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Conservative Algorithm for an Adaptive Change of Resolution in Mixed Atomistic/Coarse-Grained Multiscale Simulations

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Abstract: We derive a Hamiltonian and present a simulation protocol for mixed-resolution systems that allows for a change in resolution of selected groups of atoms during a molecular dynamics simulation. The Hamiltonian uses a low-resolution force field for the part of the system distant from an active site (for efficiency) and an atomistic force field for the active site and its direct environment (for accuracy). A microcanonical simulation protocol conserves energy and angular and linear momentum. The method is also applicable to simulations in other ensembles.

Understanding complex materials such as polymeric systems and biological functional units often requires investigating multiple and tightly coupled time and length scales. Neither atomistic nor coarse-grained simulations are able to adequately capture all the relevant scales, from the quantum mechanical to the meso- and macroscales. Atomistic models can capture the former but are too inefficient to model the latter. Coarse-grained models lump a group of atoms into a pseudoatom whose motion is governed by a simplified potential. Thus they require the evaluation of fewer interactions¹ that are often shorter ranged and “softer” than atomic interactions;^{2,3} this permits the use of longer and more efficient time steps in a molecular dynamics simulation.^{4,5} However, the loss of chemical detail and the difficulty in obtaining accurate coarse-grained potential energy parameters for strongly interacting systems, where atoms become polarized or react, limit the applicability of these models.⁶

To combine the efficiency of coarse-grained models with the accuracy of atomistic models for systems that require atomistic resolution only locally, for example at a reactive

group or defect (called the active zone), mixed-resolution models have been developed; these models use a low-resolution description for the part of the system distant from an active site and an atomistic description for the active site and its direct environment.^{7–18} The low-resolution description can be a coarse-grained model or a mixture of coarse-grained and atomistic models. Since the active zone may diffuse during a molecular simulation or ligands may exchange in and out of the inner coordination shell of the active site, the algorithm needs to permit an on-the-fly reclassification (from atomistic to low-resolution or vice versa) of atoms or groups as they transition between the high- and low-resolution regimes.

Previously, only the AdResS algorithm from Praprotnik et al.^{11,15–17} and the hybrid scheme from Ensing et al.¹⁸ permitted such a reclassification during a molecular dynamics simulation. The AdResS scheme defines an atomistic zone, a coarse-grained zone, and a mixed-resolution zone (in which the degrees of freedom are slowly switched on or off) in the simulation box and considers the reclassification of atoms or groups as a “geometry-induced first-order phase transition”. Using different force fields in each zone is equivalent to using a nonconservative force field for the whole system.¹⁹ As a result, there exists no potential energy function for the entire system, and simulations do not conserve either energy or angular momentum. The hybrid scheme from Ensing et al. integrates in essence the same force field as the AdResS scheme (a different smoothing function is used) and, to approximately conserve energy, adds or subtracts energy terms to or from the system energy whenever a group crosses a zone boundary. Considering that adding or subtracting energy terms does not alter the trajectory, the hybrid scheme from Ensing et al. does in principle not remove any of the limitations of the AdResS algorithm.

Recently, we introduced an adaptive partitioning (AP) method²⁰ for treating the potential energy function for systems with an active zone modeled at a high-level of theory (e.g., quantum mechanics) and a surrounding environmental zone modeled at a low-level of theory (e.g., molecular mechanics). This algorithm permits an on-the-fly change in level of theory of the potential energy function of an atomistic simulation as atoms or groups of atoms move between the active and environmental zones. In this letter, we present a new method called adaptive partitioning of the Lagrangian (APL) that extends our previous AP method from potential energy functions to Lagrangian functions and that can be used to derive a conservative Hamiltonian for a mixed-resolution system that allows for a change in resolution of selected groups during a simulation. Many-body force fields can be used (the AdResS method is limited to pair potentials),

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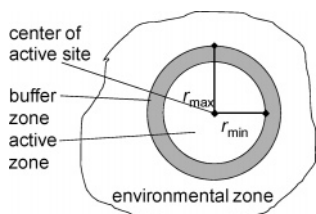


Figure 1. Partitioning of a multiscale system into an active zone, an environmental zone, and a buffer zone separating the active from the environmental zone. Groups of atoms in the active zone have a high (atomistic) resolution, groups in the environmental zone have a low (coarse-grained) resolution, and groups in the buffer zone have a mixed resolution.

