} \times \mathbf{u}_{\mu\lambda} + \cos \tau_{\mu\delta} \mathbf{u}_{\mu\lambda}). \quad (50)$$

The derivatives of \mathbf{x}_δ w.r.t. \mathbf{Z} -coordinates that are not defined to the current stage of atom δ are all zero. The derivatives of \mathbf{x}_δ w.r.t. all the previously defined R^y (differing from $r_{\lambda\delta}$, $\theta_{v\delta}$, and $\tau_{\mu\delta}$) are obtained from

$$\begin{aligned} \frac{\partial \mathbf{x}_\delta}{\partial R^y} &= \frac{\partial \mathbf{x}_\lambda}{\partial R^y} - r_{\lambda\delta} \cos \theta_{v\delta} \frac{\partial \mathbf{e}_{v\lambda}}{\partial R^y} \\ &+ r_{\lambda\delta} \sin \theta_{v\delta} \cos \tau_{\mu\delta} \frac{\partial}{\partial R^y} (\mathbf{e}_{v\lambda} \times \mathbf{u}_{\mu\lambda}) \\ &- r_{\lambda\delta} \sin \theta_{v\delta} \sin \tau_{\mu\delta} \frac{\partial \mathbf{u}_{\mu\lambda}}{\partial R^y}, \end{aligned} \quad (51)$$

where values of $\partial \mathbf{e}_{v\lambda} / \partial R^y$ and $\partial \mathbf{u}_{\mu\lambda} / \partial R^y$ are found to be, respectively,

$$\frac{\partial \mathbf{e}_{v\lambda}}{\partial R^y} = \begin{cases} \mathbf{0}, & \text{for } R^y = \text{any bond stretch coordinate,} \\ \frac{1}{r_{v\lambda}} \left(\frac{\partial \mathbf{x}_\lambda}{\partial R^y} - \frac{\partial \mathbf{x}_v}{\partial R^y} \right), & \text{otherwise,} \end{cases} \quad (52)$$

$$\frac{\partial \mathbf{u}_{\mu\lambda}}{\partial R^y} = \begin{cases} \mathbf{0}, & \text{for } R^y = \theta_{\mu\lambda} \text{ or any bond} \\ & \text{stretch coordinate,} \\ \frac{1}{\sin \theta_{\mu\lambda}} \left(\frac{\partial \mathbf{e}_{v\mu}}{\partial R^y} \times \mathbf{e}_{v\lambda} + \mathbf{e}_{v\mu} \times \frac{\partial \mathbf{e}_{v\lambda}}{\partial R^y} \right), & \text{otherwise.} \end{cases} \quad (53)$$

Similarly, the second order \mathbf{A} -matrix elements in \mathbf{Z} -coordinates can also be computed by direct differentiation. It should be noted that, with pre-determined values of $\partial \mathbf{x}_\mu / \partial R^y$, $\partial \mathbf{x}_v / \partial R^y$, and $\partial \mathbf{x}_\lambda / \partial R^y$ in the previous stages, the new method requires only values of $r_{v\lambda}$, $r_{\lambda\delta}$, $\theta_{\mu\lambda}$, $\theta_{v\delta}$, and $\tau_{\mu\delta}$, which are all \mathbf{Z} -coordinates defined from a local orientation of only four atoms, and is much easier to apply since it does not require as strict atomic ordering in constructing a proper \mathbf{Z} -matrix as the method using Eqs. (45)–(47), although it requires a few more computational steps.

Expansion to \mathbf{A} -matrix elements in all primitive internals ξ^λ can be achieved by using redundancy relations, $h^\delta(\xi) = 0$ ($\delta = 1, \dots, n - f$). Analytic redundancy relations in primitive internals corresponding to some important local molecular substructures are shown in Appendix A. Each redundancy relation can be expanded to the second order by

$$\begin{aligned}
& \sum_{\beta=1}^f a_{\beta}^{\delta} \Delta R^{\beta} + \sum_{\beta=1}^{n-f} b_{\beta}^{\delta} \Delta \zeta^{f+\beta} + \frac{1}{2} \sum_{\beta,\gamma=1}^f a_{\beta\gamma}^{\delta} \Delta R^{\beta} \Delta R^{\gamma} \\
& + \frac{1}{2} \sum_{\beta,\gamma=1}^{n-f} b_{\beta\gamma}^{\delta} \Delta \zeta^{f+\beta} \Delta \zeta^{f+\gamma} \\
& + \frac{1}{2} \sum_{\beta=1}^f \sum_{\gamma=1}^{n-f} c_{\beta\gamma}^{\delta} \Delta R^{\beta} \Delta \zeta^{f+\gamma} = 0
\end{aligned} \quad (54)$$

with $a_{\beta\gamma}^{\delta} \equiv \partial^2 h^{\delta} / \partial R^{\beta} \partial R^{\gamma}$, $b_{\beta\gamma}^{\delta} \equiv \partial^2 h^{\delta} / \partial \zeta^{f+\beta} \partial \zeta^{f+\gamma}$, and $c_{\beta\gamma}^{\delta} \equiv \partial^2 h^{\delta} / \partial R^{\beta} \partial \zeta^{f+\gamma}$, where R^{β} is not involved in the δ th redundancy relation if $a_{\beta}^{\delta} = 0$. If we define $\Phi_{\delta} \equiv \{R^{\beta} | a_{\beta}^{\delta} \neq 0\}$ and arrange so that $\zeta^{f+\delta}$ is contained in the δ th redundancy relation, then the derivatives of \mathbf{x}_{λ} w.r.t. the excluded primitive internals are found to be

$$\frac{\partial \mathbf{x}_{\lambda}}{\partial \zeta^{f+\delta}} = - \sum_{\beta \in \Phi_{\delta}} \frac{\partial \mathbf{x}_{\lambda}}{\partial R^{\beta}} \frac{b_{\beta}^{\delta}}{a_{\beta}^{\delta}}, \quad (55)$$

$$\frac{\partial^2 \mathbf{x}_{\lambda}}{\partial \zeta^{f+\delta} \partial R^{\gamma}} = - \sum_{\beta \in \Phi_{\delta}} \frac{\partial^2 \mathbf{x}_{\lambda}}{\partial R^{\beta} \partial R^{\gamma}} \frac{b_{\beta}^{\delta}}{a_{\beta}^{\delta}}, \quad (56)$$

$$\frac{\partial^2 \mathbf{x}_{\lambda}}{\partial \zeta^{f+\gamma} \partial \zeta^{f+\delta}} = \sum_{\alpha \in \Phi_{\gamma}} \sum_{\beta \in \Phi_{\delta}} \frac{\partial^2 \mathbf{x}_{\lambda}}{\partial R^{\alpha} \partial R^{\beta}} \frac{b_{\alpha}^{\gamma}}{a_{\alpha}^{\gamma}} \frac{b_{\beta}^{\delta}}{a_{\beta}^{\delta}} - \sum_{\beta \in \Phi_{\delta}} \frac{\partial \mathbf{x}_{\lambda}}{\partial R^{\beta}} \frac{b_{\beta}^{\delta}}{a_{\beta}^{\delta}}. \quad (57)$$

Therefore, from Eq. (15) the **A**-matrix elements in internal coordinates S^{γ} can be obtained by

$$\frac{\partial \mathbf{x}_{\delta}}{\partial S^{\gamma}} = \sum_{\lambda=1}^n \frac{\partial \mathbf{x}_{\delta}}{\partial \zeta^{\lambda}} V_{\gamma}^{\lambda}, \quad (58)$$

$$\frac{\partial^2 \mathbf{x}_{\lambda}}{\partial S^{\alpha} \partial S^{\beta}} = \sum_{\gamma,\omega=1}^n \frac{\partial^2 \mathbf{x}_{\lambda}}{\partial \zeta^{\omega} \partial \zeta^{\gamma}} V_{\alpha}^{\omega} V_{\beta}^{\gamma} + \sum_{\gamma=1}^n \frac{\partial \mathbf{x}_{\lambda}}{\partial \zeta^{\gamma}} V_{\alpha\beta}^{\gamma}. \quad (59)$$

3.3. Computation of *A*-matrix elements for external coordinates

For any changes in external translations, the second term on the right-hand side of Eq. (24) remains constant, so **A**-matrix elements for the external translations are simply found to be

$$\frac{\partial \mathbf{x}_{\lambda}^k}{\partial x_{\zeta}^j} = \delta_j^k, \quad (60)$$

$$\frac{\partial^2 \mathbf{x}_{\lambda}^k}{\partial x_{\zeta}^i \partial x_{\zeta}^j} = 0 = \frac{\partial^2 \mathbf{x}_{\lambda}^k}{\partial S^{\gamma} \partial x_{\zeta}^j} = \frac{\partial^2 \mathbf{x}_{\lambda}^k}{\partial x_{\zeta}^j \partial S^{\gamma}} \quad (61)$$

with S^{γ} being any generalized coordinate. The corresponding **g**-matrix elements are found to be

$$\begin{aligned}
g_{ij}^{\text{tran}} & \equiv \sum_{\lambda=1}^p m_{\lambda} \frac{\partial \mathbf{x}_{\lambda}}{\partial x_{\zeta}^i} \cdot \frac{\partial \mathbf{x}_{\lambda}}{\partial x_{\zeta}^j} \\
& = m_{\zeta} \delta_{ij} \quad (1 \leq i, j \leq 3).
\end{aligned} \quad (62)$$

The **A**-matrix elements for the external rotations given by Eq. (25) can be obtained by derivatives of Eq. (24) w.r.t. external rotation parameters. Since values of \mathbf{x}_{ζ} and $\mathbf{z}_{\lambda m}$ stay constant for any external rotations at atom ζ , we have

$$\frac{\partial \mathbf{x}_{\lambda}}{\partial \phi^j} = \frac{\partial \Xi}{\partial \phi^j} \mathbf{z}_{\lambda m}. \quad (63)$$

Considering the following two relations:

$$[\mathbf{D}_i, \mathbf{D}_j] = \varepsilon_{ijk} \mathbf{D}_k, \quad (64)$$

$$\begin{aligned}
& \exp(-\phi^k \mathbf{D}_k) \mathbf{D}_j \exp(\phi^k \mathbf{D}_k) \\
& = \mathbf{D}_j + \phi^k [\mathbf{D}_j, \mathbf{D}_k] + \frac{1}{2!} (\phi^k)^2 [[\mathbf{D}_j, \mathbf{D}_k], \mathbf{D}_k] + \cdots,
\end{aligned} \quad (65)$$

with ε_{ijk} being the Levi-Civita density, we can derive

$$\begin{aligned}
\frac{\partial \Xi(\vec{\phi})}{\partial \phi^1} & = (\cos \phi^2 \cos \phi^3 \mathbf{D}_1 + \cos \phi^2 \sin \phi^3 \mathbf{D}_2 \\
& \quad - \sin \phi^2 \mathbf{D}_3) \Xi(\vec{\phi}),
\end{aligned} \quad (66)$$

$$\frac{\partial \Xi(\vec{\phi})}{\partial \phi^2} = (\cos \phi^3 \mathbf{D}_2 - \sin \phi^3 \mathbf{D}_1) \Xi(\vec{\phi}), \quad (67)$$

$$\frac{\partial \Xi(\vec{\phi})}{\partial \phi^3} = \mathbf{D}_3 \Xi(\vec{\phi}). \quad (68)$$

