

MOLECULAR DYNAMICS SIMULATION OF RIGID MOLECULES

G. CICCOTTI

Dipartimento di Fisica, Università "La Sapienza", P. le A. Moro, 2 – 00185 Roma, Italy

and

J.P. RYCKAERT

*Pool de Physique, Université Libre de Bruxelles, Campus Plaine, CP 223, Bld du Triomphe,
1050 Bruxelles, Belgium*



1986

NORTH-HOLLAND – Amsterdam

Contents

1. Introduction	348
2. Statistical mechanics of molecular systems in Cartesian coordinates	349
2.1. The mechanical system of interest	349
2.2. Specific constraints	350
2.3. Intramolecular and intermolecular interactions	352
2.4. Generalized coordinates versus atomic Cartesian coordinates	352
2.5. Various ensembles in connection with new MD methods	357
2.6. "Extended system" methods	358
2.7. Stochastic method to simulate a canonical ensemble	365
2.8. Atomic versus molecular observables.	369
3. Dynamics of molecular systems in Cartesian coordinates	370
3.1. Lagrangian equations of motion of the first kind	370
3.2. Dynamical equations for the extended system method.	373
4. Numerical implementation	376
4.1. The evaluation of forces of constraints	377
4.2. The sampling of Cartesian atomic velocities	381
4.3. MD techniques for various ensembles.	383
5. Conclusions	388
Appendix A. Proof of the equivalence between the atomic and molecular expressions for the pressure	388
Appendix B. FORTRAN routine evaluating the constraint force displacements by the iterative technique (4.1.2)	390
References	391

MOLECULAR DYNAMICS SIMULATION OF RIGID MOLECULES

G. CICCOTTI

Dipartimento di Fisica, Università “La Sapienza”, P.le A. Moro, 2 – 00185 Roma, Italy

and

J.P. RYCKAERT

*Pool de Physique, Université Libre de Bruxelles, Campus Plaine, CP 223, Bld du Triomphe,
1050 Bruxelles, Belgium*

Received 6 May 1986

This paper is a review of the method of constraints. The method was devised to carry out Molecular Dynamics simulations of complex molecular systems with some internal degrees of freedom frozen, in terms of atomic Cartesian coordinates. The method has been subsequently generalized to treat all kinds of holonomic constraints and has been adapted to the more recent dynamical simulations in ensembles different from the microcanonical one. We start by deriving the statistical-mechanical formalism for these systems. We then proceed to derive the equations of motion. We conclude with a detailed discussion of the relevant MD algorithms. Some technical details on the FORTRAN code are presented in an appendix.

1. Introduction

In this paper we describe algorithms for use in Molecular Dynamics (MD) calculations of the macroscopic properties of molecular systems composed of fully rigid or partially rigid molecules.

The prediction of the properties of a large ensemble of interacting molecules is the aim of statistical physics. However there is little hope that analytical theories will be successful in treating complex molecular systems in condensed phase subjected to arbitrary interactions. MD simulations can successfully complement analytical theories. By MD one generates a representative statistical sample of the system which can be used to derive its macroscopic properties. The sample is given by the phase space trajectory generated by solving Newton's equations of motion for the N -particle system. Using realistic potentials, MD simulations can be used to study large systems ranging from monoatomic fluids or solids to biological systems such as membranes or proteins. We shall describe methods to solve Newton's equations of motion for molecules treated as rigid bodies and for molecules having internal degrees of freedom as well as internal geometrical constraints.

Following a classical mechanics description, atoms are modeled by point particles interacting according to a prescribed potential energy which is conveniently split into an intermolecular and an intramolecular part. The intermolecular potential is most often expressed as a sum of atom pair (or more generally site-site) interactions between centres of force located at nuclear positions. The intramolecular potential, usually written as a sum of contributions corresponding to the various bonds, bendings, torsional energies, must account for the strong forces that constrain bond lengths and bond angles to a narrow range. In the absence of "soft" internal modes, the molecule can be considered, to a first approximation, as fully rigid. This approximation, reminiscent of the Born–Oppenheimer approach in Quantum Mechanics, is justified when the frequencies of the intramolecular modes are well separated from those of intermolecular modes. Quite generally, however, when this is not the case, there are still some fast modes, such as bond-lengths or bond-angle vibrations, which can be treated as constrained. The molecule will then have internal constraints as well as internal degrees of freedom. The essential motivation to impose constraints rests on the desire to eliminate the fast vibrational modes thus allowing a larger time step to be used in the simulations. Moreover "hard" degrees of freedom are difficult to thermalise. Their freezing therefore reduces considerably the time spent to reach equilibrium.

Applying constraints implies that the atoms move on a hypersurface in phase space. This is not equivalent to the system with "hard" degrees of freedom. In particular the statistical properties of some of the "slow" variables of the system can be different in the two cases. This subtle problem must be tackled case by case because there is no general qualitative and quantitative answer.

A discussion of these matters lies far outside the scope of the present paper. We therefore simply refer the reader to the existing literature [1–3].

Once a rigid or a partially rigid model is adopted for the molecules, there are two different ways to express the equations of motion for the system:

- i) Equations of motion in generalized coordinates involving only non-constrained degrees of freedom. The Lagrange equations of the second kind are derived by the standard procedure from the Lagrangian of the whole system. For rigid bodies this leads to Newton–Euler equations, in principle very simple. In practise numerical difficulties are encountered with

Euler angle variables which either require the introduction of special integration schemes or the introduction of alternate coordinates such as the quaternion representation [4]. For molecules possessing internal degrees of freedom the quaternion equations become rapidly unmanageable, both to derive and to treat, with increasing molecular complexity.

- ii) Equations of motion in the Cartesian coordinates of all atoms, modified so as to satisfy constraints. The Cartesian equations of motion (Lagrange equations of first kind) now contain potential terms plus constraint forces. The forces of constraints depend upon a set of Lagrange multipliers which are evaluated from the constraint relationships by auxiliary calculations. This second method does not have the practical limitations of the quaternion approach, is generally applicable, even to complex macromolecules, and can be implemented in a way computationally effective. Its implementation, the so-called method of constraints, was originally developed for partially rigid molecules [5] and then generalized to other form of constraints [6,7] and to other statistical ensembles [8,9]. In this paper we concentrate entirely on the method of constraints.

Normally, MD is performed at constant volume and constant total energy, yielding a microcanonical ensemble. For various reasons this is not entirely satisfactory and various approaches have been suggested to produce a dynamics in which temperature and pressure are the independent variables [10–12]. The interest in thermostating the system is apparent in non-equilibrium situations (the so-called non-equilibrium molecular dynamics, NEMD). Indeed, in the study of irreversible processes and transport properties, the temperature must be controlled to remove the heat produced by the work done on the system to keep it in a non-equilibrium state. But even in equilibrium the control of temperature and pressure can be very convenient. In this paper we will show how to adapt these new methods to molecular models consisting of partially or totally rigid molecules.

Section 2 provides the formulation in Cartesian coordinates of statistical mechanics for rigid molecular systems. Section 3 derives the corresponding equation of motions while section 4 details the algorithms needed for the numerical implementation. In section 5 we summarize the main results discussed in the paper. We add two appendices concerning i) a useful result not easily available in English literature: the equivalence of atomic and molecular calculations of pressure [13] and ii) a FORTRAN code, for resetting constrained atomic coordinates, of wide applicability.

2. Statistical mechanics of molecular systems in Cartesian coordinates

2.1. The mechanical system of interest

Consider an assembly of N molecules each consisting of n atoms (point particles) with coordinates $\{\mathbf{r}_{i\alpha}\}$ $i = 1, \dots, n$, $\alpha = 1, \dots, N$, and masses m_i . All molecules are taken here identical with mass $M = \sum_i m_i$.

The potential energy is conveniently divided into an intramolecular and an intermolecular part. When the intramolecular potential is a sum of continuous contributions, the molecule is said to be *flexible*. If the interactions between some groups of atoms in the molecule are so stiff as to be frozen by geometrical constraints, the molecule is then *partly rigid*. When all intramolec-

ular interactions are modelled by geometrical constraints, the molecule is *fully rigid*. Partly rigid and fully rigid molecules will be collectively called *rigid molecules* in the following. These molecules are our major concern, since flexible molecules can be treated as a straightforward extension of the atomic case.

For each rigid molecule, we shall consider quite generally that l holonomic constraints

$$\sigma_k(\{\mathbf{r}_{i\alpha}\}) = 0, \quad k = 1, l, \quad (2.1)$$

relate some subsets of atoms leaving $(3n - l)$ degrees of freedom per molecule. For fully rigid molecules, $(3n - l)$ will be 6 or 5 for non-linear or linear systems, respectively so that $l = 3n - 6$ or $l = 3n - 5$ independent constraints must be imposed in the model.

2.2. Specific constraints

The most common forms of constraints are bond constraints [5]

$$\sigma_B = (\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha})^2 - d_{ij}^2 = 0 \quad (2.2)$$

and linear constraints fixing the position of an atom as a function of a set of other atomic coordinates

$$\sigma_L = \mathbf{r}_{i\alpha} - \sum_{j=1}^n C_j \mathbf{r}_{j\alpha} = 0, \quad (2.3)$$

where the constants C_j satisfy the relationship $\sum_j C_j = 1$ to guarantee the translational invariance of eq. (2.3). These last constraints have been introduced more specifically to treat fully rigid molecules where the number of atoms exceeds 2, 3 or 4 for linear, planar and 3-dimensional molecules, respectively [6]. Moreover they are quite useful when a molecule (usually a large one) has fully rigid subunits or carries extra massless centres of force or masses which are not centres of force.

As a simple example, consider the CS₂ trilinear molecule. Taking the sulphur atoms S₁ and S₂ as basic atoms, the coordinate \mathbf{r}_C is related to the other atomic coordinates by the expression

$$\mathbf{r}_C - \frac{1}{2}\mathbf{r}_{S_1} - \frac{1}{2}\mathbf{r}_{S_2} = 0. \quad (2.4)$$

This vectorial constraint, together with a bond constraint between sulphur atoms leave the linear molecule with 5 degrees of freedom as required.

Usually bond and linear kinds of constraints are sufficient for most simple molecules, e.g. fully rigid molecules or “united atoms” models of chain molecules [5]. However, partly rigid molecules represented by a full atomic model, require other forms of constraints. This was observed in the quite complex case of an n -alkane molecule [7] but it can be illustrated here on the more pedagogical example of the CH₂Cl₂ (dichloro-methane) in which all intramolecular vibrations would be frozen by geometrical constraints with the exception of the lowest vibrational mode involving the bending of the Cl–C–Cl angle ($\nu \approx 300 \text{ cm}^{-1}$, while all other

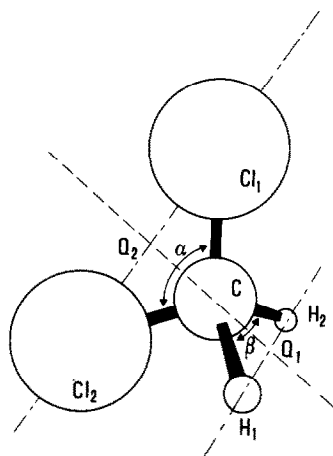


Fig. 1. Schematic representation of the dichloro-methane molecule (see text).

vibrations are above 700 cm^{-1}). If we first look at a simplified model in which the CH_2 unit is treated as a “united atom”, the molecule would be treated as a three-particle system with two rigid bonds between “carbons” and chlorine atoms. The molecule then becomes a partly rigid molecule with 3 translational, 3 rotational and 1 intramolecular degrees of freedom. If, as a refinement, we want to model the hydrogens explicitly as point particles with associated intermolecular centres of forces, we need to introduce at the same time six additional constraints if we do not want to introduce new intramolecular modes. Because the H–Cl relative distances are not conserved when the bending angle α is varying (see fig. 1), such a rigid model cannot be obtained by application of bonds, eq. (2.2) and/or linear constraints, eq. (2.3), only.

A possible scheme is the following: two bond constraints are first applied to the C–H distances d_{CH} . Consider then the midpoint Q_1 between hydrogen atoms H_1 and H_2 and the midpoint Q_2 between chlorine atoms Cl_1 and Cl_2 . We impose then that Q_1 , Q_2 and C are collinear (two constraints) and moreover that Q_1 is at fixed distance $d_{\text{CH}} \cos(\beta/2)$ from the C atom, β being the fixed value for the HCH angle. All these constraints can be written vectorially as

$$\frac{1}{2}(\mathbf{r}_{H_1} + \mathbf{r}_{H_2}) = \mathbf{r}_C - d_{\text{CH}} \cos(\beta/2)\mathbf{u}, \quad (2.4a)$$

where \mathbf{u} is a unit vector pointing along the α angle bisector, i.e.

$$\mathbf{u} = \frac{\frac{1}{2}(\mathbf{r}_{\text{Cl}_1} + \mathbf{r}_{\text{Cl}_2}) - \mathbf{r}_C}{|\frac{1}{2}(\mathbf{r}_{\text{Cl}_1} + \mathbf{r}_{\text{Cl}_2}) - \mathbf{r}_C|}. \quad (2.4b)$$

Finally, we imposed the restriction that the two vectors H_2H_1 and Cl_2Cl_1 are perpendicular by simply requiring, in addition, that

$$(\mathbf{r}_{H_2} - \mathbf{r}_{H_1}) \cdot (\mathbf{r}_{\text{Cl}_2} - \mathbf{r}_{\text{Cl}_1}) = 0. \quad (2.5)$$

In this rigid picture, the H atoms do not introduce extra degrees of freedom but “follow” the dynamics of the flexible triangle Cl_1CCl_2 .

2.3. The intramolecular and intermolecular interactions

Apart from the constraints which are an extreme case of intramolecular interactions, the most common potential, both for inter- and intramolecular interactions, is the atom-atom pair additive form, i.e.

$$U_{\text{inter}}^{\alpha\beta} = \sum_{i=1}^n \sum_{j=1}^n v_{ij}(|\mathbf{r}_{i\alpha} - \mathbf{r}_{j\beta}|), \quad (2.6a)$$

$$U_{\text{intra}}^{\alpha} = \sum'_{\substack{i,j=1 \\ (i < j)}}^n v_{ij}(|\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}|), \quad (2.6b)$$

when the sum Σ' indicates a sum over a subset of atomic pairs. Point charge Coulombic interactions, Lennard-Jones and Buckingham potentials fall into this class. Typical examples are the carbon monoxide model of the Berne and Harp study [14] and the Berendsen–Jörgensen simplified model of water [15] in which point charges are localized at the nuclear sites.

More complicated schemes are required for specific molecules:

- Centre of force may not coincide with point particle’s masses while forces remain pairwise additive. Among many examples, let us mention the nitrogen model of Barojas et al. [16], or water models like the ST2 [17] or MCY [18].
- The internal rotational potential describing the torsional vibrations of molecules such as ethane or butane [19] is usually expressed in terms of the dihedral (torsional) angle.
- Instead of a discrete point charge distribution within a molecule, Coulombic interactions are sometimes incorporated in models by electrical point multipoles associated with the whole molecule (e.g. dipole for CO [14], quadrupole for CO_2 [20] or C_6H_6 [21]) or with subgroups of atoms (e.g. C_6H_6 model of Evans–Watts [22]).

Whatever functional form the inter- (intra-) molecular potential takes, we shall represent it formally in what follows by $U(\{\mathbf{r}\})$ to indicate that ultimately it can always be considered as a function of atomic coordinates.

2.4. Generalized coordinates versus atomic Cartesian coordinates

The traditional description of a rigid molecule of n atoms with l constraints uses $(3n - l)$ generalized coordinates $\{q\}$. However, particularly for molecular models based on atom–atom interactions, the description in terms of atomic coordinates remains relevant in spite of the fact that these variables are no longer independent. The formulation of statistical mechanics for a system of rigid molecules in generalized coordinates is straightforward while within the atomic description, the corresponding formulation is not easily found in the literature. In the following we briefly recall the first formulation and we present its correspondent in Cartesian coordinates.

An assembly of N identical rigid molecules in interaction is mechanically characterized by a Lagrangian

$$L_C(q, \dot{q}) = \frac{1}{2} \sum_{\alpha=1}^N \sum_{\mu, \nu=1}^{3n-l} \dot{q}_{\mu\alpha} A_{\mu\nu}(q_\alpha) \dot{q}_{\nu\alpha} - U(\{q\}) \quad (2.7)$$

to which corresponds the Hamiltonian

$$H_C(q, p) = \frac{1}{2} \sum_{\alpha=1}^N \sum_{\mu, \nu=1}^{3n-l} p_{\mu\alpha} (A^{-1}(q_\alpha))_{\mu\nu} p_{\nu\alpha} + U(\{q\}), \quad (2.8)$$

with

$$p_{\mu\alpha} = \sum_{\nu} A_{\mu\nu} \dot{q}_{\nu\alpha}. \quad (2.9)$$

The various statistical-mechanical ensembles for such system are characterized by a probability density $\rho(q, p)$ defined in phase space volume element

$$dq \, dp = \prod_{\alpha=1}^N \prod_{\nu=1}^{3n-l} dq_{\nu\alpha} \, dp_{\nu\alpha}. \quad (2.10)$$

Given an ensemble, a macroscopic quantity $\langle F \rangle$ is given by

$$\langle F \rangle = \iint dq \, dp \, F(p, q) \rho(q, p), \quad (2.11)$$

where $F(q, p)$ is the associated dynamical quantity. When required, the ensemble average $\langle F \rangle$ will be represented by the more explicit notation $F_{\mathcal{E}}(\mathcal{E})$, where the subscript denotes the nature of the ensemble, while the argument represents the numerical values of the ensemble fixed parameters.

Typical examples are the internal energy E the pressure P or the centre-of-mass density $\langle \hat{\rho} \rangle$ given, respectively, by

$$\langle E \rangle = \iint dq \, dp \, H_C(q, p) \rho(q, p), \quad (2.12)$$

$$P = \iint dq \, dp \, (3V)^{-1} \sum_{\alpha=1}^N \left\{ \frac{\mathbf{P}_\alpha \cdot \mathbf{P}_\alpha}{M} - \mathbf{R}_\alpha \cdot \frac{\partial U}{\partial \mathbf{R}_\alpha} \right\} \rho(q, p), \quad (2.13)$$

$$\langle \hat{\rho}(\mathbf{r}) \rangle = \iint dq \, dp \, \sum_{\alpha=1}^N \delta(\mathbf{R}_\alpha - \mathbf{r}) \rho(q, p), \quad (2.14)$$

where $\{\mathbf{R}_\alpha, \mathbf{P}_\alpha\}$ are the centre of mass coordinates and conjugated momenta, systematically a subset of the generalized variables $\{q, p\}$, while \mathbf{r} is a point in physical space.