multiple active zones can be present in the simulation system, a microcanonical-ensemble (NVE) simulation protocol conserves energy, angular, and linear momentum (conservation proofs including proofs of fulfillment of Newton's third law and their group-definition requirements are presented in the Supporting Information), and the method is also well defined for any other thermodynamic ensemble. We note that both the AdResS and hybrid scheme integrate Newton's equation of motion. Considering that the degrees of freedom of a group of atoms change depending on the coordinates of the group of atoms, the kinetic energy functional of the system is both velocity and coordinate dependent. It is well-known that for coordinate-dependent kinetic energies the equations of motion are not given by Newton's equations but by the Euler–Lagrange equations (or Hamilton's equations),²¹ and it is the Lagrangian or Hamiltonian that can describe a mixed-resolution system that we derive in this letter.

The APL method starts with an atomistic description of a system and classifies all atoms into groups with group coordinates that become the interaction sites for those groups that are coarse grained in the low-resolution description of the system. We define a particular atom or a group of atoms, called the active site, as the center of an active zone that needs to be modeled atomistically. Although the scheme can involve multiple active zones and each active zone can be defined very generally, including the possibility of the active zone boundary passing through a covalent bond, the discussion here is for a single spherical active zone surrounded by a spherical-shell buffer zone (defined with inner and outer radii, r_{\min} and r_{\max}) and an environmental zone (which comprises the rest of the system, which need not be spherical), and without loss of generality we illustrate the potential energy for the case where there are no covalent bonds between groups (e.g., when the low-resolution zone is a molecular liquid solvent). At any time, all of the atoms of a given group are always considered to be in the same zone. Groups of atoms located in the environmental zone are described only by their low-resolution interaction sites. The atomistic structure of these groups is not specified, and only the group coordinates are stored. In contrast, groups in the active zone and the buffer zone possess an explicit atomistic structure. The purpose of the buffer zone is to smooth the potential and kinetic energy of the system when groups are entering or leaving the active zone. The thickness of the buffer depends on the low-resolution and atomistic description but might be, for example, a few angstroms. Figure 1 illustrates the partitioning of the system into three zones.

To keep the notation simple, we will write the equations for the case where every group has the same number A of atoms, but the generalization to A_α atoms in group α is straightforward. In addition, all equations are written here for a system following classical particle dynamics, but an extension to mixed atomistic–continuum systems^{12–14,22,23} is possible. We define a Lagrangian for v coarse-grained and μ atomistic groups

$$L^{(\mu,v)} = \sum_{\alpha=1}^v \frac{1}{2} M_\alpha U_\alpha^2 + \sum_{k=1}^{A\mu} \frac{1}{2} m_k u_k^2 - V^{(\mu,v)} \quad (1)$$

where $M_\alpha = \sum_{k=1}^A m_k^{(\alpha)}$ is the mass of group α , U_α is the velocity of its group coordinate (which may be, but need not be, at the center of mass of the group), $m_k^{(\alpha)}$ is the mass of atom k in group α , \mathbf{u}_k is its velocity vector (u_{kx}, u_{ky}, u_{kz})^T, and $V^{(\mu,v)}$ is the potential energy describing all interactions between the low-resolution and atomistic sites. For the case considered here (no covalent bonds between groups), there is considerable freedom in the choice of the mixed-resolution potential energy functional, but one reasonable possibility is

$$V^{(\mu,v)} = V^{\mu+v} + (V_{AA}^\mu - V^\mu) + 3(A-1)v k_B T_0 \quad (2)$$

where $V^{\mu+v}$ is the potential energy of the entire system described by a low-resolution force field, V_{AA}^μ is the potential energy of the active groups described by an atomistic force field, and V^μ is the potential energy of the active groups as described by the low-resolution force field. All energies are calculated in the APL scheme with reference to a point in configuration space of the all-atomistic system with all momenta equal to zero. Since most low-resolution force fields do not include energy contributions of the implicit degrees of freedom at a finite temperature, eq 2 includes $k_B T_0$ for each implicit degree of freedom in the low-resolution description of the potential energy $V^{(\mu,v)}$ where T_0 is the average temperature of the system we plan to study in our simulation. Note that the choice of $k_B T_0$ per degree of freedom is motivated by considering all implicit degrees of freedom to be harmonic,²⁴ but this does not limit the treatment to harmonic potentials for either the atomistic or coarse-grained potential functions. Because of the dependence on T_0 , the APL force field is thermodynamic-state dependent. In general, the energy contributions of the implicit degrees of freedom are system dependent and not necessarily $k_B T_0$ per degree of freedom, but the following APL procedure is independent of the specific mixed-resolution potential energy functional.