Substituting these into Eq. (63), we have with $\mathbf{z}_{\lambda} \equiv \Xi \mathbf{z}_{\lambda m}$

$$\frac{\partial \mathbf{x}_\lambda}{\partial \phi^j} = \frac{\partial \vec{\theta}}{\partial \phi^j} \times \mathbf{z}_\lambda, \quad (69)$$

where $\partial \theta^k / \partial \phi^j \equiv W_j^k$ are defined by the matrix elements of the transformation

$$\begin{pmatrix} d\theta^1 \\ d\theta^2 \\ d\theta^3 \end{pmatrix} \equiv \begin{pmatrix} \cos \phi^3 \cos \phi^2 & -\sin \phi^3 & 0 \\ \sin \phi^3 \cos \phi^2 & \cos \phi^3 & 0 \\ -\sin \phi^2 & 0 & 1 \end{pmatrix} \begin{pmatrix} d\phi^1 \\ d\phi^2 \\ d\phi^3 \end{pmatrix} \\ \equiv \mathbf{W}(\vec{\phi}) \begin{pmatrix} d\phi^1 \\ d\phi^2 \\ d\phi^3 \end{pmatrix}, \quad (70)$$

which also explicitly defines the molecule's angular velocity due to the external rotation at atom ζ by $\vec{\Omega} \equiv \vec{\theta} \equiv \mathbf{W}(\vec{\phi})\vec{\phi}$. The second-order **A**-matrix elements for the external rotations can be obtained from the derivatives of Eq. (69):

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial \phi^i \partial \phi^j} = \frac{\partial^2 \vec{\theta}}{\partial \phi^i \partial \phi^j} \times \mathbf{z}_\lambda + \frac{\partial \vec{\theta}}{\partial \phi^j} \times \left(\frac{\partial \vec{\theta}}{\partial \phi^i} \times \mathbf{z}_\lambda \right), \quad (71)$$

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial S^\gamma \partial \phi^j} = \frac{\partial \vec{\theta}}{\partial \phi^j} \times \frac{\partial \mathbf{x}_\lambda}{\partial S^\gamma} = \frac{\partial^2 \mathbf{x}_\lambda}{\partial \phi^j \partial S^\gamma} \quad (72)$$

with S^γ being an internal coordinate. Thus, the corresponding elements in θ^j become, respectively,

$$\frac{\partial \mathbf{x}_\lambda}{\partial \theta^j} = \hat{\mathbf{j}} \times \mathbf{z}_\lambda, \quad (73)$$

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial \theta^i \partial \theta^j} = \hat{\mathbf{j}} \times (\hat{\mathbf{i}} \times \mathbf{z}_\lambda), \quad (74)$$

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial S^\gamma \partial \theta^j} = \hat{\mathbf{j}} \times \frac{\partial \mathbf{x}_\lambda}{\partial S^\gamma} = \frac{\partial^2 \mathbf{x}_\lambda}{\partial \theta^j \partial S^\gamma}. \quad (75)$$

The **g**-matrix elements for external rotations of $\vec{\phi}$ are found to be

$$g_{ij}^{\text{rot}} \equiv \sum_{\lambda=1}^p m_\lambda \frac{\partial \mathbf{x}_\lambda}{\partial \phi^i} \cdot \frac{\partial \mathbf{x}_\lambda}{\partial \phi^j} = [\mathbf{W}^T \mathbf{I}_\zeta \mathbf{W}]_{ij} \quad (1 \leq i, j \leq 3) \quad (76)$$

where \mathbf{I}_ζ is the molecule's inertia tensor at atom ζ defined by

$$\mathbf{I}_\zeta^{jk} \equiv \sum_{\lambda=1}^p m_\lambda \{ (\mathbf{z}_\lambda \cdot \mathbf{z}_\lambda) \delta^{jk} - z_\lambda^j z_\lambda^k \} \\ = \sum_{\lambda=1}^p m_\lambda \frac{\partial \mathbf{x}_\lambda}{\partial \theta^j} \cdot \frac{\partial \mathbf{x}_\lambda}{\partial \theta^k}. \quad (77)$$

4. Internal coordinate dynamics with **B**-matrix

4.1. Basic formulation

We present an ICMD method that avoids direct inversion of the mass matrix of Eq. (31). Note that its inverse can be obtained by finding the inverse of the **A**-matrix. However, instead of inverting the **A**-matrix of Eq. (28), we directly use the easily computable spectroscopic **B**-matrix [35–37], which was originally devised to explain observed vibrations of molecules. Each atom constantly vibrates or changes its relative coordinates w.r.t. the local molecular orientation, and a molecule is considered to be entirely flexible. As long as a molecule is considered to be entirely flexible, the spectroscopic **B**-matrix elements for an internal coordinate, viz., the changes in the internal coordinate due to infinitesimal changes in each atomic coordinate, are nonzero only for the atoms that are involved in defining the internal coordinate.

We now show that the spectroscopic **B**-matrix computed in nonredundant coordinates of a completely flexible molecule is the exact inverse of the **A**-matrix. Since for a set of generalized coordinates S^γ we have

$$\frac{\partial x_\lambda^k}{\partial x_\nu^j} = \sum_\gamma \frac{\partial x_\lambda^k}{\partial S^\gamma} \frac{\partial S^\gamma}{\partial x_\nu^j} = \delta_\lambda^\nu \delta_j^k, \quad (78)$$

the **B**-matrix elements for external rotations, in combination with spectroscopic **B**-matrix elements for the internal coordinates, can be determined to give

$$\mathbf{AB} = \mathbf{1}_{3px3p} \quad (79)$$

with the **A**-matrix being obtained by the methods described in Section 3. (More details will follow in Section 4.2.) If the set of generalized coordinates

S^v is linearly independent, then both \mathbf{A} and \mathbf{B} are square nonsingular matrices and

$$\mathbf{BA} = \mathbf{1}_{3p \times 3p}. \quad (80)$$

Thus, the spectroscopic \mathbf{B} -matrix calculated in linearly independent coordinates of an entirely flexible molecule is the exact inverse of the \mathbf{A} -matrix computed by the methods described in Section 3. In this case, moreover, the spectroscopic matrix $\mathbf{G} \equiv \mathbf{BuB}^T$ is the inverse of the mass-matrix $\mathbf{g} \equiv \mathbf{A}^T \mathbf{u}^{-1} \mathbf{A}$, and instead of Eqs. (41) and (42), we have

$$\eta_{\gamma\delta}^{\alpha} = \begin{cases} \eta_{rs}^{\alpha} = \sum_{\lambda=1}^p \sum_{k=1}^3 B_{\lambda^k}^{\alpha} [\mathbf{A}_2]_{rs}^{\lambda^k}, \\ \eta_{rj}^{\alpha} = \sum_{\lambda=1}^p \sum_{k=1}^3 \left\{ B_{\lambda^k}^{\alpha} [\mathbf{A}_2]_{rj}^{\lambda^k} \right. \\ \quad \left. + \frac{1}{2} m_{\lambda} A_r^{\lambda^k} \sum_{l=1}^3 G^{\alpha l} [\mathbf{A}_2]_{-jl}^{\lambda^k} \right\}, \\ \eta_{ij}^{\alpha} = \frac{1}{2} \sum_{\lambda=1}^p \sum_{k=1}^3 \left\{ B_{\lambda^k}^{\alpha} [\mathbf{A}_2]_{+ij}^{\lambda^k} \right. \\ \quad \left. + m_{\lambda} \sum_{l=1}^3 G^{\alpha l} \left(A_i^{\lambda^k} [\mathbf{A}_2]_{-jl}^{\lambda^k} + A_j^{\lambda^k} [\mathbf{A}_2]_{-il}^{\lambda^k} \right) \right\}, \\ \eta_{jn}^{\alpha} = \frac{1}{2} \sum_{\lambda=1}^p m_{\lambda} \sum_{l=1}^3 G^{\alpha l} [\mathbf{A}_2]_{-jl}^{\lambda^n}, \end{cases} \quad (81)$$

$$f^{\alpha} = - \sum_{v=1}^p \sum_{j=1}^3 \frac{1}{m_v} B_{vj}^{\alpha} \frac{\partial V}{\partial x_v^j}, \quad (82)$$

which allows the entire process to be executed very efficiently (where r and s are internal coordinate indices while i, j , and l represent external rotations and n represents an external translation). Values of all nonzero $B_{\lambda^k}^{\alpha}$ are analytically calculated without any inversion of a large matrix.

If the considered generalized coordinates are subject to some redundancy relations, a spectroscopic nonsquare matrix \mathbf{B} satisfying Eq. (79) can still be obtained with the corresponding row vectors of \mathbf{B} not being independent. In this case Eq. (80) no longer holds, but we can construct a suitable set of nonredundant coordinates in a way similar to that used in Eqs. (36)–(42), viz., from an orthogonal matrix $\mathbf{P}^T \equiv (\mathbf{K}^T \mathbf{L}^T)$ that diagonalizes the spectroscopic symmetric matrix $\mathbf{G} \equiv \mathbf{BuB}^T$. Since $\mathbf{LB} = \mathbf{0}$, inserting $\mathbf{P}^T \mathbf{P}$ into the left-hand side

of Eq. (79), we have $\mathbf{AB} = \mathbf{1}_{3p \times 3p}$ with $\mathbf{A} \equiv \mathbf{AK}^T$ and $\mathbf{B} \equiv \mathbf{KB}$. Note that although \mathbf{K} is a rectangular matrix, both \mathbf{A} and \mathbf{B} are square matrices of order $3p$ and are inverses of each other so that $\mathbf{BA} = \mathbf{1}_{3p \times 3p}$. Let us define $\mathbf{G} \equiv \mathbf{BuB}^T$ and $\mathbf{g} \equiv \mathbf{A}^T \mathbf{u}^{-1} \mathbf{A}$, which are inverses of each other. Then, in terms of the new nonredundant coordinates, each molecule's equation of motion is now found to be of the same form as Eq. (40) with $\eta_{\gamma\delta}^{\alpha}$ and f^{α} being also given by Eqs. (81) and (82), respectively, neglecting the underlines. Thus, the actual dynamics can efficiently be executed in the transformed nonredundant coordinates. Whenever new values of $\mathbf{S} \equiv \mathbf{KS}$, $\mathbf{\dot{S}} \equiv \mathbf{K}\dot{\mathbf{S}}$, and $\mathbf{\ddot{S}} \equiv \mathbf{K}\ddot{\mathbf{S}}$ are determined, the corresponding values in the original redundant coordinates can be obtained by \mathbf{K}^T .