When the microscopic variable $F(q, p)$ is a purely configurational property, the integration over momenta can be explicitly performed. Consider the usual canonical ensemble probability density

$$\rho(q, p) = e^{-\beta H_C(p, q)} / Q_{NVT}, \quad (2.15a)$$

where H_C is given by eq. (2.8) and the partition function Q_{NVT} by

$$Q_{NVT} = \iint dq dp e^{-\beta H_C(q, p)}. \quad (2.15b)$$

The resulting reduced configurational probability density turns out to be

$$P(q) = |\det A(q)|^{1/2} \frac{e^{-\beta U(q)}}{Z}, \quad (2.16)$$

with

$$Z = \int dq |\det A(q)|^{1/2} e^{-\beta U(q)}. \quad (2.17)$$

In atomic Cartesian coordinates, the mechanical model introduced in eq. (2.1) is specified by the Lagrangian

$$\mathcal{L}(\mathbf{r}, \dot{\mathbf{r}}) = \frac{1}{2} \sum_{\alpha=1}^N \sum_{i=1}^{3n} m_i \dot{\mathbf{r}}_{i\alpha}^2 - U(\{\mathbf{r}\}) \quad (2.18)$$

and by the set of Nl geometrical constraints

$$\sigma_k^\alpha(\{\mathbf{r}\}) = 0, \quad \alpha = 1, N, \quad k = 1, l. \quad (2.19)$$

The corresponding Hamiltonian is

$$H(\mathbf{r}, \mathbf{p}_r) = \frac{1}{2} \sum_{\alpha=1}^N \sum_{i=1}^{3n} \frac{\mathbf{p}_{r,i\alpha}^2}{m_i} + U(\{\mathbf{r}\}), \quad (2.20)$$

where the conjugate momenta are $\mathbf{p}_{r,i\alpha} = m_i \dot{\mathbf{r}}_{i\alpha}$. As the constraints must be satisfied at all times and in the Hamiltonian description coordinates and momenta are independent variables, we need to add in this last description the requirement that

$$\dot{\sigma}_k^\alpha(\mathbf{r}, \mathbf{p}_r) = 0, \quad \alpha = 1, N, \quad k = 1, l. \quad (2.21)$$

Our aim is to express the statistical mechanics of rigid molecules in the extended phase space $\{\mathbf{r}, \mathbf{p}_r\}$. Appropriate delta functions in the probability density will be introduced to guarantee that mechanical states violating the constraints, eqs. (2.19) or (2.21) are excluded.

In order to make the bridge between the phase space of the atomic description and the one of the generalized coordinates we add to the $\{q\}$, the whole set of Nl functions $\{\sigma_k^\alpha(\{\mathbf{r}\})\}$ as additional variables [23]. The set $\{u\} = \{q, \sigma\}$ is now in a one-to-one correspondence with the atomic coordinates. In terms of these new variables, the Lagrangian, eq. (2.18), takes the form

$$\mathcal{L}(u, \dot{u}) = \frac{1}{2} \sum_{\alpha=1}^N \sum_{i,j=1}^{3n} \dot{u}_i^\alpha M_{ij}(u^\alpha) \dot{u}_j^\alpha - U(\{u\}), \quad (2.22)$$

where \mathbf{M} is a $3n \times 3n$ matrix with elements

$$M_{ij} = \sum_{k=1}^{3n} m_k \frac{\partial \mathbf{r}_{k\alpha}}{\partial u_i^\alpha} \cdot \frac{\partial \mathbf{r}_{k\alpha}}{\partial u_j^\alpha}. \quad (2.23)$$

It is straightforward to observe that imposing $\sigma = \dot{\sigma} = 0$ in eq. (2.22) reduces $\mathcal{L}(u, \dot{u})$ to $L_C(q, \dot{q})$, eq. (2.7).

Defining the conjugate momenta

$$p_{u_i}^\alpha = \sum_{j=1}^{3n} M_{ij} \dot{u}_j^\alpha, \quad (2.24)$$

the Hamiltonian in the extended space becomes

$$H(u, p_u) = \sum_{\alpha=1}^N \sum_{i=1}^{3n} \sum_{j=1}^{3n} \frac{1}{2} p_{u_i}^\alpha (M^{-1}(u^\alpha))_{ij} p_{u_j}^\alpha + U(\{u\}), \quad (2.25)$$

where by simple algebra, it can be verified that the matrix has the explicit form

$$(M^{-1})_{ij} = \sum_{k=1}^{3n} \frac{1}{m_k} \frac{\partial u_i^\alpha}{\partial \mathbf{r}_{k\alpha}} \cdot \frac{\partial u_j^\alpha}{\partial \mathbf{r}_{k\alpha}}. \quad (2.26)$$

The partition function, e.g. in the canonical ensemble, for the extended phase space can now easily be obtained in a few steps. Starting from eqs. (2.15b) and (2.8), we change the integration variables $\{q, p\}$ to $\{q, \dot{q}\}$ by using the linear transformation eq. (2.9). We get

$$Q_{NVT} = \iint d\mathbf{q} \, d\dot{\mathbf{q}} \prod_{\alpha=1}^N |\det \mathbf{A}(q^\alpha)| e^{-\beta(\sum_{\alpha=1}^N (1/2) \dot{\mathbf{q}}^{\alpha T} \mathbf{A} \dot{\mathbf{q}}^\alpha + U(\{q\})}. \quad (2.27)$$

Extending now the space to the set of variables $\{u\}$, we have also

$$Q_{NVT} = \iint du \, d\dot{u} \prod_{\alpha=1}^N \left(|\det \mathbf{A}(q^\alpha)| \prod_{k=1}^l \delta(\sigma_k^\alpha) \delta(\dot{\sigma}_k^\alpha) \right) \\ \times e^{-\beta((1/2) \sum_{\alpha=1}^N \dot{\mathbf{u}}^{\alpha T} \mathbf{M} \dot{\mathbf{u}}^\alpha + U(\{u\})}. \quad (2.28)$$

Applying now a variable change $\{\dot{u}\}$ to $\{p_u\}$, using eq. (2.24), we obtain

$$Q_{NVT} = \iint du \, dp_u \prod_{\alpha=1}^N \left(|\det \mathbf{A}(q^\alpha)| |\det \mathbf{M}(u^\alpha)|^{-1} \prod_{k=1}^l \delta(\sigma_k^\alpha) \delta(\dot{\sigma}_k^\alpha) \right) \times e^{-\beta H(u, p_u)}, \quad (2.29)$$

$$= \iint d\mathbf{r} \, d\mathbf{p}_r \prod_{\alpha=1}^N \left(|\det \mathbf{A}(q^\alpha)| |\det \mathbf{M}(u^\alpha)|^{-1} \prod_{k=1}^l \delta(\sigma_k^\alpha) \delta(\dot{\sigma}_k^\alpha) \right) \times e^{-\beta H(\mathbf{r}, \mathbf{p}_r)}, \quad (2.30)$$

where use was made of the canonical transformation $\{u, p_u\}$ to $\{\mathbf{r}, \mathbf{p}_r\}$. The last expression which is the result we were looking for can further be simplified using a property of matrices \mathbf{A} and \mathbf{M} due to Fixman [24], which states that

$$\det \mathbf{Z} = \det \mathbf{A} (\det \mathbf{M})^{-1}, \quad (2.31)$$

where \mathbf{Z} is the $l \times l$ submatrix of \mathbf{M}^{-1} corresponding to the constraint degrees of freedom, i.e.

$$Z_{ij} = \sum_k \frac{1}{m_k} \frac{\partial \sigma_{ij}}{\partial \mathbf{r}_k} \frac{\partial \sigma_j}{\partial \mathbf{r}_k} \quad i, j = 1, l. \quad (2.32)$$

Eq. (2.31) follows by first writing matrix \mathbf{M} and \mathbf{M}^{-1} in blocks referring to generalized and constraint variables

$$\mathbf{M} = \begin{pmatrix} \mathbf{A} & \mathbf{B} \\ \mathbf{B}^T & \mathbf{I} \end{pmatrix}, \quad \mathbf{M}^{-1} = \begin{pmatrix} \Delta & \mathbf{E} \\ \mathbf{E}^T & \mathbf{Z} \end{pmatrix} \quad (2.33)$$

and then taking the determinant of the identity

$$\begin{pmatrix} \mathbf{A} & \mathbf{0} \\ \mathbf{B}^T & \mathbf{I} \end{pmatrix} = \mathbf{M} \mathbf{M}^{-1} \begin{pmatrix} \mathbf{A} & \mathbf{0} \\ \mathbf{B}^T & \mathbf{I} \end{pmatrix} = \mathbf{M} \begin{pmatrix} \mathbf{I} & \mathbf{E} \\ \mathbf{0} & \mathbf{Z} \end{pmatrix}. \quad (2.34)$$

Finally eq. (2.30) becomes

$$Q_{NVT} = \iint d\mathbf{r} \, d\mathbf{p}_r \prod_{\alpha=1}^N \left(|\det \mathbf{Z}(\mathbf{r}^\alpha)| \prod_{k=1}^l \delta(\sigma_k^\alpha) \delta(\dot{\sigma}_k^\alpha) \right) e^{-\beta H(\mathbf{r}, \mathbf{p}_r)}. \quad (2.35)$$

Similar expressions apply for the probability density of the canonical ensemble

$$\rho_{NVT}^c \, d\mathbf{r} \, d\mathbf{p}_r = Q_{NVT}^{-1} \prod_{\alpha=1}^N \left(|\det \mathbf{Z}(\mathbf{r}^\alpha)| \prod_{k=1}^l \delta(\sigma_k^\alpha) \delta(\dot{\sigma}_k^\alpha) \right) e^{-\beta H(\mathbf{r}, \mathbf{p}_r)} \, d\mathbf{r} \, d\mathbf{p}_r \quad (2.36)$$

and to any statistical average of the microscopic property $F(\mathbf{r}, \mathbf{p}_r)$

$$F_{NVT}(NVT) = Q_{NVT}^{-1} \times \iint d\mathbf{r} d\mathbf{p}_r F(\mathbf{r}, \mathbf{p}_r) e^{-\beta H(\mathbf{r}, \mathbf{p}_r)} \prod_{\alpha=1}^N \left(|\det \mathbf{Z}| \prod_{k=1}^l \delta(\sigma_k^\alpha) \delta(\dot{\sigma}_k^\alpha) \right). \quad (2.37)$$

Moreover the same recipe applied for any other equilibrium ensemble.

2.5. Various ensembles in connection with new MD methods

Molecular Dynamics computer simulations of atomic and molecular systems have typically been performed by integrating Newton's equations of motion for N molecules in a cubic system of fixed volume V with periodic boundary conditions. The resulting phase space trajectory has fixed total energy E and density. The average properties obtained from the trajectory correspond to microcanonical (NVE) ensemble averages through the ergodic hypothesis. Strictly speaking, in the usual simulations the Hamiltonian also conserves linear momentum. Thus the ensemble generated is one in which all states have the same total momentum as well as constant N , V , E . We shall ignore this refinement in the following discussion although it must be kept in mind when modelling very small systems.

Recently, dynamical simulation methods have been introduced whose trajectory averages correspond to averages on other ensembles of statistical thermodynamics. In particular, (NPH), (NPT) and (NVT) ensembles, where H is the enthalpy and P , the external pressure, have been sampled by Molecular Dynamics [10,11]. For systems in the solid state, Parrinello and Rahman [12] generalized Andersen's constant pressure method to allow dynamical changes with time, not simply of the volume but also of the shape of the periodic MD cell. These new methods, originally developed for atomic systems have been subsequently adapted to molecules [8,25–27].

In this section, we discuss in detail the extension of these simulations toward rigid molecular systems. The case of flexible molecules can be easily recovered in our framework or can be obtained in a straightforward way from the atomic case. We describe here these methods from a statistical-mechanical point of view and leave the derivation and the integration of the equations of motion for the next chapter.

The constant pressure dynamical simulation has been obtained by an “extended system” method. Andersen [10] treats the volume of the periodic MD cell as an additional variable whilst Parrinello and Rahman [12] introduce extra-variables representing the components of the three vectors defining the MD periodic cell. It should be noted that the Rahman–Parrinello extension of Andersen's method, while only stable in solid phases, is fundamental to studies of solid–solid phase transitions.

The constant temperature dynamical simulation can also be formulated as an extended system method. This was done recently by Nosé [11] who introduced an additional variable coupled to the particle momenta which acts as a time scaling. Alternatively, the temperature can be controlled by other methods [27]. Generally, most of the methods proposed to thermalise a system leave the inter- and intramolecular interactions to bring about redistribution of the kinetic energy over all modes. As was recently noted in simulations of molecular solids, this

redistribution can be very slow on the timescale of the simulation [34]. We will discuss later a stochastic method due to Andersen [10] that circumvents this problem. The idea is to select at certain times one or more particles at random and to sample their velocities from the kinetic energy distribution at the desired temperature.

2.6. “Extended system” methods

2.6.1.

The easiest way to adapt the extended system method to rigid molecules to obtain an isobaric ensemble is to separate the molecular centre of mass coordinates \mathbf{R}_α , from intramolecular coordinates and then to couple the extra variable, the volume V , only to the centre of mass [8,27].

In the case of the Nosé constant temperature method, it is unclear whether coupling the time scaling parameter s to the centre of mass only is really advantageous. Therefore, the most natural way to adapt the technique to rigid systems is to couple s to all degrees of freedom explicitly [9].

We shall present in the following a unified derivation of the isobaric–isothermal dynamics and obtain the individual cases (isobaric, isoenthalpic or canonical) as particular cases. However for the pure canonical case, our derivation maintains the separation in centre of mass and relative coordinates although without any special reason.

We begin by introducing the centre of mass (com) coordinates

$$\mathbf{R}_\alpha = \sum_{i=1}^n m_i \mathbf{r}_{i\alpha} / \sum_i m_i \quad (2.38)$$

and the set of $3n$ relative coordinates

$$\mathbf{r}'_{i\alpha} = \mathbf{r}_{i\alpha} - \mathbf{R}_\alpha \quad (2.39)$$

so as to separate the translation from the internal motions. However the \mathbf{r}' 's are not independent variables because for each molecule

$$\mathbf{D}_\alpha = \sum_{i=1}^n m_i \mathbf{r}'_{i\alpha} = 0. \quad (2.40)$$

Therefore, when the mechanics or statistical mechanics of our molecular system is described in terms of the variables $\{\mathbf{r}'_{i\alpha}, \mathbf{R}_\alpha\}$, the eqs. (2.40) must be added as extra constraint relations to recover equivalence with the original Cartesian description of section 2.4.

In these new coordinates, the Lagrangian takes the form

$$\mathcal{L}' = \frac{1}{2} \sum_{\alpha=1}^N \left(M \dot{\mathbf{R}}_\alpha^2 + \sum_i m_i \dot{\mathbf{r}}_{i\alpha}'^2 \right) - U(\{\mathbf{r}'_{i\alpha} + \mathbf{R}_\alpha\}) \quad (2.41)$$

and the Hamiltonian

$$H' = \frac{1}{2} \sum_{\alpha=1}^N \left(\frac{\mathbf{P}_\alpha^2}{M} + \sum_i \frac{p_{i\alpha}'^2}{m_i} \right) + U(\{\mathbf{r}'_{i\alpha} + \mathbf{R}_\alpha\}), \quad (2.42)$$

where

$$\mathbf{P}_\alpha = M\dot{\mathbf{R}}_\alpha, \quad \mathbf{p}'_{i\alpha} = m_i\dot{\mathbf{r}}'_{i\alpha} = \mathbf{p}_{i\alpha} - (m_i/M)\mathbf{P}_\alpha. \quad (2.43)$$

To \mathcal{L}' or H' , we have still to add the intramolecular constraints, eqs. (2.19), and the extra-constraints, eq. (2.40), on the relative coordinates $\{\mathbf{r}'\}$. In terms of the new variables $\{\mathbf{R}, \mathbf{r}'\}$ the constraints, eqs. (2.19) and (2.21), keep their functional form as the geometrical constraints are translationally invariant.

The statistical average of any property $F(\mathbf{r}, \mathbf{p}_r)$ in this new description becomes then (e.g. in the canonical ensemble)

$$F_{NVT}(NVT) = Q_{NVT}^{-1}(NVT) \times \int \prod_\alpha d\mathbf{R}_\alpha d\mathbf{P}_\alpha d\mathbf{r}'_{i\alpha} d\mathbf{p}'_{i\alpha} F(\mathbf{R}_\alpha + \mathbf{r}'_{i\alpha}, \mathbf{p}'_{i\alpha} + (m_i/M)\mathbf{P}_\alpha) e^{-\beta H'} \delta_c \delta_{CM}, \quad (2.44)$$

where

$$\delta_c = \prod_{\alpha=1}^N \left(\prod_{k=1}^l \delta(\sigma_k^\alpha(\mathbf{r}')) \delta(\dot{\sigma}_k^\alpha(\mathbf{r}', \mathbf{p}')) |\det \mathbf{Z}(\mathbf{r}')| \right), \quad (2.45)$$

$$\delta_{CM} = \prod_{\alpha=1}^N (\delta(D_\alpha(\mathbf{r}')) \delta(\dot{D}_\alpha(\mathbf{r}', \mathbf{p}')) M^3). \quad (2.46)$$

The unusual separation between centre of mass and relative coordinates presented in this section is simple because it is symmetric in atomic coordinates and leaves invariant the diagonal character of the kinetic energy quadratic form. Moreover, the form of the equations of motion derived from this Lagrangian (see next chapter) conserves the simple Cartesian coordinate form, while the addition of the linear constraints, eq. (2.40), can be easily handled.

2.6.2.

The “extended system” method corresponding to fixed pressure and temperature is now introduced through a new Lagrangian \mathcal{L}_1 which is a function of a set of new variables. This Lagrangian describes an extended mechanical system closely related to the system of interest. We will first introduce this new system and then show how the time average over its dynamics will give fixed pressure-fixed temperature ensemble averages for the real system.

We apply the Andersen space scaling only to the centre of mass and the Nosé time scaling to all velocities, so we obtain the Lagrangian

$$\begin{aligned} \mathcal{L}_1 = & \sum_{\alpha=1}^N \left[\sum_{i=1}^n s^2 \frac{m_i}{2} \dot{\mathbf{r}}_{i\alpha}^2 + \frac{M}{2} s^2 Q^{2/3} \dot{\mathbf{p}}_\alpha^2 \right] \\ & - U(\{\sigma_{i\alpha} + Q^{1/3} \rho_\alpha\}) + \frac{W_Q}{2} \dot{Q}^2 + \frac{W_s}{2} \dot{s}^2 - P_{\text{ext}} Q - (3n - l) N k_B T_{\text{ext}} \ln s, \end{aligned} \quad (2.47)$$

which is a function of the so called “virtual” variables $\{\sigma_{i\alpha}, \rho_\alpha, Q, s\}$ and of their time derivatives with respect to a “virtual” time τ . To \mathcal{L}_1 , we add all constraint relations, eq.’s (2.19) and (2.40) expressed in the “virtual” relative coordinates, i.e.

$$C_k^\alpha(\sigma) = 0 \quad k = 1, l, \quad \alpha = 1, N, \quad (2.48a)$$

$$\sum_{i=1}^n m_i \sigma_{i\alpha} = 0 \quad \alpha = 1, N. \quad (2.48b)$$

The variables σ and ρ correspond to the variables r' and R in the Lagrangian \mathcal{L}' . The additional variables $Q^{1/3}$ and s play the role of dynamical space and time scaling parameters ranging from 0 to ∞ . The range of ρ is now a cube of unit side. W_Q and W_s are inertial factors appearing in the kinetic energy associated with the variables Q and s , respectively. They determine the time scale of fluctuations in Q and s . The last two terms of \mathcal{L}_1 are the potential energy contributions. Their functional form and a proper correspondence between “virtual” and real variables are the two essential ingredients to obtain the correct statistical mechanics ensemble for the *real system*. P_{ext} and T_{ext} are given numbers which play the role of external pressure and temperature, while k_B is the Boltzmann constant.