If, at one instant in time during a molecular simulation, there are M groups of atoms in the active zone, K groups of atoms in the buffer zone, and N groups of atoms in the environmental zone, then we define the mixed-resolution Lagrangian, L^{AP} , as a linear combination of all possible combinations of Lagrangian functions that are obtained by treating the active zone and a subset of the K groups in the buffer zone at a high level of resolution (and the rest at a low level of resolution)

$$L^{\text{AP}} = L^{\text{AP}}(L^{[0]}, \{L^{[1]}\}, \dots, L^{[K]}) \quad (3)$$

where $\{L^{[J]}\}$ denotes all $K!/J!(K-J)!$ possible Lagrangian

functions that can be obtained by considering various choices of J buffer-zone groups to be atomistic. To simplify the notation, we will denote the Lagrangian as $L_{\alpha\beta\cdots\theta}$ when groups $\alpha, \beta, \cdots, \theta$ in the buffer zone are considered as atomistic and groups $\gamma, \delta, \cdots, K - \theta$ are considered as having a low resolution. In the APL method all high-resolution Lagrangian contributions from groups α in the buffer zone are smoothed according to their radial coordinate r_α (distance between group α and the center of the active site)

$$L^{\text{AP}} = L + \sum_{\alpha=1,\cdots,K} S_\alpha (L_\alpha - L) + \sum_{\substack{\alpha=1,\cdots,K-1 \\ \beta=\alpha+1,\cdots,K}} S_\alpha S_\beta \{L_{\alpha\beta} - [L + \sum_{\mu=\alpha,\beta} (L_\mu - L)]\} + \sum_{\substack{\alpha=1,\cdots,K-2 \\ \beta=\alpha+1,\cdots,K-1 \\ \gamma=\beta+1,\cdots,K}} S_\alpha S_\beta S_\gamma [L_{\alpha\beta\gamma} - (L + \sum_{\mu=\alpha,\beta,\gamma} (L_\mu - L) + \sum_{(\sigma,\tau)=(\alpha,\beta),(\alpha,\gamma),(\beta,\gamma)} (L_{\sigma\tau} - [L + \sum_{\mu=\alpha,\beta} (L_\mu - L)]))] + \cdots \quad (4)$$

where L corresponds to $\theta = 0$, S_α is a fifth-order spline

$$S_\alpha(\Omega_\alpha) = -6\Omega_\alpha^5 + 15\Omega_\alpha^4 - 10\Omega_\alpha^3 + 1 \quad (5)$$

and Ω_α is given by

$$\Omega_\alpha = \frac{r_\alpha - r_{\min}}{r_{\max} - r_{\min}}, \quad \text{for } r_{\min} < r_\alpha < r_{\max} \quad (6)$$

The Supporting Information shows that eq 4 can be written as

$$L^{\text{AP}} = T^{\text{AP}} - V^{\text{AP}} = \sum_{w=x,y,z} \left[\sum_{\alpha=1}^N \frac{1}{2} M_\alpha U_{\alpha,w}^2 + \sum_{k=1}^{AM} \frac{1}{2} m_k u_{k,w}^2 + \sum_{\beta=1,\cdots,K} \frac{1}{2} (u_{1,w}^{(\beta)} \cdots u_{A,w}^{(\beta)}) \mathbf{\Lambda}^{(\beta)} \begin{pmatrix} u_{1,w}^{(\beta)} \\ \vdots \\ u_{A,w}^{(\beta)} \end{pmatrix} \right] - V^{\text{AP}} \quad (7)$$

where T^{AP} is the kinetic energy, V^{AP} is the potential energy calculated with the permuted AP method²⁰ applied to the mixed atomistic and low-resolution potential energy functions, $V^{(\mu,v)}$, $u_k^{(\beta)}$ is the velocity of atom k of group β in the buffer zone, and $\mathbf{\Lambda}^{(\beta)}$ is a coordinate-dependent mass matrix of group β . The mass matrix $\mathbf{\Lambda}^{(\beta)}$ is nonsingular for $S_\beta > 0$, and the Supporting Information shows that