It should be noted that an ICMD simulation can always be done using a suitable set of nonredundant internal coordinates, where the transformation matrix \mathbf{K} to a new set of linearly independent coordinates need not be computed. Thus, for nonredundant generalized coordinates Eqs. (40), (81) and (82) constitute an efficient MD simulation method without any inversion of a large matrix. Moreover, if we use a set of \mathbf{Z} -coordinates for internal degrees of freedom, extra transformations as in Eqs. (58) and (59) can be avoided. Even in the case that the V^S (the bonded part of the potential) is expressed in redundant coordinates, an MD simulation can always be performed by using a set of \mathbf{Z} -coordinates and external coordinates, since the required Cartesian derivatives $\partial V / \partial x_v^j$ in Eq. (82) are easily obtained from Eqs. (7) and (10). As previously assumed, we consider only nonredundant generalized coordinates and remove all the underlines if not otherwise noted. In applying the proposed new MD formalism, nonzero elements of \mathbf{A} and \mathbf{A}_2 are to be computed by one of the two methods described in Section 3 while those of \mathbf{B} are to be directly computed as in vibrational spectroscopy.

In addition to the advantage of avoiding any direct inversion of a large matrix, as in the recursive algorithms [26–28] in \mathbf{A} -matrix formulations, the new ICMD formalism based on Eqs. (40), (81), and (82) has other features. Since only a few (at most four) atoms are involved in defining an internal coordinate, the full \mathbf{B} and \mathbf{A}_2 need not be

stored if we keep related atom indices for each internal coordinate. Thus, in computing η_{rs}^α elements for the α th internal coordinate the actual multiplications in the summation of Eq. (81) need be done only for nonzero **B**-matrix elements, which significantly reduces the number of required arithmetic operations compared to using Eq. (41) with multiplications for all coordinate indices β (where even the required computation of all $\eta_{\beta\gamma\delta}$ is nontrivial). By analogy, considering only nonzero **B**-matrix elements in Eq. (82) with $\partial V/\partial x_c^{\nu\delta}$ computed from Eqs. (7) and (10) gives an effective way of computing f^α compared to using Eq. (42) with $\partial V/\partial S_c^\beta$ computed from Eq. (34). (As an example, the computation of f^α for the CCCC torsional coordinate in butane, which consists of 14 atoms, can be done only for 12 backbone Cartesian components rather than all 42 Cartesian components.)

We now consider a method to freeze some (nonredundant) internal coordinates in the course of a time trajectory. When an internal coordinate is constrained to a constant value, a movement of an atom directly related to this internal may result in a change in an adjacent internal coordinate that is not defined from this atom but from others, making the spectroscopic **B**-matrix physically ill defined in the sense that it is not the exact inverse of the **A**-matrix [30]. However, we may first construct the system's equation of motion from the spectroscopic **B**-matrix computed by regarding each molecule to be completely flexible, and next introduce the desired constraints in the equation, which simply become

$$S^r(t) = S^r(0) = \text{constant} \quad (83)$$

with r being the indices of internals to be frozen. The resulting system's equation of motion is found to be

$$\sum_{\gamma=1}^{3p} g_{\beta\gamma} \ddot{S}^\gamma + \sum_{\gamma,\delta=1}^{3p} \eta_{\beta\gamma\delta} \dot{S}^\gamma \dot{S}^\delta = -\frac{\partial V}{\partial S^\beta} + \sum_s \lambda_s \delta_{\beta s}^s, \quad (84)$$

where each additional parameter λ_s (Lagrange undetermined multiplier) represents the required constraint force to maintain the imposed constraint [38]. When each coordinate to be frozen is nonredundant, its related **B**-matrix elements are

still nonzero while its time derivatives are all zero. Thus, Eq. (84) can be solved to give

$$\ddot{S}^u + \sum_{v,w} \eta_{vw}^u \dot{S}^v \dot{S}^w = f^u + \sum_s G^{us} \lambda_s, \quad (85)$$

$$\sum_{v,w} \eta_{vw}^r \dot{S}^v \dot{S}^w = f^r + \sum_s G^{rs} \lambda_s, \quad (86)$$

where u , v , and w are indices for unconstrained coordinates, while r and s are those for constrained ones. With η_{vw}^r and f^r given by Eqs. (81) and (82), respectively, the parameters, λ_s , can be determined by solving Eq. (86). These can be substituted into Eq. (85) in order to determine new accelerations for unconstrained coordinates. Since this method requires solving a linear equation, it may be less effective in reducing operational dimensions than the **A**-matrix formalism, in which the concerned coordinates can be simply neglected since the system's kinetic energy is directly determined from the **A**-matrix [30]. Alternatively, since it is more realistic to regard each internal coordinate as flexible in a real molecule and the spectroscopic **B**-matrix is still a good approximation to the inverse of the **A**-matrix, as a useful approximation we may directly use the spectroscopic **B**-matrix elements in order to find an initial equilibrium configuration in the early stages of MD simulations by simply neglecting the fast varying internals without solving the constrained equation as in the **A**-matrix formalism. However, near the equilibrium configuration we can efficiently do full **B**-matrix ICMD without any rigid constraints in order to derive desired physical quantities.

We note that it is efficient to compute also the related nonzero spectroscopic **B**-matrix elements in **Z**-coordinates after defining new atomic coordinates from Eq. (27) at each **Z**-matrix stage. **B**-matrix elements in a set of redundant internal coordinates can alternatively be computed from these. Once all **B**-matrix elements in **Z**-coordinates are determined, those in the primitive internals can be obtained from Eq. (54) by

$$\frac{\partial \xi^\beta}{\partial x_\lambda^k} = \begin{cases} \frac{\partial R^\beta}{\partial x_\lambda^k}, & \text{for } 1 \leq \beta \leq f, \\ -\sum_{\gamma \in \Phi_\delta} \frac{a_\gamma^\delta}{b_\delta^\beta} \frac{\partial R^\gamma}{\partial x_\lambda^k}, & \text{for } \beta = f + \delta, \end{cases} \quad (87)$$

$$\frac{\partial^2 \xi^\beta}{\partial x_v^j \partial x_\lambda^k} = \begin{cases} \frac{\partial^2 R^\beta}{\partial x_v^j \partial x_\lambda^k}, & \text{for } 1 \leq \beta \leq f, \\ -\sum_{\gamma \in \Phi_\delta} \frac{a_\gamma^\delta}{b_\delta^\delta} \frac{\partial^2 R^\gamma}{\partial x_v^j \partial x_\lambda^k} - \sum_{\alpha, \gamma} \frac{a_\gamma^\delta}{b_\delta^\delta} \frac{\partial R^\alpha}{\partial x_v^j} \frac{\partial R^\gamma}{\partial x_\lambda^k}, & \text{for } \beta = f + \delta. \end{cases} \quad (88)$$

Using Eq. (14), **B**-matrix elements in (redundant) internal coordinates S^α can be alternatively obtained by

$$\frac{\partial S^\alpha}{\partial x_\lambda^k} = \sum_{\gamma=1}^n U_\gamma^\alpha \frac{\partial \xi^\gamma}{\partial x_\lambda^k}, \quad (89)$$

$$\frac{\partial^2 S^\alpha}{\partial x_v^j \partial x_\lambda^k} = \sum_{\gamma=1}^n U_\gamma^\alpha \frac{\partial^2 \xi^\gamma}{\partial x_v^j \partial x_\lambda^k} + \sum_{\beta, \gamma=1}^n U_{\beta\gamma}^\alpha \frac{\partial \xi^\beta}{\partial x_v^j} \frac{\partial \xi^\gamma}{\partial x_\lambda^k}. \quad (90)$$

4.2. B-matrix elements for external coordinates

The coordinates of atom ζ are translational parameters between the LFF and the MFF, and the **B**-matrix elements for the external translations are simply found to be

$$\frac{\partial x_\zeta^k}{\partial x_v^j} = \delta_\zeta^v \delta_j^k, \quad (91)$$

$$\frac{\partial^2 x_\zeta^k}{\partial x_\mu^i \partial x_v^j} = 0. \quad (92)$$

Since internal vibrations are the main concerns in conventional spectroscopy, **B**-matrix elements for external rotations are usually determined under the Eckart condition [45,46], which is imposed to make the interaction terms between internal vibrations and external rotations small enough to be neglected in a molecule's kinetic energy. Using Eq. (69), the interaction term between an external rotation of ϕ^j and an internal motion \dot{S}^γ in the kinetic energy expression of Eq. (30) is found to be

$$\sum_{\lambda=1}^p m_\lambda \frac{\partial \mathbf{x}_\lambda}{\partial \phi^j} \cdot \frac{\partial \mathbf{x}_\lambda}{\partial S^\gamma} = \frac{\partial \vec{\theta}}{\partial \phi^j} \cdot \left(\sum_{\lambda=1}^p m_\lambda \mathbf{z}_\lambda \times \frac{\partial \mathbf{x}_\lambda}{\partial S^\gamma} \right). \quad (93)$$

Thus, this term is guaranteed to be small when the term in parenthesis is small, viz.,

$$\sum_{\lambda=1}^p m_\lambda \mathbf{z}_\lambda \times \frac{\partial \mathbf{x}_\lambda}{\partial S^\gamma} = \mathbf{0}, \quad (94)$$

which is the Eckart condition for external rotations at atom ζ . This should not be confused with the relation

$$\sum_{\lambda=1}^p \mathbf{z}_\lambda \times \frac{\partial S^\gamma}{\partial \mathbf{x}_\lambda} = \mathbf{0} \quad (95)$$

derived from the invariance of all internal coordinates under external rotations, viz., $\partial S^\gamma / \partial \phi^j = 0$ ($j = 1, 2, 3$). It should be noted that the **A**-matrix elements $\partial x_\lambda^k / \partial S^\gamma$ for internal coordinates do not satisfy Eq. (94) in general, while the **B**-matrix elements for external rotations based on the Eckart condition of Eq. (94) do not satisfy Eqs. (79) and (80) with the **A**-matrix. Without any conditions, the correct **B**-matrix elements in $\vec{\theta}$ are found to satisfy

$$\begin{aligned} \mathbf{I}_\zeta \vec{\theta}_{v\zeta} &= \sum_{\lambda=1}^p m_\lambda \frac{\partial x_\lambda^j}{\partial \vec{\theta}} (\delta_\lambda^v - \delta_\zeta^v) \\ &\quad - \sum_{\gamma=1}^f \left(\sum_{\lambda=1}^p m_\lambda \frac{\partial \mathbf{x}_\lambda}{\partial \vec{\theta}} \cdot \frac{\partial \mathbf{x}_\lambda}{\partial S^\gamma} \right) \frac{\partial S^\gamma}{\partial x_v^j} \\ &= \sum_{\lambda=1}^p m_\lambda (\mathbf{z}_\lambda \times \hat{\mathbf{j}}) (\delta_\lambda^v - \delta_\zeta^v) \\ &\quad - \sum_{\gamma=1}^f \left(\sum_{\lambda=1}^p m_\lambda \mathbf{z}_\lambda \times \frac{\partial \mathbf{x}_\lambda}{\partial S^\gamma} \right) \frac{\partial S^\gamma}{\partial x_v^j}, \end{aligned} \quad (96)$$

where S^γ represent only internal coordinates and $\vec{\theta}_{v\zeta} \equiv \partial \vec{\theta} / \partial x_v^j$. Values of $\vec{\theta}_{v\zeta}$ can be obtained by solving Eq. (96). The second derivatives $\vec{\theta}_{\mu^i v^j} \equiv \partial^2 \vec{\theta} / \partial x_\mu^i \partial x_v^j$ can be obtained from the derivative of Eq. (96) w.r.t. x_μ^i . However, since these contain **A**₂ elements for internal coordinates (due to the second term in the right-hand side of Eq. (96)), they can alternatively be computed directly by using the relation

$$\vec{\theta}_{\mu^i v^j} = - \sum_{\alpha, \beta=1}^{3p} \left(\sum_{\lambda=1}^p \sum_{k=1}^3 \vec{\theta}_{\lambda^k} \frac{\partial^2 x_\lambda^k}{\partial S^\alpha \partial S^\beta} \right) \frac{\partial S^\alpha}{\partial x_\mu^i} \frac{\partial S^\beta}{\partial x_v^j} \quad (97)$$

obtained from a Cartesian derivative of Eq. (80). From the inverse relation of Eq. (70), the **B**-matrix elements for external rotations of $\vec{\phi}$, viz.,