The Hamiltonian H_1 of this extended system is

$$\begin{aligned} H_1 = & \sum_{\alpha} \left[\sum_i \frac{\pi_{i\alpha}^2}{2m_i s^2} + \frac{\pi_{\alpha}^2}{2Ms^2 Q^{2/3}} \right] + U(\{\sigma_{i\alpha} + Q^{1/3} \rho_{\alpha}\}) \\ & + \frac{\pi_Q^2}{2W_Q} + \frac{\pi_s^2}{2W_s} + P_{\text{ext}} Q + (3n - l) N k_B T_{\text{ext}} \ln s, \end{aligned} \quad (2.49)$$

where

$$\begin{aligned} \pi_{i\alpha} &= m_i s^2 \dot{\sigma}_{i\alpha}, \\ \pi_{\alpha} &= Ms^2 Q^{2/3} \dot{\rho}_{\alpha}, \\ \pi_Q &= W_Q \dot{Q}, \\ \pi_s &= W_s \dot{s}. \end{aligned} \quad (2.50)$$

The Hamiltonian H_1 defines the time evolution for the “extended system”. By defining a correspondence between the variables of this last system and those of the “real system” we implicitly define a time evolution of the “real system”.

The appropriate non-canonical transformation is [8–11]

$$\begin{aligned} r'_{i\alpha} &= \sigma_{i\alpha}, & p'_{i\alpha} &= \pi_{i\alpha}/s, \\ R_{\alpha} &= Q^{1/3} \rho_{\alpha}, & P_{\alpha} &= \pi_{\alpha}/s Q^{1/3}, \\ V &= Q, & P_V &= \pi_Q, \\ S &= s, & P_s &= \pi_s, \\ dt &= d\tau/s. \end{aligned} \quad (2.51)$$

By exploiting the relationship between $\{\mathbf{r}\}$ and $\{\mathbf{r}', \mathbf{R}\}$, eq. (2.39), the previous correspondence implies

$$\begin{aligned} \mathbf{r}_{i\alpha} &= \sigma_{i\alpha} + Q^{1/3} \rho_{\alpha}, \\ \mathbf{p}_{i\alpha} &= \frac{\pi_{i\alpha}}{s} + m_i \frac{\pi_{\alpha}}{MsQ^{1/3}} \end{aligned} \quad (2.52)$$

which relates the “extended system” variables to the usual atomic Cartesian coordinates of the real system.

The basic Andersen–Nosé result states that the real time average of a dynamical observable $F(\mathbf{r}, \mathbf{p}_r, V)$ is equivalent to its equilibrium isobaric–isothermal average at pressure P_{ext} and temperature T_{ext} .

$$F_{NPT}(N, P_{\text{ext}}, T_{\text{ext}}) = \lim_{|t_2 - t_1| \rightarrow \infty} |t_2 - t_1|^{-1} \int_{t_1}^{t_2} F(\mathbf{r}, \mathbf{p}_r, V) dt. \quad (2.53)$$

To obtain this result, one has to apply the ergodic theorem to the “virtual system” and use the correspondence, eq. (2.51), between virtual and real variables. The dynamical variable $F(\mathbf{r}, \mathbf{p}_r, V)$ is related through eq. (2.52) to the function $f(\sigma, \rho, Q, s)$ in the extended system. Therefore, the ergodic theorem states that

$$f_{NVE}(N, 1, E) = \lim_{|\tau_2 - \tau_1| \rightarrow \infty} |\tau_2 - \tau_1|^{-1} \int_{\tau_1}^{\tau_2} f(\sigma, \rho, Q, s) d\tau. \quad (2.54)$$

The arguments in the lhs of eq. (2.54) are, respectively, the actual number of molecules in the system, the unit volume of integration for ρ and, E , the fixed energy corresponding to the conserved quantity H_1 , eq. (2.49). As we are ultimately interested in a “real time” average over a real variable function $F(\mathbf{r}, \mathbf{p}_r, V)$, we now prove the central theorem, eq. (2.53), by first rewriting

$$\begin{aligned} \bar{F} &= \lim_{|t_2 - t_1| \rightarrow \infty} |t_2 - t_1|^{-1} \int_{t_1}^{t_2} F(\mathbf{r}, \mathbf{p}_r, V) dt \\ &= \lim_{|\tau_2 - \tau_1| \rightarrow \infty} \frac{\int_{\tau_1}^{\tau_2} (f/s) d\tau}{\int_{\tau_1}^{\tau_2} (1/s) d\tau}, \end{aligned} \quad (2.55)$$

$$= \frac{\langle f/s \rangle_{NVE}}{\langle 1/s \rangle_{NVE}}, \quad (2.56)$$

using the ergodic theorem, eq. (2.54), in both the numerator and denominator when going from eq. (2.55) to eq. (2.56). In eq. (2.55) the bar in the l.h.s. indicates a real time average. We now show that the expression (2.56) is precisely the required isobaric isothermal average of F . Both the numerator and denominator (case with $f = 1$) can be written explicitly as

$$\langle f/s \rangle_{NVE} \propto \iint dQ d\pi_Q ds d\pi_s d\rho_{\alpha}^N d\pi_{\alpha}^N d\sigma_{i\alpha}^{nN} d\pi_{i\alpha}^{nN} (f/s) \tilde{\delta}_c \tilde{\delta}_{\text{CM}} \delta(H_1 - E),$$

where

$$\begin{aligned}\tilde{\delta}_c &= \prod_{\alpha=1}^N \left\{ \prod_{k=1}^l [\delta(C_k^\alpha(\sigma_{i\alpha})) \delta(\dot{C}_k^\alpha(\sigma_{i\alpha}, \pi_{i\alpha}, s))] |\det \mathbf{Z}^\alpha(\sigma_{i\alpha})| s^{-2l} \right\}, \\ \tilde{\delta}_{\text{CM}} &= \prod_{\alpha=1}^N [\delta(\mathbf{D}^\alpha(\sigma_{i\alpha})) \delta(\dot{\mathbf{D}}^\alpha(\pi_{i\alpha}, s)) s^{-6} M^3].\end{aligned}\quad (2.57)$$

This expression is the microcanonical version of eq. (2.36) for the set of virtual variables. The origin of powers of s^2 in $\tilde{\delta}_c$ and $\tilde{\delta}_{\text{CM}}$ results from the presence of a scaling factor s^2 in the r.h.s. of eqs. (2.9) and (2.24) corresponding to the Lagrangian \mathcal{L}_1 . The double change in variables leading respectively to eqs. (2.27) and (2.29) leave an s^{-2} factor per constraint.

We now go back to real variables by first noting that, using eq. (2.51)

$$\begin{aligned}s^{-2} \delta(\dot{C}_k^\alpha(\sigma_{i\alpha}, \pi_{i\alpha}, s)) &= s^{-1} \delta(\dot{C}_k^\alpha(\mathbf{r}'_{i\alpha}, \mathbf{p}'_{i\alpha})), \quad k = 1, l \\ s^{-6} \delta(\dot{\mathbf{D}}^\alpha(\pi_{i\alpha}, s)) &= s^{-3} \delta(\dot{\mathbf{D}}^\alpha(\mathbf{p}'_{i\alpha})).\end{aligned}\quad (2.58)$$

Eq. (2.57) becomes then

$$\begin{aligned}\langle f/s \rangle_{NVE} &\propto \int \int dV dP_V dS dP_S d\mathbf{R}_\alpha^N d\mathbf{P}_\alpha^N d\mathbf{r}_{i\alpha}^{nN} d\mathbf{p}_{i\alpha}^{nN} \\ &\times S^{(3n-l)N} (F(\mathbf{r}', \mathbf{p}', \mathbf{R}, \mathbf{P}, V)/S) \delta_c \delta_{\text{CM}} \\ &\times \delta \left(H' + P_{\text{ext}} V + (3n-1) N k_B T_{\text{ext}} \ln S + \frac{P_V^2}{2W_Q} + \frac{P_S^2}{2W_S} - E \right),\end{aligned}\quad (2.59)$$

where δ_c and δ_{CM} are given by eqs. (2.45) and (2.46) respectively. Eq. (2.59) can be further expressed in terms of familiar Cartesian coordinates

$$\begin{aligned}\langle f/s \rangle &\propto \int \int dV dP_V dS dP_S d\mathbf{r}_{i\alpha}^{nN} d\mathbf{p}_{i\alpha}^{nN} \times S^{(3n-l)N} (F(\mathbf{r}, \mathbf{p}_r, V)/S) \delta_c \\ &\times \delta \left(H + P_{\text{ext}} V + (3n-l) N k_B T_{\text{ext}} \ln S + \frac{P_V^2}{2W_Q} + \frac{P_S^2}{2W_S} - E \right),\end{aligned}\quad (2.60)$$

where δ_c is now expressed in real variables $\{\mathbf{r}, \mathbf{p}_r\}$, and H is the Hamiltonian, eq. (2.20), of the real system. By solving with respect to S the δ of Dirac containing the Hamiltonian, one finds

$$\begin{aligned}&\delta \left(H + P_{\text{ext}} V + (3n-l) N k_B T_{\text{ext}} \ln S + \frac{P_V^2}{2W_Q} + \frac{P_S^2}{2W_S} - E \right) \\ &= \frac{S}{(3n-l) N k_B T} \delta \left(S - \exp \frac{H + P_{\text{ext}} V + P_V^2/2W_Q + P_S^2/2W_S - E}{(3n-l) N k_B T_{\text{ext}}} \right).\end{aligned}\quad (2.61)$$

Combining eqs. (2.56), (2.60) and (2.61), and performing explicitly the integration on S , P_V and P_S , we obtain finally

$$\begin{aligned}\bar{F} &= \frac{\langle f/s \rangle_{NVE}}{\langle 1/s \rangle_{NVE}} = \\ &= \frac{\int dV \int d\mathbf{r}_{i\alpha}^{nN} d\mathbf{p}_{i\alpha}^{nN} F \exp\{-(H - P_{\text{ext}}V)/k_B T_{\text{ext}}\}}{\int dV \int d\mathbf{r}_{i\alpha}^{nN} d\mathbf{p}_{i\alpha}^{nN} \exp\{-(H + P_{\text{ext}}V)/k_B T_{\text{ext}}\}} \\ &= \langle F \rangle_{NPT}.\end{aligned}\quad (2.62)$$

This last equality proves the identity of the real time average of F with its isothermal–isobaric average. In this dynamics, the conserved quantity is H_1 , eq. (2.49), which in terms of real variables, is

$$H_1 = H(\mathbf{r}, \mathbf{p}_r) + \frac{P_V^2}{2W_Q} + P_{\text{ext}}V + \frac{P_S^2}{2W_S} + (3n - l)Nk_B T_{\text{ext}} \ln S. \quad (2.63)$$

A word of caution is in order. The “Hamiltonian” H_1 , expressed in terms of real variables, is no longer a proper Hamiltonian because these real variables are not canonical variables for this dynamics.

In this section, we have presented the extended method for the case for which both pressure and temperature are fixed parameters. By putting ($S = 1$, $\dot{S} = 0$) or ($Q = V$, $\dot{Q} = 0$) in \mathcal{L}_1 , one recovers respectively the NPH and NVT Lagrangian. The demonstration of the equivalence of these restricted dynamics to their respective ensemble closely follows the NPT one for the NVT case, while it is a bit more tricky for the NPH case. The interested reader will find the derivation in references [8,10].

2.6.3.

The Rahman–Parrinello method is specially suited to study solid phases and structural phase transitions at constant pressure or fixed external stress. The adaptation of this technique to molecular systems closely follows the procedure presented for the Andersen case in section 2.6.2. For this reason, and because the statistical-mechanical ensemble corresponding to this approach is not a familiar one, we will limit ourselves to outline the pragmatic side of this method.

Instead of focusing the attention to the volume of the MD cell, Parrinello–Rahman describe it by a 3×3 matrix \mathbf{H} whose columns are the components of the unit cell vectors \mathbf{a} , \mathbf{b} , \mathbf{c} as in solid state terminology. The MD cell becomes triclinic with associated periodic boundary conditions along the \mathbf{a} , \mathbf{b} , \mathbf{c} directions. The volume V is given by the determinant of \mathbf{H} . As in the previous section, the constant pressure space scaling will be applied only to the centres of mass of the molecules.

Defining reduced com coordinates by

$$\mathbf{R}_\alpha = \mathbf{H}\boldsymbol{\rho}_\alpha, \quad (2.64)$$

we write the Lagrangian \mathcal{L}_2 of the extended system

$$\begin{aligned} \mathcal{L}_2 = \sum_{\alpha} \frac{1}{2} \left[\sum_{i=1}^n m_i s^2 \dot{\sigma}_{i\alpha}^2 + M s^2 \dot{\rho}^T \mathbf{h}^T \mathbf{h} \dot{\rho}_{\alpha} \right] - U(\{\sigma_{i\alpha} + \mathbf{h} \rho_{\alpha}\}) \\ + \frac{W_h}{2} \text{Tr}(\mathbf{h}^T \mathbf{h}) - P_{\text{ext}} \det \mathbf{h} + \frac{W_s}{2} \dot{s}^2 - (3n - l) N k_B T \ln s, \end{aligned} \quad (2.65)$$

where $\{\sigma_{i\alpha}, \rho_{\alpha}, \mathbf{h}, s\}$ and τ are virtual variables, W_h replaces W_Q of the Andersen Lagrangian and the superscript T stands for transpose matrix or vector. To \mathcal{L}_2 , we need to add all constraints, eqs. (2.48).

The Hamiltonian H_2 of this system, expressed in terms of the generalized conjugate momenta

$$\begin{aligned} \pi_{i\alpha} &= m_i s^2 \dot{\sigma}_{i\alpha}, \\ \pi_{\alpha} &= M s^2 \mathbf{h}^T \mathbf{h} \dot{\rho}_{\alpha}, \\ \pi_h &= W_h \dot{\mathbf{h}}, \quad \pi_s = W_s \dot{s}, \end{aligned} \quad (2.66)$$

is given by

$$\begin{aligned} H_2 = \sum_{\alpha=1}^N \frac{1}{2} \left[\sum_{i=1}^N \frac{\pi_{i\alpha}^2}{m_i s^2} + \frac{\pi_{\alpha}^T (\mathbf{h}^T \mathbf{h})^{-1} \pi_{\alpha}}{M s^2} \right] + U(\{\sigma_{i\alpha} + \mathbf{h} \rho_{\alpha}\}) \\ + \sum_{p, q=1}^3 (\pi_h)_{pq}^2 / 2W_h + P_{\text{ext}} \det \mathbf{h} + \frac{\pi_s^2}{2W_s} + (3n - l) N k_B T_{\text{ext}} \ln s. \end{aligned} \quad (2.67)$$

The real system is recovered with the variable change

$$\begin{aligned} r'_{i\alpha} &= \sigma_{i\alpha}, & p'_{i\alpha} &= \pi_{i\alpha}/s, \\ \mathbf{R}_{\alpha} &= \mathbf{h} \rho_{\alpha}, & \mathbf{P}_{\alpha} &= M s \mathbf{h} \dot{\rho}_{\alpha}, \\ \mathbf{H} &= \mathbf{h}, & \mathbf{P}_H &= \pi_h, \\ S &= s, & P_s &= \pi_s, \end{aligned} \quad (2.68)$$

while, for the real time t , $dt = d\tau/s$.

The Hamiltonian H_2 generates a dynamical trajectory of the real system such that a time average corresponds to the unusual ensemble average

$$\langle F \rangle = \int d\mathbf{H} \int d\mathbf{r} d\mathbf{p}_r F(\mathbf{r}, \mathbf{p}) \rho(\mathbf{r}, \mathbf{p}, \mathbf{H}), \quad (2.69)$$

where

$$\rho d\mathbf{H} d\mathbf{r} d\mathbf{p}_r = [N! \tilde{Q}_{NPT}]^{-1} \exp \left\{ - \frac{(H + P_{\text{ext}} V(\mathbf{H}))}{k_B T_{\text{ext}}} \right\} \delta_c d\mathbf{H} d\mathbf{r} d\mathbf{p}_r, \quad (2.70)$$

with

$$\tilde{Q}_{NPT} = (N!)^{-1} \int d\mathbf{H} \int d\mathbf{r} d\mathbf{p}_r \exp \left\{ - \frac{(H + P_{\text{ext}} V(\mathbf{H}))}{k_B T_{\text{ext}}} \right\} \delta_c \quad (2.71)$$

as “isobaric–isothermal” partition function. In terms of the real variables, the constant of motion is

$$H_2 = H(\mathbf{r}, \mathbf{p}_r) + \sum_{p, q=1}^3 \left(\frac{(\mathbf{P}_H)_{pq}^2}{2W_h} \right) + P_{\text{ext}} \det \mathbf{H} \\ + \frac{P_S^2}{2W_s} + (3n - l) N k_B T_{\text{ext}} \ln S. \quad (2.72)$$

It has been pointed out by Nosé and Klein [25] that three of nine variables \mathbf{H} represent the absolute orientation of the MD box with respect to the laboratory frame, so, in general, they are irrelevant. However, for molecular systems, Klein and Nosé showed that the presence of a non-symmetrical stress-tensor leads to an overall rotational motion of the MD box. This rotation is both undesirable and without physical meaning. To overcome such problem, one can either symmetrize the equations of motion for \mathbf{H} [25], or fix the absolute orientation of the box in the reference system [27]. In this last case, one can for example let the \mathbf{a} vector coincide with the x axis and let \mathbf{b} move in the xy plane only so as to be left with 6 variables only to describe the MD cell in such reference system. This corresponds to an upper triangular \mathbf{H} matrix. This modification must be brought in all \mathbf{H} components appearing in H_2 or \mathcal{L}_2 . From now on, we will keep this convention.

2.7. Stochastic method to simulate a canonical ensemble

In his seminal paper on isobaric–isothermal MD simulation, Andersen [10] resorted to the use of stochastic collisions to model the contact with a heat bath. Stochastic collisions are instantaneous events that affect the momentum of one particle at fixed frequency. Therefore this method is intrinsically different from the extended system’s methods of the previous section.