$$\mathbf{\Lambda}^{(\beta)} = [(1 - S_\beta) \mathbf{M}_D^{(\beta)} + S_\beta \mathbf{M}_M^{(\beta)}] \quad (8)$$

with

$$\mathbf{M}_D^{(\beta)} \equiv \left[\frac{1}{M_\beta} \begin{pmatrix} m_1^{(\beta)} \\ \vdots \\ m_A^{(\beta)} \end{pmatrix} (m_1^{(\beta)} \cdots m_A^{(\beta)}) \right] \quad (9)$$

and

$$\mathbf{M}_M^{(\beta)} \equiv \begin{bmatrix} m_1^{(\beta)} & \cdots & 0 \\ \vdots & \ddots & \vdots \\ 0 & \cdots & m_A^{(\beta)} \end{bmatrix} \quad (10)$$

Having defined a mixed-resolution Lagrangian function, we

can calculate²¹ the generalized momenta $p_i = \partial L / \partial u_i$ and the mixed-resolution Hamiltonian function H^{AP} . We obtain

$$H^{\text{AP}} = \sum_i u_i p_i - L^{\text{AP}} = \sum_{w=x,y,z} \left[\sum_{\alpha=1}^N \frac{P_{\alpha,w}^2}{2M_\alpha} + \sum_{k=1}^{AM} \frac{p_{k,w}^2}{2m_k} + \sum_{\beta=1,\cdots,K} \frac{1}{2} (p_{1,w}^{(\beta)} \cdots p_{A,w}^{(\beta)}) (\mathbf{\Lambda}^{(\beta)})^{-1} \begin{pmatrix} p_{1,w}^{(\beta)} \\ \vdots \\ p_{A,w}^{(\beta)} \end{pmatrix} \right] + V^{\text{AP}} \quad (11)$$

where P_α is the total momentum of group α .

We note that for K groups in the buffer zone, 2^K potential energy functions have to be evaluated to determine the AP potential energy, V^{AP} . (For classical mixed-resolution force fields that consist of additive many-body interaction terms the computational overhead of the APL procedure is usually negligible, which is why we based our APL scheme on the permuted AP method (that scales as $O(2^K)$) and not on the sorted AP method (that scales as $O(K)$).²⁰ For example, for pairwise potentials the computational effort scales as $[1/2(AM + N + K)(AM + N + K - 1) + 1/2AK(AM + N) + 1/2AK(AK - 1)]$ where the computational overhead of the APL procedure, $[1/2AK(AM + N) + 1/2AK(AK - 1)]$, is negligible if the number of atoms in the buffer zone, AK , is small in comparison to the number of interaction sites in the active and environmental zone, $AM + N$.)

Equation 11 shows that the mixed-resolution Hamiltonian for the system allows for a change in resolution of selected groups of atoms during a simulation by making the kinetic energy part of the adaptively partitioned Hamiltonian a functional of the splines. There are no explicit symplectic integrators for coordinate-dependent kinetic energies, but the Supporting Information presents an implicit symplectic generalization of the leapfrog algorithm²⁵ that solves Hamilton's equation of motion with a single force evaluation per time step.

APL simulations can be performed with an all-atomistic resolution in all zones (the force field has still different resolutions). In this case, the Hamiltonian propagates the atomistic structure of groups in the environmental zone in parallel to the group coordinates, and the APL scheme is time-reversible. The main disadvantage of this approach is that the all-atomistic system (including the atomistic structure of groups in the environmental zone) needs to be equilibrated using an all-atomistic force field, a step that is often computationally unfeasible. To eliminate this extra requirement, we propose to use the algorithm with reduced-dimensionality in the environmental zone, integrate only the group coordinates of groups in the environmental zone, and only insert the atomistic structure of a group as it enters the buffer zone from the environmental zone. Thus, we need an algorithm for determining atomistic structure of a group during the simulation. There are two requirements: (i) The procedure should generate appropriate atomic coordinates for the simulation conditions without changing the group coordinate. (ii) The configuration space should be sampled with a probability corresponding to that of an all-atomistic simulation. One possible procedure is to place the group coordinate on one of the atoms of the group, to generate an

atomistic configuration for the group entering the buffer zone that satisfies requirement (i), and then to perform a constrained molecular dynamics simulation to relax the newly placed atoms in the force field of all the other atoms and groups. During this process only the newly placed atoms move, and all atoms in the buffer and core zone are considered explicit. Furthermore, all group coordinates are fixed during this process. We note that in the mixed-resolution potential energy functional of eq 2, there is no change in the interaction of the environmental zone with the active and buffer zones when the group coordinates are fixed, and this interaction does not have to be evaluated. Other procedures for inserting atomistic structure based on Monte Carlo methods^{26,27} are also possible.