$\vec{\phi}_{vj} \equiv \partial \vec{\phi} / \partial x_v^j$ and $\vec{\phi}_{\mu^i vj} \equiv \partial^2 \vec{\phi} / \partial x_\mu^i \partial x_v^j$, can be determined by

$$\vec{\phi}_{vj} = \mathbf{W}^{-1}(\vec{\phi}) \vec{\theta}_{vj}, \quad (98)$$

$$\begin{aligned} \vec{\phi}_{\mu^i vj} &= \mathbf{W}^{-1}(\vec{\phi}) \left\{ \vec{\theta}_{\mu^i vj} - \frac{\partial \mathbf{W}(\vec{\phi})}{\partial \mathbf{x}_\mu^i} \vec{\phi}_{vj} \right\} \\ &= \mathbf{W}^{-1}(\vec{\phi}) \left\{ \vec{\theta}_{\mu^i vj} + \begin{pmatrix} \phi_{\mu^i}^2 \phi_{vj}^1 \cos \phi^3 \sin \phi^2 + \phi_{\mu^i}^3 (\phi_{vj}^1 \sin \phi^3 \cos \phi^2 + \phi_{vj}^2 \cos \phi^3) \\ \phi_{\mu^i}^2 \phi_{vj}^1 \sin \phi^3 \sin \phi^2 - \phi_{\mu^i}^3 (\phi_{vj}^1 \cos \phi^3 \cos \phi^2 - \phi_{vj}^2 \sin \phi^3) \\ \phi_{\mu^i}^2 \phi_{vj}^1 \cos \phi^2 \end{pmatrix} \right\}, \end{aligned} \quad (99)$$

where $\mathbf{W}^{-1}(\vec{\phi})$ is found to be

$$\mathbf{W}^{-1}(\vec{\phi}) = \begin{pmatrix} \cos \phi^3 \frac{1}{\cos \phi^2} & \sin \phi^3 \frac{1}{\cos \phi^2} & 0 \\ -\sin \phi^3 & \cos \phi^3 & 0 \\ \cos \phi^3 \frac{\sin \phi^2}{\cos \phi^2} & \sin \phi^3 \frac{\sin \phi^2}{\cos \phi^2} & 1 \end{pmatrix}. \quad (100)$$

Note that $\mathbf{W}^{-1}(\vec{\phi})$ of Eq. (100) is not well-defined when $\phi^2 = \pm\pi/2$. This is also a problem in the \mathbf{A} -matrix formulation, where \mathbf{g}^{rot} of Eq. (76) is singular and we cannot solve Eq. (32) properly. This kind of singularity may happen frequently during MM or MD simulations of a system containing many molecules. Thus, for a system of many molecules it is much better to use the Euler representation in $\mathbf{SU}(2)$ for the external rotations [38,47,29].

4.3. Euler representation of rotations in $\mathbf{SU}(2)$

A vector $\mathbf{v}_m = v_m^1 \hat{\mathbf{1}}_m + v_m^2 \hat{\mathbf{2}}_m + v_m^3 \hat{\mathbf{3}}_m$ in the MFF can be represented as

$$\mathbf{v}_m = \begin{pmatrix} v_m^3 & v_m^- \\ v_m^+ & -v_m^- \end{pmatrix} \quad (101)$$

in complex two dimensions with $v_m^+ \equiv v_m^1 + iv_m^2$ and $v_m^- \equiv v_m^1 - iv_m^2$. Thus, a rotation Ξ of \mathbf{v}_m with $\mathbf{v} = \Xi \mathbf{v}_m$ in $\{\hat{\mathbf{1}}, \hat{\mathbf{2}}, \hat{\mathbf{3}}\}$ can be regarded as a representation \mathbf{Q} with $\mathbf{v} \equiv \mathbf{Q}^\dagger \mathbf{v}_m \mathbf{Q}$ in $\mathbf{SU}(2)$ such that \mathbf{Q} is parameterized as

$$\begin{aligned} \mathbf{Q} &= \begin{pmatrix} e^0 + ie^3 & e^2 + ie^1 \\ -(e^2 - ie^1) & e^0 - ie^3 \end{pmatrix} \\ &= e^0 \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} + i\mathbf{e} \cdot \boldsymbol{\sigma} \end{aligned} \quad (102)$$

where $\boldsymbol{\sigma}_j$ ($j = 1, 2, 3$) are the Pauli spin matrices and the vector \mathbf{e} determines the direction of the rotation axis, which satisfies

$$\det(\mathbf{Q}) = e^0 e^0 + \mathbf{e} \cdot \mathbf{e} = 1. \quad (103)$$

In particular, for the rotation given by Eq. (25) the corresponding new parameters (e^0, \mathbf{e}) , which are different from the ones derived from the Euler angles [38,47,29], are found to be

$$e^0 = \cos \frac{\phi^3}{2} \cos \frac{\phi^2}{2} \cos \frac{\phi^1}{2} - \sin \frac{\phi^3}{2} \sin \frac{\phi^2}{2} \sin \frac{\phi^1}{2}, \quad (104)$$

$$e^1 = \cos \frac{\phi^3}{2} \cos \frac{\phi^2}{2} \sin \frac{\phi^1}{2} + \sin \frac{\phi^3}{2} \sin \frac{\phi^2}{2} \cos \frac{\phi^1}{2}, \quad (105)$$

$$e^2 = \cos \frac{\phi^3}{2} \sin \frac{\phi^2}{2} \cos \frac{\phi^1}{2} - \sin \frac{\phi^3}{2} \cos \frac{\phi^2}{2} \sin \frac{\phi^1}{2}, \quad (106)$$

$$e^3 = \cos \frac{\phi^3}{2} \sin \frac{\phi^2}{2} \sin \frac{\phi^1}{2} + \sin \frac{\phi^3}{2} \cos \frac{\phi^2}{2} \cos \frac{\phi^1}{2}, \quad (107)$$

and the rotation matrix Ξ in real three-dimension in terms of (e^0, \mathbf{e}) is found to be

$$\Xi(e^0, \mathbf{e}) = \begin{pmatrix} e^0 e^0 - \mathbf{e} \cdot \mathbf{e} + 2e^1 e^1 & 2e^1 e^2 - 2e^0 e^3 & 2e^1 e^3 + 2e^0 e^2 \\ 2e^1 e^2 + 2e^0 e^3 & e^0 e^0 - \mathbf{e} \cdot \mathbf{e} + 2e^2 e^2 & 2e^2 e^3 - 2e^0 e^1 \\ 2e^1 e^3 - 2e^0 e^2 & 2e^2 e^3 + 2e^0 e^1 & e^0 e^0 - \mathbf{e} \cdot \mathbf{e} + 2e^3 e^3 \end{pmatrix}. \quad (108)$$

Considering the following two relations:

$$\frac{\partial \Xi}{\partial e^0} \Xi^{-1} = 2[e^0 \mathbf{1} - \mathbf{e} \cdot \mathbf{D}], \quad (109)$$

$$\frac{\partial \Xi}{\partial e^j} \Xi^{-1} = 2[e^j \mathbf{1} + e^0 \mathbf{D}_j - (\mathbf{e} \times \mathbf{D})^j], \quad (110)$$

the time derivative of Eq. (24) in terms of (e^0, \mathbf{e}) becomes

$$\dot{\mathbf{x}}_\lambda = \dot{\mathbf{x}}_\zeta + \vec{\Omega} \times \mathbf{z}_\lambda + \Xi(e^0, \mathbf{e}) \dot{\mathbf{z}}_{\lambda m}, \quad (111)$$

where the molecule's angular momentum, $\vec{\Omega} \equiv \dot{\vec{\theta}}$, is defined by

$$\begin{pmatrix} 0 \\ \vec{\Omega} \end{pmatrix} = \mathbf{W}(e^0, \mathbf{e}) \begin{pmatrix} \dot{e}^0 \\ \dot{\mathbf{e}} \end{pmatrix} \quad (112)$$

with

$$\mathbf{W}(e^0, \mathbf{e}) \equiv 2 \begin{pmatrix} e^0 & e^1 & e^2 & e^3 \\ -e^1 & e^0 & -e^3 & e^2 \\ -e^2 & e^3 & e^0 & -e^1 \\ -e^3 & -e^2 & e^1 & e^0 \end{pmatrix}. \quad (113)$$

The \mathbf{A} -matrix elements in (e^0, \mathbf{e}) are found to be:

$$\frac{\partial \mathbf{x}_\lambda}{\partial e^m} = \frac{\partial \vec{\theta}}{\partial e^m} \times \mathbf{z}_\lambda, \quad (114)$$

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial e^l \partial e^m} = \frac{\partial}{\partial e^l} \left(\frac{\partial \vec{\theta}}{\partial e^m} \right) \times \mathbf{z}_\lambda + \frac{\partial \vec{\theta}}{\partial e^m} \times \left(\frac{\partial \vec{\theta}}{\partial e^l} \times \mathbf{z}_\lambda \right). \quad (115)$$

The first row of Eq. (112) corresponds just to the time derivative of Eq. (103). It is evident that, for all (e^0, \mathbf{e}) satisfying Eq. (103), $\mathbf{W}(e^0, \mathbf{e})$ has the well-defined unique inverse:

$$\mathbf{W}^{-1}(e^0, \mathbf{e}) = \frac{1}{4} \mathbf{W}^T(e^0, \mathbf{e}). \quad (116)$$