In a first version of this approach, the times at which a particle would suffer a stochastic collision were chosen in accord with a Poisson process and the collisions affecting different particles were uncorrelated. The evolution of the whole system between these collisions is given by the usual Newton’s equations. To perform this simulation, one has to fix two parameters: the temperature T and the mean rate of stochastic collisions per particle, ν . Given an initial state $\{\mathbf{r}_i(0), \mathbf{p}_{ri}(0)\}$ one integrates the equations of motion until the time of the first collision on a particle, say particle i . The value of the momentum of particle i is instantaneously changed by the collision to a new value chosen at random from a Maxwell–Boltzmann distribution at temperature T . All other particles are unaffected by the collision. The system is then evolved until the time of the next collision and the process is repeated.

In a later version of this stochastic method, called by Andersen [26], the method of “massive stochastic collisions”, the momenta of all particles are replaced at the same time with values

chosen at random from the Maxwell-Boltzman distribution. The times of these massive stochastic collisions are equally spaced along the trajectory and one has to fix an optimum value for the collision rate. This method has the advantage that, for the period between collisions, the system evolves according to the usual newtonian mechanics. Therefore one can compute proper time correlation functions.

In both cases, the result of such MD procedure is a trajectory such that time averages are equal to canonical ensemble averages at temperature T . Andersen has suggested that massive stochastic collisions methods, when combined with the extended variable methods for constant T and P , can significantly speed up the equilibration time by damping oscillatory transients [27].

The adaptation of the stochastic collision method to rigid molecules is formally straightforward in generalized coordinates. The conjugate momenta $\{p^q\}$ are sampled from the conditional density of probability $P(p^q|q)$ defined by eqs. (2.15a), (2.16) and (2.8) as

$$P(p^q|q) = \rho(p^q, q)/P(q) = |\det A|^{-1/2} e^{-\beta K_C(p^q, q)}, \quad (2.72)$$

where $K_C(p^q, q)$, the kinetic energy in generalized coordinates is given by

$$K_C(p^q, q) = \frac{1}{2} \sum_{\alpha} \sum_{\mu, \nu=1}^{3n-l} p_{\mu\alpha}^q (A^{-1}(q_{\alpha}))_{\mu\nu} p_{\nu\alpha}^q \quad (2.72a)$$

The form of eq. (2.72) indicates that the generalized momenta distribution is a configuration dependent multidimensional Gaussian distribution. Cartesian velocities follow from the expression

$$v_i = \sum_{\nu=1}^{3n-l} \frac{\partial \mathbf{r}_i}{\partial q_{\nu}} \dot{q}_{\nu} = \sum_{\nu} \sum_{\nu'} \frac{\partial \mathbf{r}_i}{\partial q_{\nu}} (A^{-1})_{\mu\nu'} p_{\nu'}^q. \quad (2.73)$$

This approach is not entirely satisfactory to us as it requires the explicit definition and use of generalized coordinates that we were precisely avoiding by using the method of constraints to describe the dynamics of the system in Cartesian coordinates.

In fact, Cartesian velocities can be obtained directly within a pure Cartesian description by the following two-step procedure:

i) Sample atomic Cartesian momenta $\{p'_i\}_{i=1,n}$ as independent Gaussian variables such that

$$\begin{aligned} \langle p'_{i\alpha} \rangle &= 0, \\ \langle p'^2_{i\alpha} \rangle &= m_i k_B T. \end{aligned} \quad \alpha = x, y, z, \quad (2.74)$$

ii) Subtract from the velocities their components “normal” to the constraint surfaces in the $3n$ Cartesian hyperspace in order to allow the constraints time derivatives to vanish. This is written

$$\mathbf{p}_i = \mathbf{p}'_i - \sum_{k=1}^l \lambda_k \frac{\partial \sigma_k}{\partial \mathbf{r}_i}, \quad i = 1, n, \quad (2.75)$$

where the $\{\lambda_k\}$ parameters are fixed by requiring that

$$\dot{\sigma}_k = \sum_{j=1}^l \frac{1}{m_j} \frac{\partial \sigma_k}{\partial \mathbf{r}_j} \mathbf{p}_j = 0, \quad k = 1, l. \quad (2.76)$$

Combining eqs. (2.75) and (2.76) and solving for the $\{\lambda\}$, one gets

$$\lambda_k = \sum_{k'=1}^l (\mathbf{Z}^{-1})_{kk'} \sum_{i=1}^n \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_i} \frac{\mathbf{p}_i'}{m_i}, \quad (2.77)$$

where \mathbf{Z} has been defined in eq. (2.32). We now prove that the resulting dependent variables $\{\mathbf{p}_i\}$ are sampled correctly, i.e. lead to a thermal bath interaction characteristic of the canonical ensemble of a system with constraints [28].

Combining eqs. (2.75) and (2.77), we get

$$\begin{aligned} \mathbf{p}_i &= \mathbf{p}_i' - \sum_{s=1}^n \left\{ \sum_k \sum_{k'} (\mathbf{Z}^{-1})_{kk'} \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_s} \right\} \mathbf{p}_s' / m_s \\ &= \sum_s \left\{ m_s \delta_{is} \mathbf{I} - \sum_k \sum_{k'} (\mathbf{Z}^{-1})_{kk'} \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_s} \right\} \mathbf{p}_s' / m_s, \end{aligned} \quad (2.78)$$

where \mathbf{I} is the unity matrix for the Cartesian components. The evaluation of the correlation matrix $\langle \mathbf{p}_i \mathbf{p}_j \rangle$ gives

$$\begin{aligned} \langle \mathbf{p}_i \mathbf{p}_j \rangle &= k_B T \sum_s \frac{1}{m_s} \left(m_s \delta_{is} \mathbf{I} - \sum_k \sum_{k'} (\mathbf{Z}^{-1})_{kk'} \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_s} \right) \\ &\quad \times \left(m_s \delta_{js} \mathbf{I} - \sum_{k''} \sum_{k'''} (\mathbf{Z}^{-1})_{k''k'''} \frac{\partial \sigma_{k''}}{\partial \mathbf{r}_j} \frac{\partial \sigma_{k'''}}{\partial \mathbf{r}_s} \right) \\ &= k_B T \left\{ m_i \delta_{ij} \mathbf{I} - 2 \sum_k \sum_{k'} (\mathbf{Z}^{-1})_{kk'} \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_j} \right. \\ &\quad \left. + \sum_k \sum_{k'} \sum_{k''} \sum_{k'''} (\mathbf{Z}^{-1})_{kk'} (\mathbf{Z}^{-1})_{k''k'''} \mathbf{Z}_{k'k'''} \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \frac{\partial \sigma_{k''}}{\partial \mathbf{r}_j} \right\}. \end{aligned}$$

Summing over the last term explicitly on k''' and k'' , one gets

$$\langle \mathbf{p}_i \mathbf{p}_j \rangle = k_B T \left\{ m_i \delta_{ij} \mathbf{I} - \sum_k \sum_{k'} (\mathbf{Z}^{-1})_{kk'} \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_j} \right\}. \quad (2.79)$$

The proof of the validity of the present method (formulas (2.74)–(2.77)) to generate random

Cartesian velocities follows from the fact that the $\{\mathbf{p}_i\}$, which by construction satisfy the constraints $\dot{\sigma}_k = 0$, lead to generalized momenta $\{p_v^q\}_{v=1,3n-l}$ having the correct distribution function, eq. (2.72). Using (2.9), we have

$$p_v^q = \sum_{v''} A_{vv''} \sum_i \frac{\partial q_{v''}}{\partial \mathbf{r}_i} \frac{\mathbf{p}_i}{m_i}, \quad (2.80)$$

so that they are zero average random variables with a correlation matrix given by

$$\langle p_v^q p_{v'}^q \rangle = \sum_{v''} \sum_{v''' } A_{vv''} A_{v'v'''} \sum_i \sum_j \left\langle \frac{\mathbf{p}_i}{m_i} \frac{\mathbf{p}_j}{m_j} \right\rangle \frac{\partial q_{v''}}{\partial \mathbf{r}_i} \frac{\partial q_{v'''}}{\partial \mathbf{r}_j}. \quad (2.81)$$

Substituting eq. (2.79) into eq. (2.81), we get

$$\begin{aligned} \langle p_v^q p_{v'}^q \rangle &= k_B T \left\{ \sum_{v''} \sum_{v'''} A_{vv''} A_{v'v'''} \left[\sum_i \sum_j \frac{\delta_{ij}}{m_j} \frac{\partial q_{v''}}{\partial \mathbf{r}_i} \frac{\partial q_{v'''}}{\partial \mathbf{r}_j} \right. \right. \\ &\quad \left. \left. - \sum_i \sum_j \sum_k \sum_{k'} (\mathbf{Z}^{-1})_{kk'} m_i^{-1} m_j^{-1} \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \frac{\partial q_{v''}}{\partial \mathbf{r}_i} \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_j} \frac{\partial q_{v'''}}{\partial \mathbf{r}_j} \right] \right\} \\ &= k_B T \left\{ \sum_{v''} \sum_{v'''} A_{vv''} A_{v'v'''} \left[\left(\sum_i m_i^{-1} \frac{\partial q_{v''}}{\partial \mathbf{r}_i} \frac{\partial q_{v'''}}{\partial \mathbf{r}_i} \right) \right. \right. \\ &\quad \left. \left. - \sum_k \sum_{k'} (\mathbf{Z}^{-1})_{kk'} \left(\sum_i m_i^{-1} \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \frac{\partial q_{v''}}{\partial \mathbf{r}_i} \right) \left(\sum_j m_j^{-1} \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_j} \frac{\partial q_{v'''}}{\partial \mathbf{r}_j} \right) \right] \right\} \\ &= k_B T \sum_{v''} \sum_{v'''} A_{vv''} A_{v'v'''} \left[\Delta_{v''v'''} - \sum_k \sum_{k'} (\mathbf{Z}^{-1})_{kk'} E_{v''k} E_{v'''k'} \right], \quad (2.82) \end{aligned}$$

where in the last expression, use has been made of the definitions in eq. (2.33). Using eq. (2.33), we have

$$\mathbf{A}\Delta + \mathbf{B}\mathbf{E}^T = \mathbf{I}, \quad (2.83)$$

$$\mathbf{A}\mathbf{E} + \mathbf{B}\mathbf{Z} = 0, \quad (2.84)$$

substituting $\mathbf{B} = -\mathbf{A}\mathbf{E}\mathbf{Z}^{-1}$ in eq. (2.83), we have

$$\mathbf{A}(\Delta - \mathbf{E}\mathbf{Z}^{-1}\mathbf{E}^T) = \mathbf{I}.$$

Inspection of eq. (2.82) shows that $\langle p_v^q p_{v'}^q \rangle$ is given by

$$\langle p_v^q p_{v'}^q \rangle = k_B T \sum_{v''} A_{vv''} \delta_{v'v''} = k_B T A_{vv'}. \quad (2.85)$$

The variables defined in eq. (2.80) are obtained from the $\{p_i'\}$ by a linear transformation. This concludes the proof that they are gaussian variables with the expected averages and correlation matrix.

Details regarding the numerical implementation of this scheme are given in section 4.

2.8. Atomic versus molecular observables

This paper is concerned with polyatomic molecules with internal geometrical constraints in the framework of an atomic Cartesian description. As for flexible molecules, thermodynamical properties can be equivalently related to “atomic” or “molecular” observables.

The temperature, for example, can be evaluated from the translational kinetic energy of the molecules or from the total kinetic energy of the atoms of the whole system, i.e.

$$T^{\text{mol}} = \left(\frac{3Nk_B}{2} \right)^{-1} \sum_{\alpha=1}^N K_T^{\alpha} = \left(\frac{3Nk_B}{2} \right)^{-1} \sum_{\alpha=1}^N \frac{\mathbf{P}_{\alpha}^2}{2M}, \quad (2.86)$$

$$T^{\text{atom}} = \left(\frac{N(3n-l)k_B}{2} \right)^{-1} \sum_{\alpha=1}^N K_{\text{tot}}^{\alpha} = \left(\frac{N(3n-l)k_B}{2} \right)^{-1} \sum_{\alpha=1}^N \sum_{i=1}^n \frac{\mathbf{p}_{i\alpha}^2}{2m_i}, \quad (2.87)$$

where the superscript “mol” or “atom” indicates that the property refers to an atomic or to a molecular description, respectively. K_{tot}^{α} and K_T^{α} are respectively, the total and the translational kinetic energies of molecule α . In eqs. (2.86) and (2.87) we neglected again the correction implied by momentum conservation. If linear momentum is conserved, $3N$ must be changed to $3N - 3$ in these equations.

The pressure also, can be expressed within the two different viewpoints

$$P^{\text{mol}} = \left\langle V^{-1} \left\{ \frac{2}{3} \sum_{\alpha} K_T^{\alpha} + \frac{1}{3} \sum_{\alpha} \mathbf{R}_{\alpha} \cdot \mathbf{F}_{\alpha} \right\} \right\rangle, \quad (2.88)$$

$$P^{\text{atom}} = \left\langle V^{-1} \left\{ \frac{2}{3} \sum_{\alpha} K_{\text{tot}}^{\alpha} + \frac{1}{3} \sum_{\alpha} \sum_i \mathbf{r}_{i\alpha} \cdot \mathbf{F}_{i\alpha} \right\} \right\rangle. \quad (2.89)$$

In expression (2.88), the entities are molecules located at \mathbf{R}_{α} , their centre of mass position, and subject to a total force \mathbf{F}_{α} (of intermolecular origin) whilst in eq. (2.89), the molecular system is now viewed as a “mixture” of atomic entites to which the classical formula applies. That the two expressions are equivalent has been demonstrated by Berendsen [13], see appendix A. The second expression is general whilst the first requires a real molecular concept in the sense that intramolecular forces must be sufficiently strong to prevent the decomposition of the molecules in subunits!

The adaptation of these concepts to rigid molecules does not present any special difficulty. Constraint forces must be considered as usual intramolecular forces whenever an observable contains such intramolecular contributions.

The same argument applies verbatim to the microscopic definition of local densities appearing in the generalized hydrodynamics of polyatomic systems [29]. The individual atomic contributions to the usual mass, energy or linear momentum densities can be localized either at the

atomic sites $\mathbf{r}_{i\alpha}$ or at the molecular centre of mass \mathbf{R}_α . Accordingly the local densities of any atomic property $\mu_{i\alpha}$ can be written as

$$O_\mu^{\text{atom}}(\mathbf{r}, t) = \left\langle \sum_\alpha \sum_i \mu_{i\alpha} \delta(\mathbf{r}_{i\alpha}(t) - \mathbf{r}) \right\rangle, \quad (2.90)$$

$$O_\mu^{\text{mol}}(\mathbf{r}, t) = \left\langle \sum_\alpha \sum_i \mu_{i\alpha} \delta(\mathbf{R}_\alpha(t) - \mathbf{r}) \right\rangle. \quad (2.91)$$

Marechal and Ryckaert [30] showed that both definitions lead effectively to the same transport coefficients while the current-current time correlation functions are different.

3. Dynamics of molecular systems in cartesian coordinates

3.1. Lagrangian equations of motion of the first kind

3.1.1.

For a system of N rigid molecules described by the Lagrangian (2.8) and by the l holonomic constraints (2.1) per molecule, the dynamics can be obtained from the Lagrangian equations of motion of first kind [23]

$$\frac{d}{dt} \frac{\partial \mathcal{L}}{\partial \dot{\mathbf{r}}_{i\alpha}} - \frac{\partial \mathcal{L}}{\partial \mathbf{r}_{i\alpha}} = \mathbf{G}_{i\alpha}, \quad i = 1, n, \quad \alpha = 1, N, \quad (3.1)$$

where $\mathbf{G}_{i\alpha}$, the constraint force on atom (i, α) due to all constraints involving it, is given by

$$\mathbf{G}_{i\alpha} = - \sum_{k=1}^l \lambda_k^{(\alpha)} \nabla_{i\alpha} \sigma_k^{(\alpha)}, \quad (3.1a)$$

and $\lambda_k^{(\alpha)}$ is the Lagrangian multiplier associated with the constraint $\sigma_k^{(\alpha)}$. The $3nN$ equations (3.1), supplemented with definitions (3.1a), and the Nl relations (2.19) together constitute $(3n+l)N$ equations for the $(3n+l)N$ unknowns $\{\mathbf{r}_{i\alpha}(t), \lambda_k^{(\alpha)}(t)\}$. If an initial configuration consistent with all constraints is specified, the trajectory of the system is uniquely determined.

In order to compute the trajectory starting from an initial condition at time $t = t_0$, one should know at this time the set $\lambda_k^{(\alpha)}(t_0)$ and, possibly, its time derivatives. This is easily done by exploiting the information contained in eqs. (2.19). As these equations hold at all times, their time derivatives of any order must vanish. By successive inversions of the equations obtained by putting to zero the time derivatives of the constraints, one obtains the λ 's at t_0 and their derivatives. In particular, to obtain the $\lambda_k^{(\alpha)}(t_0)$ one has to solve for each molecule the system of linear equations given by the second time derivatives of the constraints

$$\begin{aligned} \left(\frac{d^2 \sigma_k^{(\alpha)}}{dt^2} \right)_{t=t_0} &= \sum_{k'=1}^l \lambda_{k'}^{(\alpha)} \left(- \sum_{i=1}^n \frac{1}{m_i} \nabla_{i\alpha} \sigma_{k'}^{(\alpha)} \cdot \nabla_{i\alpha} \sigma_k^{(\alpha)} \right)_{t=t_0} \\ &+ \left(\sum_{i=1}^n \frac{1}{m_i} \mathbf{F}_{i\alpha} \cdot \nabla_{i\alpha} \sigma_k^{(\alpha)} + \sum_{i,j=1}^n (\dot{\mathbf{r}}_{i\alpha} \cdot \nabla_{i\alpha})(\dot{\mathbf{r}}_{j\alpha} \cdot \nabla_{j\alpha}) \sigma_k^{(\alpha)} \right)_{t=t_0} = 0. \end{aligned} \quad (3.2)$$

In this way eqs. (3.1) are reduced to ordinary second-order differential equations which could be integrated numerically.

The difficulty is now that at successive times the constraints will be fulfilled only to the order of the chosen algorithm. Moreover, the discrepancy grows in time much more quickly than linearly. This problem can be solved without introducing any additional error in the computation of the trajectory [5]. The method will be discussed in section 4.1.

3.1.2.

In the particular case of constraints linear in the atomic coordinates eq. (2.3), the equations of motion of the system can be further simplified [6]. The dynamics of the (possible) rigid subunits of the whole molecule can be reduced to the motion of “basic” subsets of atoms: two for linear units, three for planar and four for tridimensional ones.