A notable advantage of the APL scheme is that only atomic coordinates (and not velocities) have to be generated when a group enters the buffer zone from the environmental zone. For groups on the boundary between the buffer and environmental zone the atomic velocities are the same as the velocity of the group coordinate. The Hamiltonian automatically reintroduces intragroup (vibrational) velocities as a group in the buffer zone moves toward the active zone (and it removes intragroup kinetic energy as a group in the buffer zone moves toward the environmental zone). Furthermore, the AP potential energy is independent of the atomistic structure of a group on the boundary between buffer and environmental zone so that the insertion of atomic structure yields both a continuous kinetic energy and a continuous potential energy.

Finally, we illustrate how to extend the APL algorithm to perform simulations in the NVT ensemble. The average temperature, $\langle T \rangle$, during a simulation is calculated as

$$\langle T \rangle = 2 \left\langle \frac{T^{\text{AP}}}{D} \right\rangle \quad (12)$$

where $\langle \dots \rangle$ denotes a phase space average, and D is the effective number of degrees of freedom of the system for a specific configuration (time) that is calculated as

$$D = 3N + 3AM + 3K + 3 \sum_{\alpha=1, \dots, K} S_{\alpha}(A - 1) \quad (13)$$

We note that the temperature is configuration-space dependent since the kinetic energy is explicitly dependent on coordinates. The AP Hamiltonian, eq 11, is quadratic in the conjugate momenta, so that we can, for example, use the Berendsen thermostat²⁸ to perform simulations in the NVT ensemble and scale all momenta, p_i , according to

$$p_i^{\text{new}} = \sqrt{1 + \frac{\Delta t}{\tau} \left(\frac{T_{\text{desired}}}{T_{\text{instantaneous}}} - 1 \right)} p_i^{\text{old}} \quad (14)$$

where Δt is the time step, τ is a coupling parameter, and T_{desired} and $T_{\text{instantaneous}}$ are the desired and instantaneous temperature of the simulation, respectively.

The main difference between the new APL method and previous mixed resolution algorithms^{7–18} is that we define a single Lagrangian for a mixed-resolution system that allows for a change in resolution of selected groups of atoms instead of defining multiple Hamiltonians or force fields (that possess different resolutions) for different areas in space that are connected by boundary conditions. In addition, the phase

space dimensionality of a system is constant during an APL simulation and equal to the all-atomistic phase space dimensionality. Only the number of interaction sites and degrees of freedom are reduced and vary during an APL simulation. Unlike previous mixed-resolution methods, the APL scheme is therefore currently the only algorithm that solves the Euler–Lagrange equations of motion for a mixed-resolution system and that can be easily extended to any thermodynamic ensemble. The main disadvantage of the APL scheme is the need to define a mixed-resolution potential energy functional that uses the same reference state for the zero of energy for both the coarse-grained and atomistic part of the potential energy functional. In contrast, in the AdResS method the zero of energy can be defined independently for the coarse-grained and atomistic force fields.

In conclusion, we have derived a Hamiltonian and presented a simulation protocol for mixed-resolution systems that allows for a change in resolution of selected groups of atoms during a simulation. An NVE simulation protocol with this Hamiltonian conserves kinetic and potential energy and angular and linear momentum. For systems that require atomistic resolution only for a small part or parts of the simulation system, the APL algorithm permits a simulation with accuracy comparable to an atomistic one at the computational cost of a coarse-grained one.

As an application of this novel algorithm we are currently studying the structure and diffusion of hexane molecules surrounding a water molecule.

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Supporting Information Available: Derivation of the mixed-resolution Hamiltonian; conservation of energy and linear and angular momentum; constraints on low-resolution group coordinates and Newton's third law; generalized leapfrog algorithm for mixed-resolution simulations; and references. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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