Once values of $\vec{\theta}_{vj}$ and $\vec{\theta}_{\mu^i v^j}$ are calculated from Eqs. (96) and (97), the \mathbf{B} -matrix elements in (e^0, \mathbf{e}) can be obtained from the inverse relation of Eq. (112):

$$\begin{pmatrix} e_{vj}^0 \\ \mathbf{e}_{vj} \end{pmatrix} = \mathbf{W}^{-1} \begin{pmatrix} 0 \\ \vec{\theta}_{vj} \end{pmatrix}, \quad (117)$$

$$\begin{pmatrix} e_{\mu^i v^j}^0 \\ \mathbf{e}_{\mu^i v^j} \end{pmatrix} = \mathbf{W}^{-1} \begin{pmatrix} -\frac{1}{2} \vec{\theta}_{\mu^i} \cdot \vec{\theta}_{v^j} \\ \vec{\theta}_{\mu^i v^j} - \frac{1}{2} \vec{\theta}_{\mu^i} \times \vec{\theta}_{v^j} \end{pmatrix} \quad (118)$$

with

$$e_{vj}^0 \equiv \partial e^0 / \partial x_v^j, \quad \mathbf{e}_{vj} \equiv \partial \mathbf{e} / \partial x_v^j, \quad e_{\mu^i v^j}^0 \equiv \partial^2 e^0 / \partial x_{\mu^i}^i \partial x_{v^j}^j,$$

and

$$\mathbf{e}_{\mu^i v^j} \equiv \partial^2 \mathbf{e} / \partial x_{\mu^i}^i \partial x_{v^j}^j.$$

Following Eqs. (104)–(107), the case of $\vec{\phi} = \mathbf{0}$ corresponds to that of $(e^0, \mathbf{e}) = (1, \mathbf{0})$, and in the limit of $(e^0, \mathbf{e}) \rightarrow (1, \mathbf{0})$ the direction of $\dot{\mathbf{e}}$ coincides with that of $\vec{\Omega}$.

Although this treatment for external rotations not only removes the singularity problem involved in Eq. (100) but also avoids the computations of trigonometric functions inherent in using Eq. (98), we have to solve the problem arising from the constraint of Eq. (103) for each molecule. This can be solved by a treatment similar to that used in the case of dependent coordinates. Considering that \mathbf{g}^{rot} in (e^0, \mathbf{e}) is found to be

$$\mathbf{g}^{\text{rot}} = \mathbf{W}^T \begin{pmatrix} 0 & \mathbf{0} \\ \mathbf{0} & \mathbf{I}_\zeta \end{pmatrix} \mathbf{W} \quad (119)$$

and there exists an orthogonal matrix \mathbf{Q} such that

$$\mathbf{Q} \mathbf{I}_\zeta \mathbf{Q}^T = \mathbf{D} \quad (120)$$

with \mathbf{D} being diagonal, it is evident that \mathbf{g}^{rot} is diagonalized by

$$\begin{pmatrix} 1 & \mathbf{0} \\ \mathbf{0} & \mathbf{Q}^T \end{pmatrix} (\mathbf{W}^T)^{-1} \mathbf{g}^{\text{rot}} \mathbf{W}^{-1} \begin{pmatrix} 1 & \mathbf{0} \\ \mathbf{0} & \mathbf{Q} \end{pmatrix} \\ = \begin{pmatrix} 0 & \mathbf{0} \\ \mathbf{0} & \mathbf{D} \end{pmatrix}. \quad (121)$$

Therefore, a desired transformation matrix \mathbf{K} to new nonredundant rotation coordinates $\underline{\mathbf{e}}$ can be taken as

$$\mathbf{K} \equiv (\mathbf{0} \ \mathbf{Q})\mathbf{W}$$

$$= 2\mathbf{Q} \begin{pmatrix} -e^1 & e^0 & -e^3 & e^2 \\ -e^2 & e^3 & e^0 & -e^1 \\ -e^3 & -e^2 & e^1 & e^0 \end{pmatrix} \quad (122)$$

where \mathbf{Q} has to be constructed from eigenvectors of nonzero eigenvalues of \mathbf{I}_ζ . The time derivative of $\underline{\mathbf{e}}$ becomes

$$\dot{\underline{\mathbf{e}}} \equiv \mathbf{K} \begin{pmatrix} \dot{e}^0 \\ \dot{\mathbf{e}} \end{pmatrix} = \mathbf{Q}\dot{\underline{\theta}} = \mathbf{Q}\dot{\underline{\Omega}}, \quad (123)$$

which is the angular velocity in the frame of principal axes of \mathbf{I}_ζ , while the new rotation coordinates are the null coordinates since

$$\underline{\mathbf{e}} \equiv \mathbf{K} \begin{pmatrix} e^0 \\ \mathbf{e} \end{pmatrix} = \mathbf{0}. \quad (124)$$

For nonlinear molecules, it is more efficient to transform $\underline{\mathbf{e}}$ to new rotation parameters, $\underline{\tilde{\theta}}$, by \mathbf{Q}^T : $\underline{\tilde{\theta}} \equiv \mathbf{Q}^T \underline{\mathbf{e}}$, $\dot{\underline{\tilde{\theta}}} \equiv \mathbf{Q}^T \dot{\underline{\mathbf{e}}}$, and $\ddot{\underline{\tilde{\theta}}} \equiv \mathbf{Q}^T \ddot{\underline{\mathbf{e}}}$. Thus, the transformation matrix from Euler parameters (e^0, \mathbf{e}) to $\underline{\tilde{\theta}}$ is found to be

$$\mathbf{N} \equiv \mathbf{Q}^T \mathbf{K} = 2 \begin{pmatrix} -e^1 & e^0 & -e^3 & e^2 \\ -e^2 & e^3 & e^0 & -e^1 \\ -e^3 & -e^2 & e^1 & e^0 \end{pmatrix}, \quad (125)$$

which is the submatrix taken from the second row to the fourth row of $\mathbf{W}(e^0, \mathbf{e})$. Then, the corresponding \mathbf{B} - and \mathbf{A} -matrix elements become, respectively,

$$\underline{\tilde{\theta}}_{vj} \equiv \mathbf{N} \begin{pmatrix} e_{vj}^0 \\ \mathbf{e}_{vj} \end{pmatrix} = \tilde{\theta}_{vj}, \quad (126)$$

$$\underline{\tilde{\theta}}_{\mu^i vj} \equiv \mathbf{N} \begin{pmatrix} e_{\mu^i vj}^0 \\ \mathbf{e}_{\mu^i vj} \end{pmatrix} = \tilde{\theta}_{\mu^i vj} - \frac{1}{2} \tilde{\theta}_{\mu^i} \times \tilde{\theta}_{vj}, \quad (127)$$

$$\frac{\partial \mathbf{x}_\lambda}{\partial \underline{\tilde{\theta}}^j} = \sum_{k=1}^3 \sum_{l=0}^3 \frac{\partial \mathbf{x}_\lambda}{\partial \theta^k} \frac{\partial \theta^k}{\partial e^l} \frac{\partial e^l}{\partial \underline{\tilde{\theta}}^j} = \frac{\partial \mathbf{x}_\lambda}{\partial \theta^j}, \quad (128)$$

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial \underline{\tilde{\theta}}^i \partial \underline{\tilde{\theta}}^j} = \frac{\partial^2 \mathbf{x}_\lambda}{\partial \theta^i \partial \theta^j}, \quad (129)$$

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial S^v \partial \underline{\tilde{\theta}}^j} = \frac{\partial^2 \mathbf{x}_\lambda}{\partial S^v \partial \theta^j} = \frac{\partial^2 \mathbf{x}_\lambda}{\partial \underline{\tilde{\theta}}^j \partial S^v}, \quad (130)$$

which are computed from Eqs. (73)–(75) and (96)–(97) with S^v being internal coordinates.

Finally, we briefly summarize how the above results can be used in applying the proposed new ICMD formalism to model systems. Initial Euler parameters (e^0, \mathbf{e}) specify the relative rotation matrix Ξ between the MFF and LFF by Eq. (108), while those of \mathbf{x}_ζ determine the translations between the two frames. The dynamics equation, Eq. (40), with Eqs. (81) and (82) is most efficiently executed in a nonredundant set of \mathbf{Z} -coordinates, \mathbf{x}_ζ (translations), and $\underline{\tilde{\theta}}$ (rotations), for a nonlinear molecule. From the given initial values of \mathbf{Z} -coordinates, we generate each molecule's atomic coordinates \mathbf{x}_λ in the LFF by using Eqs. (24) and (27). At each stage of atomic coordinate generation we also compute nonzero elements of \mathbf{A} , \mathbf{A}_2 , and \mathbf{B} in \mathbf{Z} -coordinates directly. (The method of computing spectroscopic \mathbf{B} -matrix elements can be found elsewhere [35–37].) Next, we compute \mathbf{A} - and \mathbf{B} -matrix elements for external coordinates. Those for \mathbf{x}_ζ are obtained from Eqs. (60), (61), and (91), while those for $\underline{\tilde{\theta}}$ are obtained from Eqs. (128)–(130) and (126) with Eqs. (73)–(75) and (96) being used. The time trajectory of (e^0, \mathbf{e}) is obtained in the following way. Initial values of $(\dot{e}^0, \dot{\mathbf{e}})$ are transformed to those of $\dot{\underline{\tilde{\theta}}}$ by \mathbf{N} , and from Eq. (40) new values of $\dot{\underline{\tilde{\theta}}}$ are computed and transformed back to values of $(\ddot{e}^0, \ddot{\mathbf{e}})$ by $\mathbf{N}^T/4$. These are then used to determine new values of (e^0, \mathbf{e}) by Eq. (43).