To achieve this result, let us divide the n atoms composing a molecule into i) n_b primary particles, the basic ones, linked by l_b constraints of general type (usually bonds constraints) and ii) $n_s = n - n_b$ secondary particles linked to the basic structure only by $l_s = 3n_s$ constraints

$$\sigma_p(\{\mathbf{R}_i\}) = 0, \quad p = 1, l_b, \quad (3.3a)$$

$$\tau_\alpha = \sum_{i=1}^{n_b} C_{\alpha i} \mathbf{R}_i - \mathbf{r}_\alpha = 0, \quad \alpha = 1, n_s, \quad (3.3b)$$

$$\sum_{i=1}^{n_b} C_{\alpha i} = 1, \quad (3.3c)$$

where $\mathbf{R}_i(\mathbf{r}_\alpha)$ denotes the coordinates of the i th (α th) particle of the basic (secondary) structure, while to avoid confusion, primary and secondary particles are labelled by latin and greek indices respectively. Note that in this section α, β, \dots are no longer used to label molecules. Starting from eq. (3.3) the molecular index is kept implicit to simplify the notation. The set $\{C_{\alpha i}\}$ is defined by the geometry of the rigid subunits of the molecule and can be obtained giving the positions of the n atoms in any reference frame. For each secondary particle, eqs (3.3b, c) give a non-singular system of linear equations in $C_{\alpha i}$. The equations of motion for each particle are now given by

$$M_i \ddot{\mathbf{R}}_i = \mathbf{F}_i + \mathbf{G}_i = \mathbf{F}_i - \sum_{p=1}^{l_b} \lambda_p \nabla_i \sigma_p - \sum_{\beta=1}^{n_s} \nabla_i (\mu_\beta \cdot \tau_\beta), \quad i = 1, n_b, \quad (3.4a)$$

$$m_\alpha \ddot{\mathbf{r}}_\alpha = \mathbf{f}_\alpha + \mathbf{g}_\alpha = \mathbf{f}_\alpha - \sum_{\beta=1}^{n_s} \nabla_\alpha (\mu_\beta \cdot \tau_\beta), \quad \alpha = 1, n_s, \quad (3.4b)$$

where $\mathbf{F}_i(\mathbf{f}_\alpha)$ is the force on particle $i(\alpha)$ resulting from the total potential while $\mathbf{G}_i(\mathbf{g}_\alpha)$ is the total constraint force on the particle. $\lambda_p(\mu_\alpha)$ are the Lagrange multipliers associated to the constraints $\sigma_p(\tau_\alpha)$.

Eqs (3.4b) do not need to be integrated explicitly since the constraint relations, eq. (3.3b), give the $\{\mathbf{r}_\alpha(t)\}$ once the evolution of $\{\mathbf{R}_i(t)\}$ is known. This dynamics can be obtained solving $\{\mu_\alpha\}$

in terms of the atomic forces F_i , f_α and the remaining Lagrangian parameters $\{\lambda_p\}$. In terms of theoretical mechanics this corresponds to transferring the atomic forces on secondary particles to the basic ones by equivalence operations.

Eqs. (3.4) are then rewritten more explicitly as

$$M_i \ddot{\mathbf{R}}_i = \mathbf{F}_i - \sum_p \lambda_p \nabla_i \sigma_p - \sum_\beta C_{\beta i} \boldsymbol{\mu}_\beta, \quad (3.5a)$$

$$m_\alpha \ddot{\mathbf{r}}_\alpha = \mathbf{f}_\alpha + \boldsymbol{\mu}_\alpha. \quad (3.5b)$$

Consider now the equations coming from the second time derivative of the linear constraints, eq. (3.3b)

$$\ddot{\mathbf{r}}_\alpha = \sum_i C_{\alpha i} \ddot{\mathbf{R}}_i - \ddot{\mathbf{r}}_\alpha = 0. \quad (3.6)$$

Substituting eqs (3.5a-b) in eq. (3.6), one gets

$$\sum_\beta A_{\alpha\beta} \boldsymbol{\mu}_\beta = \mathbf{T}_\alpha - \sum_p \lambda_p \mathbf{B}_\alpha^p, \quad (3.7)$$

where

$$A_{\alpha\beta} = \frac{\delta_{\alpha\beta}}{m} + \sum_i \frac{C_{\alpha i} C_{\beta i}}{M_i},$$

$$\mathbf{T}_\alpha = \sum_i \frac{C_{\alpha i} \mathbf{F}_i}{M_i} - \mathbf{f}_\alpha / m_\alpha,$$

$$\mathbf{B}_\alpha^p = \sum_i \frac{C_{\alpha i}}{M_i} \nabla_i \sigma_p.$$

Solving for $\boldsymbol{\mu}_\alpha$, by inverting the time independent matrix $A_{\alpha\beta}$, and substituting the solution in eq. (3.5a) we obtain, after some algebra

$$M_i \ddot{\mathbf{R}}_i = \mathcal{J}_i - \sum_p \lambda_p \Delta_{i,p}, \quad (3.8)$$

where

$$\mathcal{J}_i = \mathbf{F}_i - \sum_{\alpha, \beta} C_{\alpha i} (A^{-1})_{\alpha\beta} \mathbf{T}_\beta \quad (3.9)$$

and

$$\Delta_{i,p} = \nabla_i \sigma_p - \sum_j \sum_{\alpha, \beta} C_{\alpha i} (A^{-1})_{\alpha\beta} \frac{C_{\beta j}}{M_j} \nabla_j \sigma_p. \quad (3.10)$$

Eqs. (3.8) are the closed set of equations of motion for the basic particles, while the constraints relations, eq. (3.3b), give the time evolution of all secondary particles. It is transparent from eq. (3.8) that the equations of motion of the basic particles have the same structure of the usual equations for a system with constraints after a proper redefinition of the force arising from the potential and of the constraint forces, eqs. (3.9), (3.10).

3.1.3.

The simplification achieved by going from eqs. (3.4) to eqs. (3.8) can be particularly useful when the molecular model is no longer built up of point masses coincident in space with the centres of force. There are then i) point masses which are not centres of forces and ii) massless points which are centres of forces. Consider first i). These particles play just an inertial role in the molecular motion, therefore it can be convenient to take them as secondary particles transferring their effect on the basic ones. ii) These points can be taken as secondary particles for which their zero mass implies that the equations of motion are

$$0 = m_\alpha \ddot{\mathbf{r}}_\alpha = \mathbf{f}_\alpha + \boldsymbol{\mu}_\alpha. \quad (3.11)$$

Inserting $\boldsymbol{\mu}_\alpha = -\mathbf{f}_\alpha$ in eq. (3.5a) one simply gets rid of these extra degrees of freedom. Note that, in this special case, the force transferred on particle \mathbf{R}_i is simply $C_{\alpha i} \mathbf{f}_\alpha$.

The same approach can be applied whenever a vector constraint $\boldsymbol{\tau}_\alpha$ is linear in \mathbf{r}_α but no longer in \mathbf{R}_i :

$$\boldsymbol{\tau}_\alpha = \boldsymbol{\varphi}(\mathbf{R}_i) - \mathbf{r}_\alpha = 0. \quad (3.12)$$

The transfer is still possible but now the force transferred on particle \mathbf{R}_i is $-\nabla_i(\boldsymbol{\varphi}(\mathbf{R}_i)) \cdot \mathbf{f}_\alpha$. This observation can be useful when an extra centre of force lies outside of the space engendered by the basic subunits [6].

3.2. Dynamical equations of motion for the extended system method

As we have seen in section 2, the starting point to introduce a dynamical simulation of both isobaric and isothermal ensembles is an “extended” mechanical system defined by its Lagrangian function.

The constant pressure method introduces isotropic (Andersen [10]) or anisotropic (Parrinello–Rahman [12]) scaling of both positions and velocities while a scaling in time affecting only velocities is required by Nosé’s procedure for constant temperature [11].

In this section, we derive the equations of motion in real variables corresponding to the isotropic and anisotropic version of the isobaric–isothermal ensemble for systems with constraints [8,9]. The special case in which one scales only space or time can be easily recovered from the combined version.

3.2.1. The isotropic case

For the extended system defined by the Lagrangian \mathcal{L}_1 in eq. (2.47), the equations of motion

expressed with respect to “virtual” time τ are

$$m_i s^2 \ddot{\sigma}_{i\alpha} = \mathbf{F}_{i\alpha} + \mathbf{G}_{i\alpha} - m_i \mu_\alpha - 2m_i \dot{s} s \dot{\sigma}_{i\alpha}, \quad (3.13a)$$

$$M s^2 \ddot{\rho}_\alpha = Q^{-1/3} \mathbf{F}_\alpha - 2M(\dot{s} s + s^2 \dot{Q}(3Q)^{-1}) \dot{\rho}_\alpha, \quad (3.13b)$$

$$W_Q \ddot{Q} = \left(\sum_{\alpha=1}^N M s^2 Q^{2/3} \dot{\rho}_\alpha^2 + Q^{1/3} \mathbf{F}_\alpha \cdot \rho_\alpha \right) (3Q)^{-1} - P_{\text{ext}}, \quad (3.13c)$$

$$W_s \ddot{s} = \sum_{\alpha=1}^N \left[\left(\sum_{i=1}^n m_i s \dot{\sigma}_{i\alpha}^2 \right) + M Q^{2/3} s \dot{\rho}_\alpha^2 \right] - (3n - l) N k_B T_{\text{ext}} s^{-1}, \quad (3.13d)$$

where the notations are those of section 2.6.2. $\mathbf{F}_{i\alpha}$ (\mathbf{F}_α) is the total force on atom $i\alpha$ (molecule α) deriving from the potential U . $\mathbf{G}_{i\alpha} = -\sum_k \lambda_k^{(\alpha)} \nabla_{\sigma_{i\alpha}} \sigma_k^{(\alpha)}$ is the constraint force acting on atom i of molecule α due to all constraints, eq. (2.48a), implying this particle. $\lambda_i^{(\alpha)}$ and μ_α are, as usual, the Lagrange multipliers associated to the constraints in eqs. (2.48a) and (2.48b), respectively. Substituting eqs. (3.13a) in the time second derivative of eq. (2.48b), one gets immediately rid of this parameter since $\mu_\alpha = \mathbf{F}_\alpha / M$.

These dynamical equations can now be expressed in terms of real coordinates and with respect to real time. Using eqs. (2.52) and (2.53) and remembering that $d/d\tau = (dt/d\tau)d/dt$, one finds, after some algebra,

$$m_i \ddot{\mathbf{r}}_{i\alpha} = \mathbf{F}_{i\alpha} + \mathbf{G}_{i\alpha} - \dot{S} S^{-1} \mathbf{p}_{i\alpha} + m_i \left(\ddot{V} - \frac{2}{3} \dot{V}^2 V^{-1} \right) \mathbf{R}_\alpha (3V)^{-1}, \quad (3.14a)$$

$$W_Q \ddot{V} = W_Q \dot{S} S^{-1} \dot{V} + S^2 \left\{ \sum_{\alpha=1}^N \left(\mathbf{P}_\alpha^2 / M + \mathbf{F}_\alpha \cdot \mathbf{R}_\alpha \right) (3V)^{-1} - P_{\text{ext}} \right\}, \quad (3.14b)$$

$$W_s \ddot{S} = W_s \dot{S}^2 S^{-1} + S \sum_{\alpha=1}^N \sum_{i=1}^n \mathbf{p}_{i\alpha}^2 / m_i - (3n - l) N k_B T_{\text{ext}}, \quad (3.14c)$$

where, to simplify the expressions, we have used the variables \mathbf{R}_α , \mathbf{P}_α and $\mathbf{p}_{i\alpha}$. They are simply known functions of the atomic coordinates and their time derivatives. \mathbf{R}_α is defined by eq. (2.38), while \mathbf{P}_α and $\mathbf{p}_{i\alpha}$, defined in eqs. (2.51) and (2.52), respectively, turn out to be, when expressed in terms of real time derivatives and real coordinates

$$\begin{aligned} \mathbf{P}_\alpha &= M(\dot{\mathbf{R}}_\alpha - \mathbf{R}_\alpha \dot{V} / 3V), \\ \mathbf{p}_{i\alpha} &= m_i(\dot{\mathbf{r}}_{i\alpha} - \mathbf{R}_\alpha \dot{V} / 3V). \end{aligned} \quad (3.15)$$

They represent the conjugate momenta of \mathcal{L}_1 expressed in “real” variables and in “real” time. It is apparent from eqs. (3.14) that the usual force term $\mathbf{F} + \mathbf{G}$, is the same whatever ensemble is considered. The coupling with an heat bath and/or an external pressure manifests itself through the presence of extra terms in the r.h.s. of the equations of motion. Moreover, it can be easily verified that these extra terms do not contribute to the constraint forces. In particular, the

simplification developed in section 3.1.2 for linear constraints is still applicable and one can reduce the motion of the whole set of atoms to a restricted set of basic atoms. The extra terms due to the external coupling which are present in the equations of motions of the basic atoms remain unchanged after that transformation. Eqs. (3.14) describe the dynamics of an extended system whose restriction to real space variables $\{\mathbf{r}_{i\alpha}, \mathbf{p}_{i\alpha}\}$ samples an isothermal–isobaric ensemble. The dynamics corresponding to the canonical or isoenthalpic–isobaric ensembles can be deduced from eqs. (3.14) by putting $s = \text{constant} = 1$ or $Q = \text{constant} = V$, respectively, in the Lagrangian \mathcal{L}_1 , eq. (2.47). The resulting equations of motion resemble closely the NPT ones, eqs. (3.14). Only one relevant auxiliary variable, eq. (3.14b) or (3.14c) has to be considered. Then, the transformation $s = 1$ or $Q = V$ in the remaining equations furnishes the final result.

3.2.2. The anisotropic case

As has been said in section 2.6.3, the Parrinello–Rahman method is based on an anisotropic scaling of the space coordinates which can be described by a matrix \mathbf{H} . For reasons already discussed, see section 2.6.3, this matrix will be taken upper triangular. The equations of motion for this new extended system are derived, in virtual variables, from the Lagrangian \mathcal{L}_2 in eq. (2.65), taking account again of the molecular constraints, eqs. (2.48). The same manipulations we described in section 3.2.1, performed on the new Lagrangian, give for the equations of motion in terms of “real” variables and “real” time

$$m_i \ddot{\mathbf{r}}_{i\alpha} = \mathbf{F}_{i\alpha} + \mathbf{G}_{i\alpha} - \dot{S} S^{-1} \mathbf{p}_{i\alpha} + \ddot{\mathbf{H}} \mathbf{H}^{-1} \mathbf{R}_\alpha + [\dot{\mathbf{H}} \mathbf{H}^{-1} - (\dot{\mathbf{H}} \mathbf{H}^{-1})^T] \mathbf{P}_\alpha, \quad (3.16a)$$

$$W_h \ddot{\mathbf{H}} = W_h \dot{S} S^{-1} \dot{\mathbf{H}} - S^2 \det(\mathbf{H}) P_{\text{ext}} (\mathbf{H}^{-1})^T + S^2 \mathbf{H}^{-1} \left\{ \sum_{\alpha=1}^N \left[\frac{1}{M} \mathbf{P}_\alpha \mathbf{P}_\alpha + \mathbf{R}_\alpha \mathbf{F}_\alpha \right] \right\}, \quad (3.16b)$$

$$W_s \ddot{S} = W_s \dot{S}^2 S^{-1} + S \left[\sum_{\alpha=1}^N \sum_{i=1}^n \frac{1}{m_i} \mathbf{p}_{i\alpha}^2 - (3n - l) N k_B T_{\text{ext}} \right], \quad (3.16c)$$

where, in eq. (3.16b), only the upper triangular elements of matrix \mathbf{H} must be considered and, as before, \mathbf{R}_α , \mathbf{P}_α and $\mathbf{p}_{i\alpha}$ are abbreviated symbols for their definitions in terms of atomic velocities and positions. \mathbf{R}_α is the centre of mass coordinate, eq. (2.38), while \mathbf{P}_α and $\mathbf{p}_{i\alpha}$ are given by

$$\begin{aligned} \mathbf{P}_\alpha &= M (\dot{\mathbf{R}}_\alpha - \dot{\mathbf{H}} \mathbf{H}^{-1} \mathbf{R}_\alpha), \\ \mathbf{p}_{i\alpha} &= m_i (\dot{\mathbf{r}}_{i\alpha} - \dot{\mathbf{H}} \mathbf{H}^{-1} \mathbf{R}_\alpha), \end{aligned} \quad (3.17)$$

and represent the conjugate momenta of \mathcal{L}_2 expressed in “real” variables and “real” time.

Eqs. (3.16) have the same general behaviour described in the previous section. However, extra care is needed when applying periodic boundary conditions to find the minimum image interaction pair [9]. To recover the usual procedure, the cutoff of the potential energy must be less than half the minimum distance L_{min} , between opposite faces of the MD box.

4. Numerical implementation

This section is devoted to the technical aspects of the simulation by MD of a set of rigid molecules (fully rigid or partially rigid), when the dynamics is expressed in terms of the Cartesian coordinates of the constituting atoms. The relevant equations of motion were derived in the previous section. For the traditional MD simulation at fixed number of molecules, volume, and total energy, these equations are Newton's equations of motion in which the total force is the sum of the forces deriving from the potential energy and the forces of constraint. When other ensembles at fixed pressure and/or temperature are sampled by the extended variable MD technique, the accelerations contain additional coupling terms describing the fixed external pressure or heat bath influences on the system of interest.

Let us mention immediately that the numerical integration of all these equations will be performed using the Verlet algorithm or one of its close variants. This algorithm owes its popularity to its simplicity and to its stability. It predicts the value of a variable x at a later time using the propagation

$$x(t+h) = -x(t-h) + 2x(t) + h^2\ddot{x}(t) + \mathcal{O}(h^4), \quad (4.1)$$

where t is the running time and h the time step.

Velocities at times t are only computed after completion of the step in eq. (4.1) using

$$\dot{x}(t) = \frac{x(t+h) - x(t-h)}{2h} + \mathcal{O}(h^2). \quad (4.2)$$

A limitation of this algorithm is that one sometimes does not have the two successive configurations required to describe the mechanical state of the system. This is true, for example, at the beginning where it is far more simple to fix positions and velocities of the atoms. Also, to adjust the temperature of the system, it is necessary, during the "equilibration part" of the MD run to modify the atomic velocities either by a uniform scaling or by stochastic methods. In all these cases where one needs to (re)start with explicit velocities, we have used the simple truncated Taylor expansion scheme,

$$x(t+h) = x(t) + h\dot{x}(t) + (h^2/2)\ddot{x}(t) + \mathcal{O}(h^3). \quad (4.3)$$

Such a simple algorithm does not introduce major errors as it is only used to get two successive configurations of the system in order to restart the former algorithm, eq. (4.1).

When \ddot{x} is velocity dependent, the Verlet algorithm is no longer applicable as such [31]. This is the case for the extended variable systems when the MD simulation is performed at fixed pressure and/or fixed temperature (see section 3.2). One then needs to predict the velocity at time t say, then apply the sequence of eqs. (4.1) and (4.2) with iterations. The scheme adapted to this case uses the prediction

$$\dot{x}(t) = (3x(t) - 4x(t-h) + x(t-2h))/2h + \mathcal{O}(h^2) \quad (4.4a)$$

or

$$\dot{x}(t) = x(t-h) + h\ddot{x}(t-h) + \mathcal{O}(h^2). \quad (4.4b)$$

Eq. (4.4a) is generally used except when at the previous time (here $t - h$) the integration scheme was restarted with eq. (4.3) in which case eq. (4.4b) is used.

The presence of geometrical constraints in the molecules requires specific techniques which will be presented here prior to a more systematic and detailed discussion of the numerical integration algorithms.

4.1. The evaluation of the forces of constraint

In a previous section, 3.1, it has been shown that the force of constraint $\mathbf{G}_{i\alpha}$ acting on atom (i, α) pertaining to a molecule with l constraints, has the general form

$$\mathbf{G}_{i\alpha} = - \sum_{k=1}^l \lambda_k^{(\alpha)} \left(\frac{\partial \sigma_k^{(\alpha)}}{\partial \mathbf{r}_{i\alpha}} \right), \quad (4.5)$$

where the Lagrange multiplier $\lambda_k^{(\alpha)}$ is a function of the coordinates and velocities of the atoms of that molecule, see eq. (3.2). The explicit expression for $\lambda_k^{(\alpha)}$ is obtained by requiring that, for all k , $\ddot{\sigma}_k^{(\alpha)}$ vanishes at all times. Therefore, if we start from an initial configuration in which $\{\sigma_k^{(\alpha)} = 0\}$ and $\{\dot{\sigma}_k^{(\alpha)} = 0\}$, the constraints themselves should be satisfied at all later times. This is true for the exact solution but it is only approximate when a numerical integration algorithm is used to propagate the dynamics. If it is clear that $\sigma_k^{(\alpha)}$ must be conserved within the error of the integration algorithm, the practice has shown [5] that $\sigma_k^{(\alpha)}$ tends to drift systematically away from its original value at a rate depending on the time step.

This numerical problem was overcome by the following procedure. The set of Lagrange multipliers $\{\lambda_k^{(\alpha)}(t)\}$ is no longer evaluated by solving eq. (3.2), but instead they are considered as free parameters $\{\gamma_k^{(\alpha)}\}$. They are fixed a posteriori by requiring that the atomic coordinates at the next time step (at time $t + h$), as propagated by the adopted integration algorithm, depending parametrically on $\{\gamma_k^{(\alpha)}\}$, do satisfy the constraints exactly.

This procedure was originally devised with the Verlet algorithm, eq. (4.1), to integrate the equations of motion of rigid molecules according to the traditional *NVE* Molecular Dynamics. We will now detail this method as it is the most transparent to illustrate the explicit evaluation of constraint forces. It is also the most extensively used so far. Note however that schemes based on other algorithm have been proposed [32,33].

4.1.1. The matrix method

– *Example 1.* Let us first illustrate this method on the simple case of the heteronuclear rigid diatomic. The constraint is

$$\mathbf{r}_{12}^2 - d^2 = 0, \quad (4.6)$$

where we have written for compactness $\mathbf{r}_{12} = \mathbf{r}_1 - \mathbf{r}_2$, so d is the fixed internuclear distance. The constraint forces are, eq. (4.5)

$$\mathbf{G}_1 = -\mathbf{G}_2 = -2\lambda \mathbf{r}_{12}. \quad (4.7)$$

The Verlet algorithm for both atoms, in the usual *NVE* Molecular Dynamics is, eq. (4.1)

$$\begin{aligned} \mathbf{r}_1(t+h) &= \mathbf{r}'_1(t+h) - 2(\lambda/m_1)\mathbf{r}_{12}(t), \\ \mathbf{r}_2(t+h) &= \mathbf{r}'_2(t+h) + 2(\lambda/m_2)\mathbf{r}_{12}(t), \end{aligned} \quad (4.8)$$

where

$$\mathbf{r}'_i(t+h) = -\mathbf{r}_i(t-h) + 2\mathbf{r}_i(t) + (h^2/m_i)\mathbf{F}_i(t) \quad (4.9)$$

are the predicted positions at time $t+h$ according to all forces in the system except the constraint one.

Combining eqs. (4.6) and (4.8) in which we have substituted formally λ_k by parameter γ_k and writing $\mathbf{r}'_{12} = \mathbf{r}'_1 - \mathbf{r}'_2$, we get a quadratic equation in γ_k giving

$$\gamma_k h^2 = \frac{-(\mathbf{r}_{12} \cdot \mathbf{r}'_{12}) + \sqrt{(\mathbf{r}_{12} \cdot \mathbf{r}'_{12})^2 - d^2(d^2 - \mathbf{r}_{12}^2)}}{2\mu^{-1}d^2}, \quad (4.10)$$

where $\mu = (m_1^{-1} + m_2^{-1})^{-1}$ is the reduced mass of the diatomic molecule. Note that the above solution, among the two possible, is the physical one such that the r.h.s. goes to zero when $\mathbf{r}'_{12} \rightarrow \mathbf{r}_{12}$, i.e. when $h \rightarrow 0$. Substitution of eq. (4.10) in eq. (4.8) gives the final positions at time $t+h$.

This procedure does not require the knowledge of $\dot{\mathbf{r}}_i(t)$, the velocities at time t , to compute γ_k , the (approximate) value of $\lambda_k(t)$. These velocities can be evaluated using eq. (4.2), as usual in the Verlet scheme.

When a molecule contains a set of l arbitrary constraints $\{\sigma_k = 0\}_{k=1,l}$, the procedure is generalized in a straightforward way. For any atom i , eq. (4.8) becomes

$$\mathbf{r}_i(t+h) = \mathbf{r}'_i(t+h) - \frac{h^2}{m_i} \sum_{k=1}^l \gamma_k \left(\frac{\partial \sigma_k}{\partial \mathbf{r}_i} \right)_{\{\mathbf{r}_i(t)\}}, \quad (4.11)$$

where \mathbf{r}'_i keeps its original definition, eq. (4.9). Substituting eq. (4.11) in the constraints leads to a set of l equations in γ_k that we will write

$$\sigma_k(\{\mathbf{r}_i(t+h)\}_{i=1,n}) = T_k(\{\gamma_{k'}\}_{k'=1,l}) = 0. \quad (4.12)$$

$\{T_k = 0\}_{k=1,l}$ is a set of algebraic equations of order greater than unity except in the case of linear constraints. Neglecting this last case in which the resolution of eq. (4.12) can be simplified (see eq. (3.8)) the evaluation of the $\{\gamma_{k'}\}$ requires an iterative method in general.

A direct application of the Newton–Raphston iterative method is possible. Writing collectively as B_k all terms of order 2 or higher in $h^2\gamma$ in T_k , we rewrite eq. (4.12) as

$$T_k = \sigma'_k + \sum_{k'=1}^l A_{kk'} h^2 \gamma_{k'} + B_k(h^2\gamma) = 0, \quad (4.13)$$

where

$$A_{kk'} = h^{-2} \left(\frac{\partial T_k}{\partial \gamma_{k'}} \right)_{\gamma=0} = \sum_{i=1}^n m_i^{-1} \left(\frac{\partial \sigma_k}{\partial \mathbf{r}_i} \right)_{\mathbf{r}'(t+h)} \cdot \left(\frac{\partial \sigma_{k'}}{\partial \mathbf{r}_i} \right)_{\mathbf{r}(t)}, \quad (4.13a)$$

where σ'_k is a short symbol for $\sigma_k(\{\mathbf{r}'(t+h)\})$ and the subscripts $\gamma=0$, $\mathbf{r}'(t+h)$ and $\mathbf{r}(t)$ mean that the partial derivatives are computed at the indicated values. Rewriting finally eq. (4.13) in a form directly suitable for the iterative procedure, the n th approximation of γ , $\gamma^{(n)}$ is evaluated as

$$h^2 \gamma_k^{(n)} = - \sum_{k=1}^l (A^{-1})_{k'k} \{ \sigma'_k + B_k(h^2 \gamma^{(n-1)}) \}. \quad (4.14)$$

This procedure, starting with $h^2 \gamma_k^{(0)} = 0$ converges rapidly [5]. Note that, in practice, the computer time for the iterative part is negligible in comparison with inversion of matrix **A**.

– *Example 2.* As an illustration, consider a flexible trimer with three equivalent beads of mass $m_i = m$ ($i = 1, 3$) connected by two rigid bonds of equal length d . The constraints are written

$$\begin{aligned} \sigma_1 &= \mathbf{r}_{12}^2 - d^2 = 0, \\ \sigma_2 &= \mathbf{r}_{23}^2 - d^2 = 0. \end{aligned} \quad (4.15)$$

After deriving the equations of motion for all beads, the algorithm (eq. (4.11)) becomes in this specific case

$$\begin{aligned} \mathbf{r}_1(t+h) &= \mathbf{r}'_1(t+h) - 2 \frac{h^2}{m} \gamma_1 \mathbf{r}_{12}, \\ \mathbf{r}_2(t+h) &= \mathbf{r}'_2(t+h) + 2 \frac{h^2}{m} (\gamma_1 \mathbf{r}_{12} - \gamma_2 \mathbf{r}_{23}), \\ \mathbf{r}_3(t+h) &= \mathbf{r}'_3(t+h) + 2 \frac{h^2}{m} \gamma_2 \mathbf{r}_{23}. \end{aligned} \quad (4.16)$$

Substituting eq. (4.16) in eq. (4.15), eq. (4.13) is obtained, with

$$\mathbf{A} = \begin{pmatrix} -\frac{8}{m} \mathbf{r}'_{12} \cdot \mathbf{r}_{12} & \frac{4}{m} \mathbf{r}'_{12} \cdot \mathbf{r}_{23} \\ \frac{4}{m} \mathbf{r}'_{23} \cdot \mathbf{r}_{12} & -\frac{8}{m} \mathbf{r}'_{23} \cdot \mathbf{r}_{23} \end{pmatrix}, \quad (4.17a)$$

$$\mathbf{B} = \begin{pmatrix} \left(\frac{4h^2}{m} \gamma_1 \mathbf{r}_{12} - 2 \frac{h^2}{m} \gamma_2 \mathbf{r}_{23} \right)^2 \\ \left(2 \frac{h^2}{m} \gamma_1 \mathbf{r}_{12} - 4 \frac{h^2}{m} \gamma_2 \mathbf{r}_{23} \right)^2 \end{pmatrix}. \quad (4.17b)$$

Such a method works well but requires a matrix inversion for each molecule at each time step. Therefore, it is efficient only as long as the number of constraints, which correspond to the size of matrix \mathbf{A} , remains relatively small ($l < 30$ or 40). When l gets larger, as in chain molecules [34] or in proteins [32], the computing time of the constraint forces would quickly be greater than the time required to evaluate the usual forces in a MD experiment. Moreover, the elements of \mathbf{A} and \mathbf{B} become tedious to evaluate explicitly for such large molecules. Note that while \mathbf{A}^{-1} must be evaluated once per molecule and per time step, \mathbf{B} is evaluated again at each iteration.

4.1.2. The iterative method on individual constraints

A different route to solve eq. (4.12) is based on an iterative process where each loop treats all constraints individually in succession. This method originally called SHAKE, has been devised for molecules with bond constraints only [5]. However, it can be generalized to arbitrary constraints [7] and we present here this last version.

Let us focus on a given constraint k (out of the l ones) at the \mathcal{N} th iterative loop and let $\{\mathbf{r}_j^{\text{OLD}}\}$ be the subset of the n_k atomic positions involved in the specific constraint σ_k at the given stage of the iterative process. The effect of the corresponding constraint forces on these atoms is written (cf. eq. (4.11))

$$\mathbf{r}_j^{\text{NEW}} = \mathbf{r}_j^{\text{OLD}} - h^2 \frac{\gamma_k^{(\mathcal{N})}}{m_j} \frac{\partial \sigma_k}{\partial \mathbf{r}_j}, \quad j = 1, n_k. \quad (4.18)$$

The single parameter $\gamma_k^{(\mathcal{N})}$ is now evaluated as the first order solution of the scalar equation $\sigma_k(\{\mathbf{r}_j^{\text{NEW}}\}) = 0$. This is obtained by expanding this last equation in powers of $\gamma_k^{(\mathcal{N})}$ and neglecting all terms of order larger than unity. So we get

$$\gamma_k^{(\mathcal{N})} = h^{-2} \sigma_k(\{\mathbf{r}_j^{\text{OLD}}\}) / \sum_{j=1}^{n_k} m_j^{-1} \left(\frac{\partial \sigma_k}{\partial \mathbf{r}_j} \right)_{\mathbf{r}^{\text{OLD}}} \cdot \left(\frac{\partial \sigma_k}{\partial \mathbf{r}_j} \right)_{\mathbf{r}(t)}, \quad (4.19)$$

where the sum in the denominator runs over the n_k atoms involved by σ_k . If the iterative procedure is started with the “unconstrained” positions $\mathbf{r}_i'(t+h)$, eq. (4.9), the coordinates after completion of steps eqs. (4.18) and (4.19) for the σ_k constraint at the \mathcal{N} th loop can be written

$$\mathbf{r}_i^{\text{NEW}} = \mathbf{r}_i'(t+h) - \frac{h^2}{m_i} \sum_{k'=1}^l \beta_{k'}^{k,\mathcal{N}} \left(\frac{\partial \sigma_{k'}}{\partial \mathbf{r}_i} \right)_{\mathbf{r}(t)}, \quad (4.20)$$

where

$$\begin{aligned} \beta_{k'}^{k,\mathcal{N}} &= \sum_{\mathcal{N}'=1}^{\mathcal{N}} \gamma_{k'}^{(\mathcal{N}')} , \quad k' \leq k, \\ \beta_{k'}^{k,\mathcal{N}} &= \sum_{\mathcal{N}'=1}^{\mathcal{N}-1} \gamma_{k'}^{(\mathcal{N}')} , \quad k' > k. \end{aligned} \quad (4.21)$$

The convergence of the iterative process is controlled by $X^{\mathcal{N}}$, the maximum deviation of $\sigma_k(\{\mathbf{r}_j^{\text{OLD}}\})$ from 0 for all constraints $k = 1, l$, within the \mathcal{N} th cycle. When $X^{\mathcal{N}}$ becomes smaller than some tolerance value at cycle M say, the final positions

$$\mathbf{r}_i^{\text{NEW}} = \mathbf{r}'_i(t+h) - \frac{h^2}{m_i} \sum_{k=1}^l \beta_k'^M \left(\frac{\partial \sigma_k}{\partial \mathbf{r}_i} \right)_{\mathbf{r}(t)} \quad (4.22)$$

are accepted as the new configuration, $\{\mathbf{r}_i(t+h)\}$. The choice of $\mathbf{r}'_i(t+h)$ to start the iterative procedure should guarantee that the numerical process converges to the physical solution among the different solutions of the set of non-linear algebraic eqs. (4.12).

All programming work rests on the two formulae (4.18) and (4.19). Considering all constraints in succession in a cyclic way, $\gamma_k^{(\mathcal{N})}$ is evaluated at the \mathcal{N} th iterative loop for constraint k and then incorporated in eq. (4.18) to produce a set of refined coordinates at the next time step. A few tens of loops are usually sufficient to reach a relative accuracy of 10^{-6} – 10^{-7} on the Cartesian coordinates solution of eq. (4.12) [5,7].

The two different routes to compute constraint forces presented in this section can equivalently be adapted to different numerical integration algorithms [32,33]. In the simple Taylor algorithm, mentioned at the beginning of chapter 4, eq. (4.3), eqs. (4.9) and (4.11), take the form, for atom i

$$\begin{aligned} \mathbf{r}'_i(t+h) &= \mathbf{r}_i(t) + h\dot{\mathbf{r}}_i(t) + (h^2/2m_i)\mathbf{F}_i, \\ \mathbf{r}_i(t+h) &= \mathbf{r}'_i(t+h) - \frac{h^2}{2m_i} \sum_{k=1}^l \gamma_k' \left(\frac{\partial \sigma_k}{\partial \mathbf{r}_i} \right)_{\mathbf{r}(t)}. \end{aligned} \quad (4.23)$$

As usual, the $\{\gamma_k'\}$ parameters are obtained by substituting (4.23) into the constraint relations and solving for the unknowns. Given the analogy of eqs. (4.11) and (4.23), the same routine can be used in both cases to evaluate the Lagrange parameters provided that γ_k is identified with $\gamma_k/2$.

4.2. The sampling of Cartesian atomic velocities

Sampling velocities in the equilibrium distribution function may be performed for two purposes. In section 2.6.4. we mentioned that it was possible to simulate a canonical ensemble by MD if, at certain times, velocities were instantaneously modified to new suitably sampled values. On another hand, in order to start a new MD experiment, random velocities are often given to all individual atoms (molecules), usually located on a regular lattice (crystal structure). In this way, for a solid simulation, all modes are activated whilst, for a liquid simulation, this initial thermal motion helps in melting the initial structure. For highly anharmonic solids or liquids, such velocity randomisation should be repeated a few times in order to bring the system to a well defined equilibrium state.

The sampling of atomic velocities appears to be a useful method, quite generally, to sample the phase space of a given system in a more efficient way. Our own experience on simulation by MD of crystals of partly rigid molecules with intramolecular potentials has shown that this sampling

is the only practical way to achieve a reasonable equipartition of kinetic energy among all modes [34].

In section 2.7, we already outlined the method to generate random cartesian velocities for a set of atoms connected by geometrical constraints. As we now illustrate, its application to specific cases resembles the computation of the Lagrange multipliers in the constraint forces evaluation see section 4.1.

For a system with l constraints, the relevant Lagrange parameters, eq. (2.77), are now the solution of a set of l linear equations. In practice, this requires the evaluation of the elements of the $l \times l$ matrix \mathbf{Z} eq. (2.32) and its inversion.

However, these velocities may alternatively be obtained via a method which, though indirect, is much more simple to implement in an existing MD program. This method, borrowed from an idea used in a somewhat different context [35], consists in performing a virtual time step of all atoms implied by stochastic collisions.

If $\{\mathbf{v}'_i\}$ is the set of unconstrained velocities sampled from a Gaussian distribution of zero mean and standard deviation $(kT/m_i)^{1/2}$, one evaluates

$$\mathbf{r}'_i(t + h^*) = \mathbf{r}_i(t) + h^* \mathbf{v}'_i, \quad i = 1, n, \quad (4.24)$$

where $\{\mathbf{r}_i(t)\}$ are the atomic coordinates at the time of “collisions” and h^* is a virtual time step. Its order of magnitude is defined below. The resulting positions are then “readjusted” by applying the constraint routine used in an ordinary MD step. The final positions $\mathbf{r}^*_i(t + h^*)$ and the initial positions $\mathbf{r}_i(t)$ give the required velocities by numerical differentiation, i.e.

$$\mathbf{v}_i(t) = (\mathbf{r}^*_i(t + h^*) - \mathbf{r}_i(t))/h^*. \quad (4.25)$$

The normal MD integration can then be restarted for these atoms with the Taylor scheme, eq. (4.3), using the velocities in eqs. (4.25).