5. Multiple time step algorithm

With J_c^γ being the conjugate momenta of the generalized coordinates S_c^γ as in Eq. (35), the system's Hamiltonian is expressed by

$$H(\mathbf{S}, \mathbf{J}) = \frac{1}{2} \sum_{c=1}^{N_{\text{mol}}} \mathbf{J}_c^T \mathbf{g}_c^{-1} \mathbf{J}_c + V(\mathbf{S}) \quad (131)$$

which provides for the system's Hamiltonian equations of motion

$$j_c^z = \frac{\partial H}{\partial S_c^z} = -\frac{1}{2} \dot{\mathbf{S}}_c^T \frac{\partial \mathbf{g}_c}{\partial S_c^z} \dot{\mathbf{S}}_c + \frac{\partial V}{\partial S_c^z}, \quad (132)$$

$$\dot{S}_c^\alpha = \frac{\partial H}{\partial J_c^\alpha} = [\mathbf{g}_c^{-1} \mathbf{J}_c]^\alpha. \quad (133)$$

While Eq. (133) is equivalent to the definition of J_c^γ , Eq. (132) is equivalent to Eq. (32), the system's Euler–Lagrange equation of motion. Let us concentrate on the c th molecule of the system and remove the molecular index. Then, the molecule's Liouville operator \mathbf{L} can be defined by

$$i\mathbf{L} \equiv \sum_\beta \left(\dot{S}^\beta \frac{\partial}{\partial S^\beta} + \dot{J}^\beta \frac{\partial}{\partial J^\beta} \right), \quad (134)$$

which is Hermitian and propagates the initial values of $\{\mathbf{S}(0), \mathbf{J}(0)\}$ to those of

$$\{\mathbf{S}(t), \mathbf{J}(t)\} = \exp(i\mathbf{L}t)\{\mathbf{S}(0), \mathbf{J}(0)\} \quad (135)$$

at time t . Note that in the generalized coordinates S^γ the fast varying degrees of freedom, e.g., bond stretches or angle bend coordinates, can be explicitly separated from the slowly varying degrees of freedom such as torsions, external translations, or external rotations. So, we can decompose the Liouville operator into two parts for simplicity:

$$\begin{aligned} i\mathbf{L} &= i\mathbf{L}_s + i\mathbf{L}_f \\ &\equiv \sum_r \left(\dot{S}^r \frac{\partial}{\partial S^r} + \dot{J}^r \frac{\partial}{\partial J^r} \right) \\ &\quad + \sum_u \left(\dot{S}^u \frac{\partial}{\partial S^u} + \dot{J}^u \frac{\partial}{\partial J^u} \right), \end{aligned} \quad (136)$$

where r and u are coordinate indices for slowly varying and fast varying coordinates, respectively. This enables us to write, to the order of $O(\Delta t^3)$ [12],

$$\begin{aligned} \exp(i\mathbf{L}\Delta t) &\cong \exp\left(i\mathbf{L}_s \frac{\Delta t}{2}\right) \exp(i\mathbf{L}_f \Delta t) \exp\left(i\mathbf{L}_s \frac{\Delta t}{2}\right) \\ &= \exp\left(i\mathbf{L}_s \frac{\Delta t}{2}\right) \{\exp(i\mathbf{L}_f \delta t)\}^n \\ &\quad \times \exp\left(i\mathbf{L}_s \frac{\Delta t}{2}\right) \end{aligned} \quad (137)$$

where the inner fast varying part is further resolved by a smaller time step of $\delta t \equiv \Delta t/n$ (n can be chosen to give an optimized process). The state at time Δt is determined by applying this propagator to the initial state of $\{\mathbf{S}(0), \mathbf{J}(0); 0\}$:

(a) $\exp(i\mathbf{L}_s \Delta t/2)\{\mathbf{S}(0), \mathbf{J}(0); 0\}$ provides the state of $\{S^r(\Delta t/2), J^r(\Delta t/2); \Delta t/2\}$ and $\{S^u(0), J^u(0); \Delta t/2\}$, where $S^r(\Delta t/2)$ and $J^r(\Delta t/2)$ are found to be, respectively,

$$S^r\left(\frac{\Delta t}{2}\right) = S^r(0) + \frac{\Delta t}{2} \dot{S}^r(0), \quad (138)$$

$$J^r\left(\frac{\Delta t}{2}\right) = J^r(0) + \frac{\Delta t}{2} \dot{J}^r(0). \quad (139)$$

Instead of Eq. (139), with Eq. (40) we can equivalently use

$$\dot{S}^r\left(\frac{\Delta t}{2}\right) = \dot{S}^r(0) + \frac{\Delta t}{2} \ddot{S}^r(0). \quad (140)$$

(b) $\exp(i\mathbf{L}_f \delta t)\{\mathbf{S}(\Delta t/2), \mathbf{J}(\Delta t/2); \Delta t/2\}$ provides the state of $\{S^r(\Delta t/2), J^r(\Delta t/2); \Delta t/2 + \delta t\}$ and $\{S^u(\delta t), J^u(\delta t); \Delta t/2 + \delta t\}$. Applying this operation a total of n times, which is equivalent to using the velocity Verlet integrator iteratively n times on the system with only fast varying degrees of freedom, generates the state of $\{S^r(\Delta t/2), J^r(\Delta t/2); \Delta t/2\}$ and $\{S^u(\Delta t), J^u(\Delta t); \Delta t\}$.

(c) Applying $\exp(i\mathbf{L}_s \Delta t/2)$ to the final state of step (b) provides the state of $\{\mathbf{S}(\Delta t), \mathbf{J}(\Delta t); \Delta t\}$.

Thus, we may use MTS depending on the nature of the degrees of freedom: a longer time step for slowly varying degrees of freedom while a smaller time step for fast varying degrees of freedom. This is different from the conventional MTS algorithm [10–13], where the Liouville operator is decomposed depending on the classification of interaction distances, since the forces acting on an atom due to atoms located at far distances stay roughly constant while those arising from near atoms change fast. In fact, each molecule changes its position and the classes of interaction distances may also change in time, which reduces the effectiveness of the conventional method. It should be mentioned that, if we follow the spectroscopic \mathbf{B} -matrix formulation, at each time step, whether it is for fast or slow moving degrees of freedom, we have to solve a linear equation to determine the Lagrange undetermined multipliers introduced to freeze internal degrees of freedom. However, as a way to obtain an initial rough equilibrium configuration, we may also explore the trajectories

that result from simply neglecting the frozen coordinates, as in the **A**-matrix formalism. Such configurations could then be used for further unconstrained dynamics.

6. Concluding remarks

Based on the spectroscopic **B**-matrix in nonredundant generalized coordinates, we propose a new ICMD formalism that does not require any matrix inversion except for the 3×3 inertia tensor, which makes it useful for MD simulations on systems of large molecules. The inversion of the mass-matrix is avoided by directly computing the desired spectroscopic **B**-matrix that gives the exact inverse of the conventional **A**-matrix. It turns out that the **B**-matrix elements for external rotations under the Eckart conditions [45,46] do not provide such an exact inverse of the **A**-matrix. Instead, the correct **B**-matrix elements for external rotations are obtained (by solving Eq. (96)) without any conditions. The sparsity in the spectroscopic **B**-matrix enhances the efficiency of the proposed formalism by significantly reducing the number of arithmetic operations required. This approach is ideal for MD simulations of many-molecule systems in combination with the proposed dynamics method of singularity free external rotations in a representation of $SU(2)$ algebra [38]. Based on the explicit separability between fast varying degrees of freedom and slowly varying ones, we introduce an MTS method in generalized coordinates in which the nontrivial classification of interaction distances [10–12] is not required.

An MD simulation in redundant internal coordinates can be done by finding a transformation to a new set of independent coordinates, in which the actual dynamics equation is solved. Since this may involve nontrivial computations of eigenvectors of the spectroscopic matrix **G**, the proposed **B**-matrix formalism is then not optimal. In every case, however, we can easily find a suitable set of nonredundant internal coordinates for MD simulations. In particular, if we use a proper set of **Z**-coordinates, which are linearly independent and orthogonal to each other, the transformations to other (redundant or nonredundant) internals are

not necessary, giving an efficient set of internal coordinates for the proposed **B**-matrix formalism. Even in the case that the bonded part of the potential energy function contains terms expressed in redundant internal coordinates, its Cartesian derivatives are easily computed and substituted into Eq. (82) so that the actual dynamics simulation can be performed in **Z**-coordinates.

Although the spectroscopic **B**-matrix is not well-defined for rigid constraints on internal coordinates [30], it is still a good approximation to the inverse of the **A**-matrix for real macromolecules. Thus, as an effective way of finding an approximate initial equilibrium configuration before any full rigorous MD process, this approach can be used by simply neglecting the constrained coordinates to reduce the operational dimension, as in the **A**-matrix ICMD formalism. This may also be a useful way of finding a folding path from an arbitrary extended conformation of a macromolecule like a protein or high polymer to its stable (native) structure in a solvent.

The proposed **B**-matrix ICMD formalism is under implementation in our laboratory and it will be applied to realistic model systems and compared with other MD simulation methods.

Acknowledgements

We are indebted to Weili Qian for many helpful discussions. This research was supported by NSF grants MCB-9903991 and DMR-9902727. Additional support was provided by the Air Force Research Laboratory/Materials & Manufacturing Directorate and by the Common High Performance Software Support Initiative of the Department of Defense High Performance Computing Program.

Appendix A. Redundancy relations in primitive internals

Most redundancy relations in primitive internals of a molecule can be derived from a basic equation that is related to a local structure of five atoms. This local structure can be best represented by the one from atom 1 to atom 5 in Fig. 1. Using

Eq. (27), from the atomic ordering for this local structure we have

$$\mathbf{e}_{34} = -\cos\theta_{24}\mathbf{e}_{23} + \sin\theta_{24}(\cos\tau_{14}\mathbf{e}_{23} \times \mathbf{u}_{13} - \sin\tau_{14}\mathbf{u}_{13}), \quad (\text{A.1})$$

$$\mathbf{e}_{35} = -\cos\theta_{25}\mathbf{e}_{23} + \sin\theta_{25}(\cos\tau_{15}\mathbf{e}_{23} \times \mathbf{u}_{13} - \sin\tau_{15}\mathbf{u}_{13}). \quad (\text{A.2})$$

Since $\mathbf{u}_{13} \cdot (\mathbf{e}_{23} \times \mathbf{u}_{13}) = 0$, we obtain a relation between the excluded (from \mathbf{Z} -coordinates) bond angle θ_{45} ($\cos\theta_{45} \equiv \mathbf{e}_{34} \cdot \mathbf{e}_{35}$) and \mathbf{Z} -coordinates θ_{24} , θ_{25} , τ_{14} , and τ_{15} [48]:

$$\cos\theta_{45} = \cos\theta_{24}\cos\theta_{25} + \sin\theta_{24}\sin\theta_{25}\cos(\tau_{14} - \tau_{15}). \quad (\text{A.3})$$

When $\tau_{14} - \tau_{15} = \pm\pi$, viz., a planar local structure, θ_{45} is independent of τ_{14} and τ_{15} :

$$\theta_{45} + \theta_{24} + \theta_{25} = 2\pi. \quad (\text{A.4})$$

Redundancy relations for a locally tetrahedral structure can be easily derived by applying Eq. (A.3). As an illustration, we consider the left-end local structure in Fig. 1. Assume that the coordinates of atoms 9, 10, and 11 are defined starting not from atom 7 but from atom 2, viz., the primitive internals θ_{19} , θ_{110} , θ_{111} , τ_{29} , τ_{210} , and τ_{211} belong to the \mathbf{Z} -coordinates, while θ_{910} , θ_{911} , θ_{1011} , τ_{79} , τ_{710} , and τ_{711} do not. The redundancy relations for θ_{910} , θ_{911} , and θ_{1011} in terms of \mathbf{Z} -coordinates are found to be, respectively,

$$\cos\theta_{910} = \cos\theta_{19}\cos\theta_{110} + \sin\theta_{19}\sin\theta_{110}\cos(\tau_{29} - \tau_{210}), \quad (\text{A.5})$$

$$\cos\theta_{911} = \cos\theta_{19}\cos\theta_{111} + \sin\theta_{19}\sin\theta_{111}\cos(\tau_{29} - \tau_{211}), \quad (\text{A.6})$$

$$\cos\theta_{1011} = \cos\theta_{110}\cos\theta_{111} + \sin\theta_{110}\sin\theta_{111}\cos(\tau_{210} - \tau_{211}). \quad (\text{A.7})$$

Note that $\cos\theta_{910}$ also satisfies

$$\cos\theta_{910} = \cos\theta_{19}\cos\theta_{110} + \sin\theta_{19}\sin\theta_{110}\cos(\tau_{79} - \tau_{710}). \quad (\text{A.8})$$

Substitution of Eq. (A.8) into Eq. (A.5) provides another redundancy relation

$$\cos(\tau_{79} - \tau_{710}) = \cos(\tau_{29} - \tau_{210}). \quad (\text{A.9})$$

Similar considerations to $\cos\theta_{810}$ and $\cos\theta_{910}$ lead to, respectively,

$$\cos(\tau_{79} - \tau_{711}) = \cos(\tau_{29} - \tau_{211}), \quad (\text{A.10})$$

$$\cos(\tau_{710} - \tau_{711}) = \cos(\tau_{210} - \tau_{211}). \quad (\text{A.11})$$

Next, we consider the redundancy relations in benzene, which is a basic cyclic structure. Each atom is numbered as in Fig. 2, and the unnecessary bond length and bond angle internal coordinates for the \mathbf{Z} -matrix construction are designated by dashed lines while those of \mathbf{Z} -coordinates are shown by solid lines. Related to the excluded bond vector \mathbf{x}_{112} , thirteen primitive internals excluded from the \mathbf{Z} -matrix construction are listed to be not only θ_{122} , θ_{111} , τ_{91} , τ_{102} , τ_{114} , τ_{121} , and τ_{123} , but also the six coordinates r_{112} , θ_{92} , θ_{113} , τ_{72} , τ_{93} , and τ_{115} coming from the inside hexagonal carbon ring. Ten analytic redundancy relations can be obtained in ways similar to the above:

$$\cos\theta_{122} = \cos\theta_{912}\cos\theta_{92} + \sin\theta_{912}\sin\theta_{92}\cos(\tau_{712} - \tau_{72}), \quad (\text{A.12})$$

$$\cos\theta_{912} = \cos\theta_{92}\cos\theta_{122} + \sin\theta_{92}\sin\theta_{122}\cos(\tau_{91} - \tau_{121}), \quad (\text{A.13})$$

$$\cos\theta_{113} = \cos\theta_{111}\cos\theta_{113} + \sin\theta_{111}\sin\theta_{113}\cos(\tau_{91} - \tau_{93}), \quad (\text{A.14})$$

$$\cos\theta_{111} = \cos\theta_{13}\cos\theta_{113} + \sin\theta_{13}\sin\theta_{113}\cos(\tau_{15} - \tau_{115}), \quad (\text{A.15})$$

$$\cos(\tau_{72} - \tau_{712}) = \cos(\tau_{102} - \tau_{1012}), \quad (\text{A.16})$$

$$\cos(\tau_{72} - \tau_{102}) = \cos(\tau_{712} - \tau_{1012}), \quad (\text{A.17})$$

$$\cos(\tau_{93} - \tau_{91}) = \cos(\tau_{123} - \tau_{121}), \quad (\text{A.18})$$

$$\cos(\tau_{93} - \tau_{123}) = \cos(\tau_{91} - \tau_{121}), \quad (\text{A.19})$$

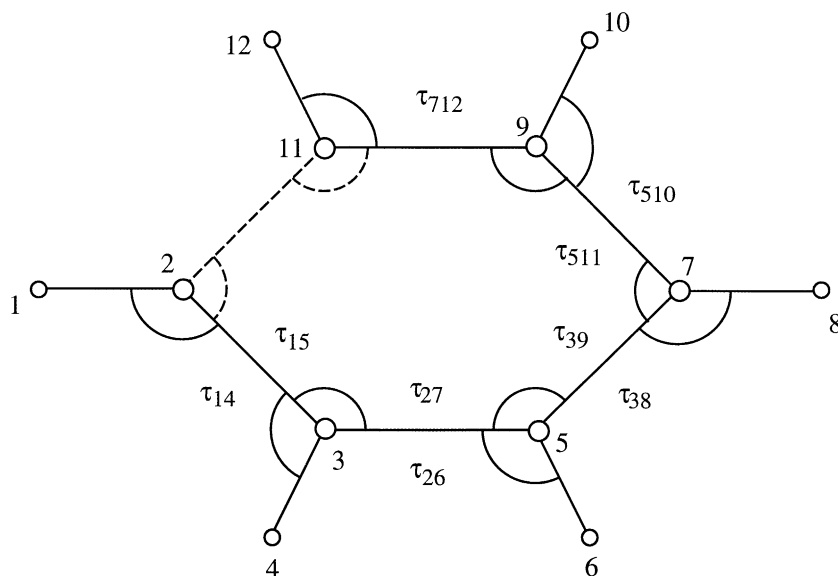


Fig. 2. Schematic drawing of the benzene molecule with atomic numbering consistent with a **Z**-matrix construction.

$$\cos(\tau_{115} - \tau_{114}) = \cos(\tau_{15} - \tau_{14}), \quad (\text{A.20})$$

$$\cos(\tau_{115} - \tau_{15}) = \cos(\tau_{114} - \tau_{14}). \quad (\text{A.21})$$

The remaining three redundancy relations can be obtained from a closure condition of the internal carbon ring:

$$\mathbf{P} \equiv \mathbf{x}_{23} + \mathbf{x}_{35} + \mathbf{x}_{57} + \mathbf{x}_{79} + \mathbf{x}_{911} + \mathbf{x}_{112} = \mathbf{0}. \quad (\text{A.22})$$

For example, redundancy relations belonging to planar symmetry species A_{1g} , B_{2u} , and E_{2g} can be found, respectively, from [36]

$$\mathbf{P} \cdot (\mathbf{x}_{23} + \mathbf{x}_{35} + \mathbf{x}_{57} + \mathbf{x}_{79} + \mathbf{x}_{911} + \mathbf{x}_{112}) = 0, \quad (\text{A.23})$$

$$\mathbf{P} \cdot (\mathbf{x}_{23} - \mathbf{x}_{35} + \mathbf{x}_{57} - \mathbf{x}_{79} + \mathbf{x}_{911} - \mathbf{x}_{112}) = 0, \quad (\text{A.24})$$

$$\mathbf{P} \cdot (\mathbf{x}_{23} - 2\mathbf{x}_{35} + \mathbf{x}_{57} + \mathbf{x}_{79} - 2\mathbf{x}_{911} + \mathbf{x}_{112}) = 0. \quad (\text{A.25})$$

In order to compute all the dot products in Eqs. (A.23)–(A.25), which will provide relations in terms of primitive internals, we need relations similar to

$$\begin{pmatrix} \mathbf{e}_{57} \\ \mathbf{e}_{57} \times \mathbf{u}_{37} \\ -\mathbf{u}_{37} \end{pmatrix}_5 = \mathbf{T}_{35}(\theta_{25}, \tau_{14}) \begin{pmatrix} \mathbf{e}_{35} \\ \mathbf{e}_{35} \times \mathbf{u}_{25} \\ -\mathbf{u}_{25} \end{pmatrix}_3, \quad (\text{A.26})$$

where $\{\mathbf{e}_{35}, \mathbf{e}_{35} \times \mathbf{u}_{25}, -\mathbf{u}_{25}\}$ can be considered as the basis of a local coordinate system at atom 3 and the transformation matrix $\mathbf{T}_{35}(\theta_{25}, \tau_{14})$, which can be obtained from local geometric relations and Eq. (27), is found to be

$$\begin{aligned} \mathbf{T}_{35}(\theta_{25}, \tau_{14}) &= \exp(-i[\pi - \theta_{24}]\mathbf{D}_3) \exp(-i\tau_{14}\mathbf{D}_1) \\ &= \begin{pmatrix} -\cos \theta_{24} & \sin \theta_{24} \cos \tau_{14} & \sin \theta_{24} \sin \tau_{14} \\ -\sin \theta_{24} & -\cos \theta_{24} \cos \tau_{14} & -\cos \theta_{24} \sin \tau_{14} \\ 0 & -\sin \tau_{14} & \cos \tau_{14} \end{pmatrix}. \end{aligned} \quad (\text{A.27})$$

From the ring closure, we should have

$$\mathbf{T}_{35}\mathbf{T}_{57}\mathbf{T}_{79}\mathbf{T}_{911}\mathbf{T}_{112}\mathbf{T}_{23} = \mathbf{1}, \quad (\text{A.28})$$

which contains no bond length dependency. The underlying essence in Eqs. (A.22) and (A.28) can be applied to any molecular ring structure. It should be noted that Eq. (A.28) provides three additional redundancy relations. For simplicity, we can choose

$$(\mathbf{T}_{35}\mathbf{T}_{57}\mathbf{T}_{79}\mathbf{T}_{911}\mathbf{T}_{112}\mathbf{T}_{23})\hat{\mathbf{1}} = \hat{\mathbf{1}}, \quad (\text{A.29})$$

since bringing the vector \mathbf{e}_{35} to the initial state through cyclic symmetry transformations is equivalent to bringing the other two vectors $\mathbf{e}_{35} \times \mathbf{u}_{25}$ and $-\mathbf{u}_{25}$ to the starting position. For the case of the benzene molecule, where six hydrogen atoms are sticking out from the internal carbon ring, the three redundancy relations from Eq. (A.28) are not necessary, since Eqs. (A.12)–(A.21) provide all the requirements.