The justification of the “corrected” velocity sampling is quite straightforward. The constraint scheme on the $\{\mathbf{r}'_i(t + h^*)\}$ positions implies that the final positions $\{\mathbf{r}^*_i(t + h)\}$ have been obtained as

$$\mathbf{r}^*_i(t + h^*) = \mathbf{r}'_i(t + h^*) - \frac{h^*}{m_i} \sum_{k=1}^l \gamma_k^* \frac{\partial \sigma_k}{\partial \mathbf{r}_i}. \quad (4.26)$$

In eq. (4.26), the $\{\gamma_k^*\}_{k=1,l}$ parameters are fixed as usual by requiring that all constraints $\{\sigma_k = 0\}_{k=1,l}$ are satisfied by the new virtual positions $\{\mathbf{r}^*_i(t + h^*)\}$. Note that the constraint term is here of order h^* as the correction has the order of the velocities.

Assuming h^* sufficiently small, $\sigma_k(\mathbf{r}^*_i)$ can be expanded in series around $\{\mathbf{r}_i(t)\}$, so that

$$\begin{aligned} 0 &= \sigma_{k'}(\{\mathbf{r}^*_i(t + h^*)\}) = \sigma_{k'}(\{\mathbf{r}_i(t)\}) + \sum_{i=1}^n \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_i} \cdot (\mathbf{r}^*_i(t + h^*) - \mathbf{r}_i(t)) + \dots \\ &= h^* \sum_{i=1}^n \frac{\partial \sigma_{k'}}{\partial \mathbf{r}_i} \cdot \left(\mathbf{v}'_i - \frac{1}{m_i} \sum_{k=1}^l \gamma_k^* \frac{\partial \sigma_k}{\partial \mathbf{r}_i} \right) + \mathcal{O}(h^{*2}), \end{aligned} \quad (4.27)$$

where eq. (4.26) has been used in the second step. The result is

$$\gamma_k^* = \sum_{k'=1}^l (Z^{-1})_{kk'} \left(\frac{\partial \sigma_{k'}}{\partial \mathbf{r}_i} \cdot \mathbf{v}_i' \right) + \mathcal{O}(h^*). \quad (4.28)$$

Substitution of eq. (4.28) back in eq. (4.26) and use of eq. (4.25) gives the required result, eqs. (2.75) and (2.76) up to first order in h^* for the velocities. This is why h^* must be adjusted properly so that, in the next Taylor step, the error on the velocity does not lead to errors larger than $\mathcal{O}(h^3)$ on the positions at time $t+h$. This suggests that a good choice should be $h^* \nu m^{-1} (\mathbf{F}^2 / \mathbf{v}^2)^{1/2} h^2$, with obvious meaning of the symbols.

4.3. Molecular dynamics techniques for various ensembles

4.3.1. The “traditional” MD experiment (NVE ensemble)

Most of the technical details concerning the MD of molecules with constraints have been presented in the sections 4.1 and 4.2. Therefore we content ourselves here in presenting the general structure of the MD program.

A dynamic step going from the configuration of the system at time t to the next configuration at time $t+h$, h being the time step, goes as follows when Verlet scheme is used

- 1) to start, two successive configurations $\{\mathbf{r}_{i\alpha}(t-h)\}$ and $\{\mathbf{r}_{i\alpha}(t)\}$ for all atoms of all molecules are stored in memory.
- 2) the force on each atom $\mathbf{F}_{i\alpha} = -\partial U / \partial \mathbf{r}_{i\alpha}$, deriving from the inter + intramolecular potential energy, is computed for the positions $\{\mathbf{r}_{i\alpha}(t)\}$. This step is usually a CALL to a force subroutine.
- 3) all molecules $\alpha = 1, N$ are now considered in succession
 - 3a) the predicted positions $\mathbf{r}_{i\alpha}'(t+h)$ (without forces of constraints) are evaluated according to eq. (4.9).
 - 3b) a version of the method of constraints is applied to evaluate $\mathbf{r}_i(t+h)$ with $\mathbf{r}_i'(t+h)$ as input. Step 3b is usually a CALL to a subroutine (see appendix B for the subroutine based on the method of section 4.1.2).
 - 3c) atomic velocities $\{\dot{\mathbf{r}}_{i\alpha}(t)\}$ are then calculated according to eq. (4.2).
 - 3d) the dynamical step is performed for molecule α by replacing in the memory of the past configuration $\{\mathbf{r}_{i\alpha}(t-h)\}$ by $\{\mathbf{r}_{i\alpha}(t)\}$ and in the memory of the present configuration $\{\mathbf{r}_{i\alpha}(t)\}$ by $\{\mathbf{r}_{i\alpha}(t+h)\}$.
 - 3e) go back to 3a for the next molecule. When the last molecule $\alpha = N$ has been treated, go back to step 2 for the next MD step.

During the preliminary equilibration run, it is usual to force the system to attain a prescribed temperature T even if, afterwards, the production run is performed in microcanonical conditions. This is achieved by modifying from time to time the atomic velocities. The technical implications are identical to those of Andersen canonical MD simulation [10] applied to rigid molecules.

4.3.2. The stochastic collision method of Andersen (NVT ensemble)

According to the two variants of this method [26], the stochastic collisions suffered by individual atoms can be either applied at random times for particles chosen at random or applied

to all atoms at times equally spaced. For rigid molecules, we will in any case thermalise all atoms ($i = 1, n$) of a chosen molecule at the same time. The following steps are required at this occasion:

- i) sample Gaussian velocities $\{\mathbf{v}'_{i\alpha}\}$ of zero mean and standard deviation $(kT/m_i)^{1/2}$.
 - ii) apply one of the schemes of section 4.2 to obtain the corresponding velocities $\{\mathbf{v}_{i\alpha}\}$ distributed according to the canonical measure of a system with constraints.
 - iii) restart the trajectory for that particular molecule with the algorithm given by eq. (4.3).
- Apart from this, the usual dynamical scheme of section 4.3.1 is applicable between stochastic collisions.

4.3.3. MD at fixed pressure in a cubic cell (HPN ensemble)

The combination of Andersen fixed pressure method [10] with the method of constraints results in the eqs. (3.14) where we do not consider the irrelevant s variable dynamics necessary only for fixed temperature simulations. From the Verlet scheme, eq. (4.1), one gets:

$$\mathbf{r}_{i\alpha}(t+h) = -\mathbf{r}_{i\alpha}(t-h) + 2\mathbf{r}_{i\alpha}(t) + \frac{h^2}{m_i}(\mathbf{F}_{i\alpha}(t) + \mathbf{G}_{i\alpha}(t)) + \Delta\mathbf{R}_\alpha, \quad (4.29)$$

$$V(t+H) = -V(t-h) + 2V(t) + h^2\ddot{V}(t), \quad (4.30)$$

where

$$\Delta\mathbf{R}_\alpha = \frac{h^2}{3V(t)}(\ddot{V}(t) - \frac{2}{3}\dot{V}^2(t)V^{-1}(t))\mathbf{R}_\alpha(t), \quad (4.31)$$

$$\ddot{V}(t) = W_Q^{-1} \left\{ (3V(t))^{-1} \sum_{\alpha=1}^N \left(M(\dot{\mathbf{R}}_\alpha(t) - (3V(t))^{-1}\dot{V}(t)\mathbf{R}_\alpha(t))^2 + \mathbf{R}_\alpha \cdot \mathbf{F}_\alpha \right) - P_{\text{ext}} \right\}. \quad (4.32)$$

$\Delta\mathbf{R}_\alpha$ is the molecular displacement due to the isotropic contraction or dilation of the cubic cell. Multiplying eq. (4.29) by m_i and summing over all atoms of molecule α one gets the centre of mass dynamical evolution

$$\mathbf{R}_\alpha(t+h) = -\mathbf{R}_\alpha(t-h) + 2\mathbf{R}_\alpha(t) + \frac{h^2}{M}\mathbf{F}_\alpha + \Delta\mathbf{R}_\alpha \quad (4.33)$$

in which \mathbf{F}_α is the total force on α .

These formulac cannot be used directly because the first derivatives $\dot{V}(t)$ and $\dot{\mathbf{R}}_\alpha(t)$ are not known. We have then to resort to a prediction followed by an iterative procedure to solve the problem. Note that, as the individual atomic velocities are not required, the iterative procedure can be performed on the centre of mass and volume variables separately before applying the atomic dynamical step, eq. (4.29).

4.3.3.1. The centre of mass dynamical step. Let us introduce $\mathbf{R}_\alpha^{(k)}$, $V^{(k)}$, $\dot{\mathbf{R}}_\alpha^{(k)}$, ..., the k th order estimate of $\mathbf{R}_\alpha(t+h)$ and $V(t+h)$ and their time derivatives $\dot{\mathbf{R}}_\alpha(t)$, $\dot{V}(t)$.

- 1) predict $\dot{V}(0)$ and $\{\dot{\mathbf{R}}_\alpha^{(0)}\}$ according to the eqs. (4.4a) or (4.4b). In the usual case, eq. (4.4a) is used i.e.

$$\dot{x}^{(0)}(t) = \frac{3x(t) - 4x(t-h) + x(t-2h)}{2h} + \mathcal{O}(h^2), \quad (4.34)$$

where x stands for any variable. Set index k to 0.

- 2) compute $\dot{V}^{(k)}$ and $\Delta \mathbf{R}_\alpha$ according to eqs. (4.32) and (4.31) using $\dot{V}^{(k)}$ and $\dot{\mathbf{R}}_\alpha^{(k)}$
 3) predict $V^{(k)}(t+h)$ and $\mathbf{R}_\alpha^{(k)}(t+h)$ using eq. (4.30) and (4.33)
 4) compute new estimate of $\dot{V}^{(k+1)}$ and $\dot{\mathbf{R}}_\alpha^{(k+1)}$ using eq. (4.2), i.e.

$$\dot{x}^{(k+1)}(t) = \frac{x^{(k)}(t+h) - x(t-h)}{2h}, \quad (4.35)$$

- 5) go back to step 2) after increasing k index to $k+1$.

Convergence is usually obtained in 2 or 3 loops, the output of which is $V(t+h)$, $\{\mathbf{R}_\alpha(t+h)\}$ and $\{\Delta \mathbf{R}_\alpha\}$.

4.3.3.2. The atomic dynamical step. This step can now be performed in a way similar to the NVE case of section 4.3.1. In the present case, the $\{\mathbf{r}'_{i\alpha}(t+h)\}$ should be identified with

$$\mathbf{r}'_{i\alpha}(t+h) = -\mathbf{r}_{i\alpha}(t-h) + 2\mathbf{r}_{i\alpha}(t) + \frac{h^2}{m_i} \mathbf{F}_{i\alpha} + \Delta \mathbf{R}_\alpha \quad (4.36)$$

which are finally transformed to $\mathbf{r}_{i\alpha}(t+h)$ by the constraint force routine.

All these equations are dealing with real variables $\{\mathbf{r}_{i\alpha}\}$, V defined in eq. (2.51). To make the bridge with the statistical mechanical formulation, we still need to relate the real variables $\{\mathbf{p}_{i\alpha}\}$, eq. (2.52), to the $\{\mathbf{r}_{i\alpha}\}$, V dynamics. This is provided by eq. (3.15). Time averages of any property $F(\{\mathbf{r}_{i\alpha}, \mathbf{p}_{i\alpha}\})$ over the extended system dynamics can now be realised with the algorithm given by eqs. (4.29–4.36) of this section. It provides an estimate of the isobaric–isoenthalpic ensemble average of F .

The accuracy of the numerical procedure can be tested by following the time evolution of the Hamiltonian, eq. (2.63), corresponding to this particular extended system. In terms of real variables, this conserved quantity reads

$$H_1 = H(\{\mathbf{r}_{i\alpha}, \mathbf{p}_{i\alpha}\}) + P_V^2/2W_Q + P_{\text{ext}}V, \quad (4.37)$$

where $P_V = W_Q \dot{V}$. Note here that it is possible to combine the present method (with externally applied pressure) with the stochastic collisions method of Andersen simulating a heat bath contact at a given temperature. This is again useful to bring the system to a prescribed temperature during the equilibration period preceeding a simulation at fixed pressure only. Moreover it can provide a method to realise *NPT* simulations.

The stochastic collisions are realised by sampling the $\{\mathbf{p}_{i\alpha}\}$ according to the method of section 4.2 and P_V in a simple maxwellian distribution function. The atomic velocities $\{\dot{\mathbf{r}}_{i\alpha}\}$ are then evaluated by inverting eq. (3.15) and introduced in the simple Taylor scheme given by eq. (4.3), (4.4b).

4.3.4. The Rahman–Parrinello constant pressure method

The integration scheme for the isotropic case, (see previous section) can be generalised to the present case without difficulty. The counterpart of equations (4.29–4.33) read, respectively (see eq. (3.16))

$$\mathbf{r}_{i\alpha}(t+h) = -\mathbf{r}_{i\alpha}(t-h) + 2\mathbf{r}_{i\alpha}(t) + \frac{h^2}{m_i}(\mathbf{F}_{i\alpha}(t) + \mathbf{G}_{i\alpha}(t)) + \Delta\mathbf{R}_\alpha, \quad (4.38)$$

$$\mathbf{H}(t+h) = -\mathbf{H}(t-h) + 2\mathbf{H}(t) + h^2\ddot{\mathbf{H}}(t), \quad (4.39)$$

where

$$\Delta\mathbf{R}_\alpha = h^2 \left[(\dot{\mathbf{H}}\mathbf{H}^{-1} - (\dot{\mathbf{H}}\mathbf{H}^{-1})^T)(\dot{\mathbf{R}}_\alpha - \dot{\mathbf{H}}\mathbf{H}^{-1}\mathbf{R}_\alpha) + \ddot{\mathbf{H}}\mathbf{H}^{-1}\mathbf{R}_\alpha \right], \quad (4.40)$$

$$\ddot{\mathbf{H}}(t) = W^{-1}(\Pi - P_{\text{ext}}\mathbf{I})\boldsymbol{\sigma}, \quad (4.41)$$

$$\text{with } \boldsymbol{\sigma} = \Omega(\mathbf{H}^{-1})^T, \quad \Omega = \det(\mathbf{H})$$

and

$$\Omega\Pi = \sum_{\alpha} M_{\alpha}(\dot{\mathbf{R}}_{\alpha} - \dot{\mathbf{H}}\mathbf{H}^{-1}\mathbf{R}_{\alpha})(\dot{\mathbf{R}}_{\alpha} - \dot{\mathbf{H}}\mathbf{H}^{-1}\mathbf{R}_{\alpha}) + \mathbf{R}_{\alpha}\mathbf{F}_{\alpha}.$$

The com displacement, eq. (4.33) applied with the present expression of $\Delta\mathbf{R}_\alpha$, eq. (3.40). As in the isotropic case, it is necessary to iterate on the com and \mathbf{H} matrix velocities before performing the individual atomic displacements so that the only difference in the numerical integration scheme results from the matrix character of \mathbf{H} instead of the scalar volume V .

4.3.5. The Nosé constant temperature method

The use of the Verlet algorithm to integrate the Nosé equations of motion for a system coupled to a heat bath (eq. (3.14), where V is a constant) presents a drawback due to the dependence of the atomic accelerations on atomic velocities. The constraint forces evaluation a posteriori, in which the Lagrangian multipliers are calculated by requiring that the final positions satisfy the constraint relations exactly, is coupled with the iterative process on the velocities.

The numerical scheme is the following

$$\mathbf{r}_{i\alpha}(t+h) = -\mathbf{r}_{i\alpha}(t-h) + 2\mathbf{r}_{i\alpha}(t) + \frac{\mathbf{F}_{i\alpha}}{m_i}h^2 + \frac{\mathbf{G}_{i\alpha}}{m_i}h^2 - \dot{S}S^{-1}\dot{\mathbf{r}}_{i\alpha}h^2, \quad (4.42)$$

$$S(t+h) = -S(t-h) + 2S(t) + h^2\ddot{S}(t), \quad (4.43)$$

with

$$\ddot{S}(t) = \dot{S}^2(t)S^{-1}(t) + W_S^{-1}S(t) \left\{ \sum_{\alpha=1}^N \sum_{i=1}^n m_i \dot{\mathbf{r}}_{i\alpha}^2 - (3n-l)Nk_{\text{B}}T_{\text{ext}} \right\}, \quad (4.44)$$

It is convenient to introduce at this stage

$$\mathbf{r}_{i\alpha}''(t+h) = -\mathbf{r}_{i\alpha}(t-h) + 2\mathbf{r}_{i\alpha}(t) + \frac{\mathbf{F}_{i\alpha}}{m_i}h^2, \quad (4.45)$$

$$\mathbf{r}_{i\alpha}'(t+h) = \mathbf{r}_{i\alpha}''(t+h) - \dot{\mathbf{S}}(t)\mathbf{S}^{-1}(t)\mathbf{r}_{i\alpha}(t)h^2. \quad (4.46)$$

For small molecules, for which the evaluation of constraint forces takes a minor amount of computer time, the following iterative scheme can be used:

- 1) compute $\mathbf{r}_{i\alpha}''(t+h)$ according to eq. (4.45)
- 2) predict $\dot{\mathbf{r}}_{i\alpha}^{(0)}$, $\dot{\mathbf{S}}^{(0)}$ time derivatives according to the usual expression (4.4a) and set the index k to 0.
- 3) compute $\ddot{\mathbf{S}}^{(k)}$ according to eqs. (4.44) using the set $\{\dot{\mathbf{r}}_{i\alpha}^{(k)}, \dot{\mathbf{S}}^{(k)}\}$.
- 4) estimate $\mathbf{S}^{(k)}(t+h)$ and $\mathbf{r}_{i\alpha}^{(k)}$ using eqs. (4.43) and (4.46).
- 5) compute the set $\{\mathbf{r}_{i\alpha}^{(k)}(t+h)\}$ by applying the constraint force routine to $\{\mathbf{r}_{i\alpha}^{(k)}\}$.
- 6) compute a new estimate of time derivatives $\dot{\mathbf{S}}^{(k+1)}$ and $\{\dot{\mathbf{r}}_{i\alpha}^{(k+1)}\}$ using usual velocity expression, eq. (4.35).
- 7) go back to step 3) after increasing the index k to $k+1$.

Convergence is usually obtained in 2 or 3 loops so that the need to apply the constraint routine at each iteration loop does not affect the computer time per step in a significant way.

For large molecules, one usually uses the iterative method of section 4.1.2. In such a case where the computer time for the constraint part can be important, an alternative route is possible in which the overall time spent to compute the constraint forces contributions can be kept equivalent to the usual standard MD case.