Appendix B. External coordinates in the center of mass frame

From a molecule's atomic coordinates \mathbf{x}_λ in $\{\hat{\mathbf{1}}, \hat{\mathbf{2}}, \hat{\mathbf{3}}\}$, the center of mass (c.m.) position, \mathbf{c} , is defined by

$$\mathbf{c} \equiv \frac{1}{M} \sum_{\lambda=1}^p m_\lambda \mathbf{x}_\lambda. \quad (\text{B.1})$$

If we define \mathbf{y}_λ as the distance vector from the c.m. to the λ th atom, then the equivalent to Eq. (24) is expressed by

$$\mathbf{x}_\lambda = \mathbf{c} + \mathbf{y}_\lambda \quad (\text{B.2})$$

with $\mathbf{y}_\lambda \equiv \Xi \mathbf{y}_{\lambda m}$, where Ξ represents the relative rotation between the LFF and the c.m. frame (CMF). The definition of Eq. (B.1) in combination with Eq. (B.2) provides

$$\sum_{\lambda=1}^p m_\lambda \mathbf{y}_\lambda = \mathbf{0}. \quad (\text{B.3})$$

If we regard the components of \mathbf{c} as translational parameters, the corresponding **A**- and **B**-matrix elements are found to be

$$\frac{\partial \mathbf{x}_\lambda^k}{\partial c^j} = \delta_j^k, \quad (\text{B.4})$$

$$\frac{\partial^2 \mathbf{x}_\lambda^k}{\partial c^i \partial c^j} = 0 = \frac{\partial^2 \mathbf{x}_\lambda^k}{\partial S^\gamma \partial c^j} = \frac{\partial^2 \mathbf{x}_\lambda^k}{\partial c^j \partial S^\gamma}, \quad (\text{B.5})$$

$$\frac{\partial \mathbf{c}}{\partial \mathbf{x}_v^j} = \frac{m_v}{M} \hat{\mathbf{j}}, \quad (\text{B.6})$$

$$\frac{\partial^2 \mathbf{c}}{\partial \mathbf{x}_\mu^i \partial \mathbf{x}_v^j} = \mathbf{0} \quad (\text{B.7})$$

with S^γ being internal coordinates. Since for rotations at the c.m., \mathbf{c} and the internal coordinates S^γ remain constant, the **A**-matrix elements in $\bar{\theta}$ are found to be

$$\frac{\partial \mathbf{x}_\lambda}{\partial \theta^j} = \hat{\mathbf{j}} \times \mathbf{y}_\lambda, \quad (\text{B.8})$$

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial \theta^i \partial \theta^j} = \hat{\mathbf{j}} \times (\hat{\mathbf{i}} \times \mathbf{y}_\lambda), \quad (\text{B.9})$$

$$\frac{\partial^2 \mathbf{x}_\lambda}{\partial S^\gamma \partial \theta^j} = \hat{\mathbf{j}} \times \frac{\partial \mathbf{x}_\lambda}{\partial S^\gamma} = \frac{\partial^2 \mathbf{x}_\lambda}{\partial \theta^j \partial S^\gamma}. \quad (\text{B.10})$$

It should be noted that, in general for flexible molecules, a slight change in \mathbf{x}_λ or in internal coordinates S^γ will result in changes in the c.m. position, giving

$$\frac{\partial c^j}{\partial S^\gamma} = \sum_{\lambda=1}^p \sum_{k=1}^3 \frac{\partial c^j}{\partial \mathbf{x}_\lambda^k} \frac{\partial \mathbf{x}_\lambda^k}{\partial S^\gamma} \neq 0. \quad (\text{B.11})$$

Thus, Eq. (80) no longer holds. However, if we take the reference frame as the CMF making $\mathbf{c} = \mathbf{0}$, the corresponding **A** and **B** satisfy the required Eqs. (79) and (80) for **B**-matrix ICMD simulations. Since $\partial \mathbf{y}_\lambda^k / \partial \mathbf{x}_v^j = (\delta_\lambda^v - m_v/M) \delta_j^k$ and $\partial \mathbf{x}_v^j / \partial \mathbf{y}_\lambda^k = \delta_k^j$, the desired elements of **B** and **A** for internal coordinates S^γ in CMF are obtained by, respectively,

$$\frac{\partial S^\gamma}{\partial \mathbf{y}_v^j} = \frac{\partial S^\gamma}{\partial \mathbf{x}_v^j}, \quad (\text{B.12})$$

$$\frac{\partial \mathbf{y}_v^j}{\partial S^\gamma} = \frac{\partial \mathbf{x}_v^j}{\partial S^\gamma} - \frac{1}{M} \sum_{\lambda=1}^p m_\lambda \frac{\partial \mathbf{x}_\lambda^j}{\partial S^\gamma}. \quad (\text{B.13})$$

Eq. (B.13) holds also for external coordinates with $\partial x_v^j / \partial S^\gamma$ being given by Eqs. (B.4) and (B.8). The elements of \mathbf{A}_2 in CMF are obtained from derivatives of Eq. (B.13). Thus, the desired elements of \mathbf{B} for external rotations, $\vec{\theta}_{vj} \equiv \partial \vec{\theta} / \partial y_v^j$, can be obtained by solving the relation equivalent to Eq. (96):

$$\begin{aligned} \mathbf{I}_{cm} \vec{\theta}_{vj} &= m_v \frac{\partial y_v^j}{\partial \vec{\theta}} - \sum_{\gamma=1}^f \left(\sum_{\lambda=1}^p m_\lambda \frac{\partial \mathbf{y}_\lambda}{\partial \vec{\theta}} \cdot \frac{\partial \mathbf{y}_\lambda}{\partial S^\gamma} \right) \frac{\partial S^\gamma}{\partial y_v^j} \\ &= m_v \mathbf{y}_v \times \hat{\mathbf{j}} - \sum_{\gamma=1}^f \left(\sum_{\lambda=1}^p m_\lambda \mathbf{y}_\lambda \times \frac{\partial \mathbf{y}_\lambda}{\partial S^\gamma} \right) \frac{\partial S^\gamma}{\partial y_v^j} \end{aligned} \quad (\text{B.14})$$

with \mathbf{I}_{cm}^{jk} , the molecule's inertia tensor w.r.t. its c.m., being given by

$$\begin{aligned} \mathbf{I}_{cm}^{jk} &\equiv \sum_{\lambda=1}^p m_\lambda \{ (\mathbf{y}_\lambda \cdot \mathbf{y}_\lambda) \delta^{jk} - y_\lambda^j y_\lambda^k \} \\ &= \sum_{\lambda=1}^p m_\lambda \frac{\partial y_\lambda^j}{\partial \theta^j} \cdot \frac{\partial y_\lambda^k}{\partial \theta^k}. \end{aligned} \quad (\text{B.15})$$

Note that the quantity in parenthesis on the right-hand side of Eq. (B.14) is nonzero in general.

References

- [1] M.P. Allen, D.J. Tildesley, Computer Simulation of Liquids, Clarendon Press, Oxford, 1987.
- [2] J.A. McCammon, S.C. Harvey, Dynamics of Proteins and Nucleic Acids, Cambridge University Press, Cambridge, 1987.
- [3] J.P. Ryckaert, G. Ciccotti, H.J.C. Berendsen, J. Comput. Phys. 23 (1977) 327.
- [4] H.C. Andersen, J. Comput. Phys. 52 (1983) 24.
- [5] J.P. Ryckaert, J. Comput. Phys. 55 (1985) 549.
- [6] R. Edberg, D.J. Evans, G.P. Morriss, J. Chem. Phys. 84 (1986) 6933.
- [7] D.J. Tobias, C.L. Brooks III, J. Chem. Phys. 89 (1988) 5115.
- [8] E. Barth, K. Kuczera, B. Leimkuhler, R.D. Skeel, J. Comput. Chem. 16 (1995) 1192.
- [9] R. Kutteh, J. Chem. Phys. 111 (1999) 1394.
- [10] W.B. Streett, D.J. Tildesley, G. Saville, Mol. Phys. 35 (1978) 639.
- [11] H. Grubmüller, H. Heller, A. Windemuth, K. Schulten, Mol. Simul. 6 (1991) 121.
- [12] M. Tuckerman, B.J. Berne, G.J. Martyna, J. Chem. Phys. 97 (1992) 1990.
- [13] D.D. Humphreys, R.A. Friesner, B.J. Berne, J. Phys. Chem. 98 (1994) 6885.
- [14] J.J. Biesiadecki, R.D. Skeel, J. Comput. Phys. 109 (1993) 318.
- [15] J.A. Izaguirre, S. Reich, R.D. Skeel, J. Chem. Phys. 110 (1999) 9853.
- [16] C.S. Peskin, T. Schlick, Commun. Pure Appl. Math. 42 (1989) 1001.
- [17] G. Zhang, T. Schlick, J. Chem. Phys. 101 (1994) 4995.
- [18] B. Paizs, G. Fogarasi, P. Pulay, J. Chem. Phys. 109 (1998) 6571.
- [19] J. Baker, D. Kinghorn, P. Pulay, J. Chem. Phys. 110 (1999) 4986.
- [20] W.L. Jorgensen, J. Tirado-Rives, J. Phys. Chem. 100 (1996) 14508.
- [21] N. Gö, H.A. Scheraga, Macromolecules 3 (1970) 178.
- [22] T. Noguti, N. Gö, J. Phys. Soc. Jpn. 52 (1983) 3283.
- [23] A.K. Mazur, R.A. Abagyan, J. Biomol. Struct. Dyn. 6 (1989) 815.
- [24] A.K. Mazur, R.A. Abagyan, J. Biomol. Struct. Dyn. 6 (1989) 833.
- [25] K.D. Gibson, H.A. Scheraga, J. Comput. Chem. 11 (1990) 468.
- [26] A. Jain, N. Vaidehi, G. Rodriguez, J. Comput. Phys. 106 (1993) 258.
- [27] L.M. Rice, A.T. Brünger, Proteins 19 (1994) 277.
- [28] J. Turner, P. Weiner, B. Robson, R. Venugopal, H. Schubele III, R. Singh, J. Comput. Chem. 16 (1995) 1271.
- [29] G.R. Kneller, K. Hinsien, Phys. Rev. E 50 (1994) 1559.
- [30] S. He, H.A. Scheraga, J. Chem. Phys. 108 (1998) 271.
- [31] A.K. Mazur, J. Chem. Phys. 111 (1999) 1407.
- [32] A. Amadei, A.B.M. Linssen, H.J.C. Berendsen, Proteins 17 (1993) 412.
- [33] D.-S. Bae, E.J. Haug, Mech. Struct. Mach. 15 (3) (1987) 359.
- [34] G. Rodriguez, A. Jain, K. Kreutz-Delgado, J. Astronaut. Sci. 40 (1992) 27.
- [35] E.B. Wilson, J.C. Decius, P.C. Cross, Molecular Vibrations, McGraw-Hill, New York, 1955.
- [36] S. Califano, Vibrational States, Wiley, New York, 1976.
- [37] S.-H. Lee, K. Palmo, S. Krimm, J. Comput. Chem. 20 (1999) 1067.
- [38] H. Goldstein, Classical Mechanics, Addison-Wesley, Reading, MA, 1971.
- [39] H.J.C. Berendsen, Science 282 (1998) 642.
- [40] Y. Duan, P.A. Kollman, Science 282 (1998) 740.
- [41] K. Palmo, L.-O. Pietila, S. Krimm, J. Comput. Chem. 12 (1991) 385.
- [42] K. Palmo, L.-O. Pietila, S. Krimm, Comput. Chem. 17 (1993) 67.
- [43] K. Palmo, N.G. Mirkin, S. Krimm, J. Phys. Chem. A 102 (1998) 6448.
- [44] W.D. Allen, A.G. Császár, J. Chem. Phys. 98 (1993) 2983.
- [45] C. Eckart, Phys. Rev. 47 (1935) 552.
- [46] A. Sayvetz, J. Chem. Phys. 7 (1939) 383.
- [47] D.J. Evans, Mol. Phys. 34 (1977) 317.
- [48] T. Schlick, J. Comput. Chem. 9 (1988) 861.