- 1) compute $\{\mathbf{r}_{i\alpha}''\}$ according to eq. (4.45).
- 2) apply the constraint subroutine to $\{\mathbf{r}_{i\alpha}''\}$ to produce $\{\tilde{\mathbf{r}}_{i\alpha}\}$ just as if the last term of eq. (4.42) was absent. In fact this term affects the constraints only at order h^4 .
- 3) predict the $\{\dot{\mathbf{r}}_{i\alpha}^{(0)}\}$, $\dot{\mathbf{S}}^{(0)}$ time derivatives according to the usual expression (4.4.a) and set index k to 0.
- 4) compute $\ddot{\mathbf{S}}^{(k)}$ according to eq. (4.44) using the set $\{\dot{\mathbf{r}}_{i\alpha}^{(k)}\}$, $\dot{\mathbf{S}}^{(k)}$.
- 5) estimate the set $\{\mathbf{r}_{i\alpha}^{(k)}\}$ by applying the constraint force routine to $\tilde{\mathbf{r}}_{i\alpha} - \dot{\mathbf{S}}^{(k)}\mathbf{S}^{-1}\dot{\mathbf{r}}_{i\alpha}^{(k)}h^2$.
- 6) compute the new estimate of time derivatives $\dot{\mathbf{S}}^{(k+1)}$ and $\dot{\mathbf{r}}_{i\alpha}^{(k+1)}$ using eq. (4.35).
- 7) go back to step 4) after increasing the index k to $k+1$.

In this last procedure, the number of iterations necessary to obtain $\{\tilde{\mathbf{r}}_{i\alpha}\}$ in step 2 is certainly similar to an ordinary MD step. However, in step 5, the heat bath coupling term leads to deviations of order h^4 on the constraint satisfaction, so that the number of additional iterations in the constraint force routine must be much smaller.

The accuracy of the numerical procedure can be tested by looking at the conservation of the Hamiltonian of this extended system. In terms of real variables the conserved quantity is

$$H_1 = H(\{\mathbf{r}_{i\alpha}, \mathbf{p}_{i\alpha}\}) + \frac{P_s^2}{2W_s} + (3n-l)Nk_B T_{\text{ext}} \ln S, \quad (4.47)$$

where $P_s = W_s \dot{\mathbf{S}} \mathbf{S}^{-1}$.

5. Conclusions

This review discusses various algorithms needed to perform MD simulations in Cartesian coordinates for molecular systems composed of partially or fully rigid molecules. A survey of the literature on MD simulations of polyatomic systems [36] reveals that in a majority of cases the intramolecular structure is taken to be totally or partially rigid. With the exception of fully rigid molecules for which an efficient technique has been developed by Evans [4], there is no real alternative to the use of the method of constraints. Moreover the method is particularly useful when the potential is expressed as a sum of atom pair (or site–site) interactions. In our experience the stability and efficiency of the algorithms presented here is superior to that of schemes not based on the Verlet algorithm. In particular, the stability of this algorithm and the time step magnitude are not altered when one goes from the traditional MD (Newton's equations) to extended variable methods where the accelerations are velocity dependent so that velocities are obtained by an iterative technique. In section 2 we discussed in detail the statistical mechanics formulation in atomic description of a system of molecules subjected to holonomic constraints. The probability measure associated with such systems is a “singular” function on the atomic phase space. This formulation is lacking in standard textbooks although it is essential to prove the validity of the various dynamical schemes that have been introduced to simulate ensembles different from the microcanonical one. Moreover it is quite useful to clarify the old question of the differences between rigid and flexible molecular systems [2,3,37,38].

The method of constraints has a large flexibility. With a judicious choice of potentials it can be (and has been already) used to understand and predict properties of large systems of complex molecules ranging from molecular fluids and solids to macromolecules, liquid crystals, micelles, surfaces and chemical reactions. A discussion of the applications of the method is far outside the scope of this review. However there are a number of recent excellent reviews of what can be learned by simulation of molecular systems [36,39,40].

Lastly we refer the interested reader to the useful complementary review of the method of constraints by Berendsen and van Gunsteren [41].

Acknowledgements

We would like to thank A. Bellemans, H.J.C. Berendsen, M. Ferrario, I.R. McDonald and C. Moser for collaboration and criticism of much of the work described here. We are also grateful to M. Ferrario and I.R. McDonald for a critical reading of the manuscript. This work has been partially supported by the exchange program of FNRS (Belgium)–CNR(Italy) and by the NATO Grant no. 1865.

Appendix A. Proof of the equivalence between the atomic and molecular expression for the pressure [13]

We want to prove that the internal pressure of a molecular system with internal degrees of freedom can be equivalently expressed as the ensemble average of the atomic pressure, eq. (2.88)

$$P = \langle \hat{P}_{\text{atom}} \rangle = \langle (1/3V) \left[\sum_{\alpha} \sum_i (m_i \dot{r}_{i\alpha}^2 + \mathbf{r}_{i\alpha} \cdot \mathbf{F}_{i\alpha}) \right] \rangle, \quad (\text{A.1})$$

or molecular pressure, eq. (2.89)

$$P = \langle \hat{P}_{\text{molecule}} \rangle = \langle (1/3V) \left[\sum_{\alpha} (M \dot{\mathbf{R}}_{\alpha}^2 + \mathbf{R}_{\alpha} \cdot \mathbf{F}_{\alpha}) \right] \rangle. \quad (\text{A.2})$$

In eq. (A.1), $\mathbf{F}_{i\alpha}$ is the total force acting on atom i in molecule α , including possible constraints forces, while in eq. (A.2) \mathbf{F}_{α} is the total force acting on the com of molecule α , $\mathbf{F}_{\alpha} = \sum_i \mathbf{F}_{i\alpha}$. \mathbf{R}_{α} is, as usual, the com coordinate

$$\mathbf{R}_{\alpha} = (1/M) \sum_i m_i \mathbf{r}_{i\alpha}. \quad (\text{A.3})$$

Eq. (A.1) is the definition of the Clausius virial theorem for a molecular system, so that to prove eq. (A.2) we need only to show the equivalence of the r.h.s. of eqs. (A.1) and (A.2). To do this let us start by manipulating the force term in the rhs of eq. (A.2)

$$\begin{aligned} \sum_{\alpha} \langle \mathbf{R}_{\alpha} \cdot \mathbf{F}_{\alpha} \rangle &= \sum_{\alpha} 1/M \sum_i \sum_j m_i \langle \mathbf{r}_{i\alpha} \cdot \mathbf{F}_{j\alpha} \rangle \\ &= \sum_{\alpha} 1/M \sum_{ij} \langle m_i (\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}) \cdot \mathbf{F}_{j\alpha} + m_i \mathbf{r}_{j\alpha} \cdot \mathbf{F}_{j\alpha} \rangle \\ &= \sum_{\alpha} 1/M \left\{ \sum_{ij} \left[\frac{1}{2} \langle (\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}) \cdot (m_i \mathbf{F}_{j\alpha} - m_j \mathbf{F}_{i\alpha}) \rangle \right] + M \sum_j \langle \mathbf{r}_{j\alpha} \cdot \mathbf{F}_{j\alpha} \rangle \right\} \\ &= - \sum_{\alpha} 1/M \sum_{ij} \left[\frac{1}{2} \langle m_i m_j (\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}) \cdot (\ddot{\mathbf{r}}_{i\alpha} - \ddot{\mathbf{r}}_{j\alpha}) \rangle \right] + \sum_{\alpha} \sum_j \langle \mathbf{r}_{j\alpha} \cdot \mathbf{F}_{j\alpha} \rangle, \end{aligned} \quad (\text{A.4})$$

where, in the last equality, Newton's equations, $\mathbf{F}_{i\alpha} = m_i \ddot{\mathbf{r}}_{i\alpha}$, have been used.

Now the vector $\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}$ satisfies the relation

$$(\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}) \cdot (\ddot{\mathbf{r}}_{i\alpha} - \ddot{\mathbf{r}}_{j\alpha}) = \frac{d}{dt} [(\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}) \cdot (\dot{\mathbf{r}}_{i\alpha} - \dot{\mathbf{r}}_{j\alpha})] - (\dot{\mathbf{r}}_{i\alpha} - \dot{\mathbf{r}}_{j\alpha})^2. \quad (\text{A.5})$$

The first term in the r.h.s. of eq. (A.5) is zero in the average if $\langle (\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}) \cdot (\dot{\mathbf{r}}_{i\alpha} - \dot{\mathbf{r}}_{j\alpha}) \rangle$ exists. In fact, in equilibrium, it is possible to interchange the phase space integral, implied by the average, with the time derivative if the average of the observable to be derived exists. This is the case for atoms belonging to the same molecule because they cannot go too far apart one from the other in space or velocity. Moreover $\langle (\mathbf{r}_{i\alpha} - \mathbf{r}_{j\alpha}) \cdot (\dot{\mathbf{r}}_{i\alpha} - \dot{\mathbf{r}}_{j\alpha}) \rangle$ is a time independent quantity and its time derivative is zero. Note that for atoms rigidly connected the first term in the r.h.s. of eq. (A.5) is zero mechanically and not simply in the average. Substituting this result in eq. (A.4) one finds

$$\langle \sum_{\alpha} \mathbf{R}_{\alpha} \cdot \mathbf{F}_{\alpha} \rangle = \sum_{\alpha} \frac{1}{2M} \sum_{i,j} m_i m_j \langle (\dot{\mathbf{r}}_{i\alpha} - \dot{\mathbf{r}}_{j\alpha})^2 \rangle + \sum_{\alpha} \sum_i \langle \mathbf{r}_{i\alpha} \cdot \mathbf{F}_{i\alpha} \rangle. \quad (\text{A.6})$$

The first term can be further simplified by developing $(\dot{\mathbf{r}}_{i\alpha} - \dot{\mathbf{r}}_{j\alpha})^2$ and using the com velocity, $\dot{\mathbf{R}}_\alpha = (1/M)\sum_i m_i \dot{\mathbf{r}}_{i\alpha}$, to find

$$\sum_\alpha \frac{1}{2M} \sum_{ij} m_i m_j \langle (\dot{\mathbf{r}}_{i\alpha} - \dot{\mathbf{r}}_{j\alpha})^2 \rangle = \sum_\alpha \sum_i m_i \langle \dot{\mathbf{r}}_{i\alpha}^2 \rangle - \sum_\alpha M \langle \dot{\mathbf{R}}_\alpha^2 \rangle. \quad (\text{A.7})$$

Substituting eq. (A.7) in (A.6) and this last in (A.2) we find the result. To conclude this appendix, we have proven that $\hat{P}_{\text{atom}} = \hat{P}_{\text{molecule}}$ for rigid molecules and that $\langle \hat{P}_{\text{atom}} \rangle = \langle \hat{P}_{\text{molecule}} \rangle$ for flexible molecules.

Appendix B. FORTRAN routine evaluating the constraint forces displacements by the iterative technique, section 4.1.2

a – List of variables (not exhaustive)

On INPUT:	XP,YP,ZP	atomic positions $\{r'(t+h)\}$
	X,Y,Z	atomic positions $\{r(t)\}$
	HM	atomic masses
	TOL	tolerance
	ITMAX	maximum number of allowed iterations
On OUTPUT:	XP,YP,ZP	atomic positions $\{r(t+h)\}$ within the tolerance (no message) or atomic positions after ITMAX loops over all constraints (message: "CONVERGENCE PROBLEM DISCR = ..."). DISCR gives the largest discrepancy among the constraints within the last loop.
In ROUTINE:	N	number of atoms in the molecule
	NK	number of atoms implied by constraint k (In the FORTRAN, by a DO loop on $I = 1, NK$, we mean that the loop considers the NK specific atoms implied by a given constraint.)
	L	number of scalar constraints per molecule
	DISCR	at the end of the iterative loop on all constraints, DISCR is zero if all constraints are satisfied within the tolerance. Otherwise it gives the maximum deviation of $\{\sigma_k(r_j^{\text{OLD}})\}$ from zero found within the same loop.

b – Sketch of the subroutine.

```

SUBROUTINE GAMMA (XP,YP,ZP,X,Y,Z,HM,TOL,ITMAX)
DIMENSION XP(N),YP(N),ZP(N),X(N),Y(N),Z(N),HM(N)
DO 1 K = 1, L          consider all constraints
DO 1 I = 1, NK         consider the NK specific atoms involved in constraint K

```

```

DSX(K,I) = ...
DSY(K,I) = ...           compute  $(\frac{\partial \sigma_k}{\partial \mathbf{r}_i})_{\mathbf{r}(t)}$  using X,Y,Z
DSZ(K,I) = ...

1 CONTINUE
DO 9000 ITER = 1,ITMAX    central iterative loop on all constraints

    DISCR = 0.
    DO 2 K = 1,L           consider all constraints
    SIGOLD = ...           compute  $\sigma_k(\{\mathbf{r}_i^{\text{OLD}}\})$  using XP,YP,ZP

    IF(ABS(SIGOLD).LT.TOL)GOTO2
    IF(DISCR.LT.ABS(SIGOLD))DISCR = ABS(SIGOLD)
    DENOM = 0.
    DO 3 I = 1,NK          consider all specific atoms involved in constraint K

    DSXP(I) = ...
    DSY(I) = ...           compute  $(\frac{\partial \sigma_k}{\partial \mathbf{r}_i})_{\mathbf{r}_i^{\text{OLD}}}$  using XP,YP,ZP
    DSZ(I) = ...

    3 DENOM = DENOM + (DSXP(I)*DSX(I) + ... + ...)/HM(I)
    GAMK = SIGOLD/DENOM    Lagrange parameter  $\gamma_k$ 
    DO 4 I = 1,NK
    XP(I) = XP(I)-GAMK*DSX(K,N)  $\mathbf{r}_i^{\text{NEW}} = \mathbf{r}_i^{\text{OLD}} - \gamma_k(\frac{\partial \sigma_k}{\partial \mathbf{r}_i})_{\mathbf{r}(t)}$ 
    YP(I) = YP(I)-GAMK*DSY(K,N) with substitution of  $\mathbf{r}_i^{\text{OLD}}$  by  $\mathbf{r}_i^{\text{NEW}}$ 
    4 ZP(I) = ZP(I) - GAMK*DSZ(K,N)
    2 CONTINUE
    IF(DISCR.EQ.0)GOTO9001    if DISCR = 0, end of iteration
    IF (ITER.EQ.ITMAX)PRINT 100, DISCR
100  FORMAT(1H,'CONVERGENCE PROBLEM DISCR ='E10.3)
9000 CONTINUE
9001 RETURN
    END

```

References

- [1] H.J.C. Berendsen and W.F. van Gunsteren, in: The Physics of Superionic Conductors and Electrode Materials, ed. J.W. Perram NATO ASI B92 (Plenum Press New York, 1983) p. 221.
- [2] E. Helfand, J. Chem. Phys. 71 (1979) 5000.
- [3] W.F. van Gunsteren, Mol. Phys. 40 (1980) 1015.
- [4] D.J. Evans, Mol. Phys. 34 (1977) 317.

- [5] J.P. Ryckaert, G. Ciccotti and H.J.C. Berendsen, *J. Comput. Phys.* 23 (1977) 327.
- [6] G. Ciccotti, M. Ferrario and J.P. Ryckaert, *Mol. Phys.* 47 (1982) 1253.
- [7] J.P. Ryckaert, *Mol. Phys.* 55 (1985) 549.
- [8] J.P. Ryckaert and G. Ciccotti, *J. Chem. Phys.* 78 (1983) 7368.
- [9] M. Ferrario and J.P. Ryckaert, *Mol. Phys.* 54 (1985) 587.
- [10] H.C. Andersen, *J. Chem. Phys.* 72 (1980) 2384.
- [11] S. Nosé, *Mol. Phys.* 52 (1984) 255; *J. Chem. Phys.* 81 (1984) 511.
- [12] M. Parrinello and A. Rahman, *J. Appl. Phys.* 52 (1981) 7182; *J. Chem. Phys.* 76 (1982) 2662.
- [13] H.J.C. Berendsen, Lecture notes on: Druk en Viriaal in Moleculaire Dynamica, unpublished.
- [14] B.J. Berne and G.D. Harp, *Advan. Chem. Phys.* 17 (1970) 63.
- [15] W.L. Jorgensen, *J. Am. Chem. Soc.* 103 (1981) 335.
H.J.C. Berendsen, J.P.N. Postma, W.F. van Gunsteren and J. Hermans, in: *Intermolecular Forces*, ed B. Pullman (Reidel, Dordrecht, Holland, 1981).
- [16] J. Barojas and D. Levesque, *Phys. Rev. A* 7 (1973) 1092.
- [17] F.H. Stillinger and A. Rahman, *J. Chem. Phys.* 60 (1974) 1545.
- [18] O. Matsuoka, E. Clementi and M. Yoshimine, *J. Chem. Phys.* 64 (1976) 1351.
- [19] J.P. Ryckaert and A. Bellemans, *Chem. Phys. Lett.* 30 (1975) 123.
- [20] C.S. Murthy, K. Singer and I.R. McDonald, *Mol. Phys.* 44 (1981) 135.
- [21] M. Claessens, M. Ferrario and J.P. Ryckaert, *Mol. Phys.* 50 (1983) 217.
- [22] D.J. Evans and R.O. Watts, *Mol. Phys.* 31 (1976) 83.
- [23] K.R. Symon, *Mechanics* (Addison-Wesley, Reading MA, 1967) Chap. IX.
- [24] M. Fixman, *Proc. Nat. Acad. Sci. USA* 71 (1974) 3050.
- [25] S. Nosé and M.J. Klein, *Mol. Phys.* 50 (1983) 1055.
- [26] T.A. Andrea, W.C. Swope and H.C. Andersen, *J. Chem. Phys.* 79 (1983) 4576.
- [27] Report of CECAM Workshop on Constraint Techniques in the Simulation of Transport and Structural Phase Transitions (1984) Orsay.
- [28] J.P. Ryckaert and G. Ciccotti, to be published in *Mol. Phys.*
- [29] R.D. Olmsted and R.F. Snider, *J. Chem. Phys.* 65 (1976) 3407, 68 (1978) 2477.
- [30] G. Maréchal and J.P. Ryckaert, *Chem. Phys. Lett.* 101 (1983) 548.
- [31] H.J.C. Berendsen and W.F. van Gunsteren, in: *Proc. of 1985 Varenna Summer School*, see ref. [40].
- [32] W.F. Van Gunsteren and H.J.C. Berendsen, *Mol. Phys.* 34 (1977) 1311.
- [33] H.C. Andersen, *J. Comput. Phys.* 52 (1983) 24.
- [34] J.P. Ryckaert and M.J. Klein, to be published in *J. Chem. Phys.*
- [35] W.F. van Gunsteren, H.J.C. Berendsen and J.A.C. Rullmann, *Mol. Phys.* 44 (1982) 69.
- [36] D. Levesque, J.J. Weis and J.P. Hansen, *Topics in Current Physics* 36 (1984) 37 (see table 2.1).
- [37] H.A. Kramers, *Physica* 7 (1940) 284.
- [38] N.G. van Kampen, *Appl. Sci. Res.* 37 (1981) 67.
- [39] D.J. Tildesley, in: *Molecular Liquids, Dynamics and interactions*, eds A.J. Barnes, W.J. Orville-Thomas and J. Yarwood NATO ASI C135 (Plenum Press, New York, 1984) p. 519.
- [40] *Proc. of 1985 Varenna Summer School on: MD Simulation of Statistical Mechanical Systems*, to appear (North-Holland, Amsterdam, 1986).
- [41] H.J.C. Berendsen and W.F. Van Gunsteren, in: *Molecular Liquids, Dynamics and Interactions*, see ref. [39], p. 475.