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Non-periodic Molecular Dynamics simulations of coarse grained lipid bilayer in water

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ABSTRACT

We present a multiscale algorithm that couples coarse grained molecular dynamics (CGMD) with continuum solver. The coupling requires the imposition of non-periodic boundary conditions on the coarse grained Molecular Dynamics which, when not properly enforced, may result in spurious fluctuations of the material properties of the system represented by CGMD. In this paper we extend a control algorithm originally developed for atomistic simulations [3], to conduct simulations involving coarse grained water molecules without periodic boundary conditions. We demonstrate the applicability of our method in simulating more complex systems by performing a non-periodic Molecular Dynamics simulation of a DPPC lipid in liquid coarse grained water.

1. Introduction

Interfaces between biomembranes and water are significant components of living cells because biological processes, such as ion exchange and neural signal transmission, take place in the proximity of these interfaces. Understanding their structural characteristics and their dependence on surrounding biomolecules and nanoscale flows will be the key to emerging fields such as single-molecule medicine and nanotechnology based medical applications. Studying relevant systems is usually hindered by their complexity. All-atom models are computationally expensive, therefore coarse grained models have been proposed [1] to access larger length and time scales. However, these coarse grained models are subject to periodic boundary conditions (BCs). Non-periodic BCs are often more appropriate in cases where the nanoscale domain interfaces a microscale flow or in cases where biomolecules are transported electrophoretically through membranes [2]. An approach is thus needed to couple mesoscopic descriptions to continuum ones. This coupling is achieved by using the control algorithm developed by Kotsalis et al. [3] and shows its applicability for liquid water in its coarse grained description.

2. Methodology

The atomistic region is described by Molecular Dynamics (MD) simulations subject to non-periodic boundary conditions. The position $\mathbf{r}_i = (x_i, y_i, z_i)$ and velocities $\mathbf{v}_i = (u_i, v_i, w_i)$ of the ith particle evolve according to Newton's equation of motion:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbf{r}_i = \mathbf{v}_i(t)$$

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$$m_i \frac{\mathrm{d}}{\mathrm{d}t}\mathbf{v}_i = \mathbf{F}_i = -\sum_{j\neq i} \nabla U(r_{ij}),$$

where m_i is the mass and $\mathbf{F}_i$ the force on particle i. The interaction potential $U(r_{ij})$ models the physics of the system. In the case of pure bulk coarse grained water (CGW) we consider:

$$U(r_{ij}) = U_{12\text{-}6}(r_{ij}) + U_m(r_w),$$

where $U_{12\text{-}6}$ is the 12–6 Lennard–Jones (LJ) potential:

$$U_{12\text{-}6}(r_{ij}) = 4\epsilon\left[\left(\frac{\sigma}{r_{ij}}\right)^{12} - \left(\frac{\sigma}{r_{ij}}\right)^{6}\right], \tag{1}$$

and r_{ij} denotes the distance between the i and j atom, and σ and ϵ are the length and energy scales of the LJ potential (for CGW: $\epsilon = 5.0\,\mathrm{kJ\,mol^{-1}}$ and $\sigma = 0.47\,\mathrm{nm}$ [1]). The term $U_m(r_w)$ accounts for the interaction of the mesoscopic region with the surrounding continuum medium. It depends on the distance to the outer boundary of the atomistic domain r_w [5]. In hybrid algorithms, the elimination of periodic boundary conditions in the atomistic domain hampers the maintenance of a uniform density across the domain. The potential U_m replaces the missing interactions for the particles close to the mesoscopic–continuum interface. The equations of motion are integrated using the leap-frog scheme with a time step of 20 fs.

3. Results

3.1. Coarse grained water

We examine the validity of the method for the case of water, namely ($T = 300\ K$, $\rho = 1.0\ \mathrm{g\,cm^{-3}}$). The size of the computational domain is 5 nm × 5 nm × 5 nm. The periodicity is broken only in the x direction. The system is weakly coupled to a Berendsen thermostat [4] with a time constant of 0.1 ps. All the potentials are truncated smoothly after a cutoff r_c of 1.2 nm [1].

In this paper we apply the method proposed by Kotsalis et al. [3]. We develop a mean external boundary force using a control algorithm to minimize the density perturbations in the MD system subject to non-periodic BCs. The control approach is sketched in Fig. 1. An iteration progresses as follows: we start by applying no external boundary force. Then we measure the density in short time intervals filtering away the noise. This improves the convergence of the method and makes it more suitable for coupling the mesoscopic to the continuum description. The density $\rho^{m'}$ is measured with a spatial resolution δx of 0.04 nm in time intervals of 4 ps and processed twice through a Gaussian filter. We then obtain ρ^m as:

$$\rho^{m''}(x) = \frac{1}{\epsilon}\int \rho^{m'}(x)\exp\left(-\frac{(x-y)^2}{\epsilon^2}\right)\mathrm{d}y$$

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where $\epsilon = 2\delta x$. The cutoff used for the discrete evaluation of the convolution is $3\delta x$ and the filter can be expressed in the following discrete form:

$$\rho_i^{m''} = \begin{cases} \rho_i^{m'} & \text{for } i = 1 \text{ or } i = N \\ 0.3045\rho_{i\pm1}^{m'} + 0.3910\rho_i^{m'} & \text{for } i = 2 \text{ or } i = N-1 \\ 0.1117\rho_{i\pm2}^{m'} + 0.2365\rho_{i\pm1}^{m'} + 0.3036\rho_i^{m'} & \text{for } i = 3 \text{ or } i = N-2 \\ 0.0301\rho_{i\pm3}^{m'} + 0.1050\rho_{i\pm2}^{m'} + 0.2223\rho_{i\pm1}^{m'} + 0.2854\rho_i^{m'} & \text{for } 4 \le i \le N-3 \end{cases}$$

where N is the number of the measured density values.

We then evaluate the error as:

$$e(r_w) = \rho^t - \rho^m(r_w), \tag{2}$$

where r_w is the distance to the boundary, ρ^t the desired constant target density and ρ^m the measured filtered value. We compute the gradient of this error as $\epsilon(r_w) = \nabla e(r_w) = -\nabla\rho^m(r_w)$ and amplify this with a factor K_i^P to obtain the adjustment ΔF to the boundary force as:

$$\Delta F_i = K_i^P \epsilon_i,$$

for each ith bin, where $K^P(r_w) = k_p\sqrt{(r_c - r_w)}$. We let K^P depend on the distance from the wall because the magnitude of the density disturbances reduce as the distance increases. The boundary force is finally computed as:

$$F_i^{\mathrm{new}} = F_i^{\mathrm{old}} + \Delta F_i.$$

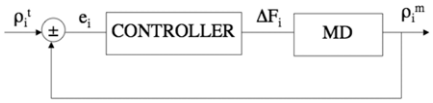

Fig. 1. Sketch of the control algorithm.

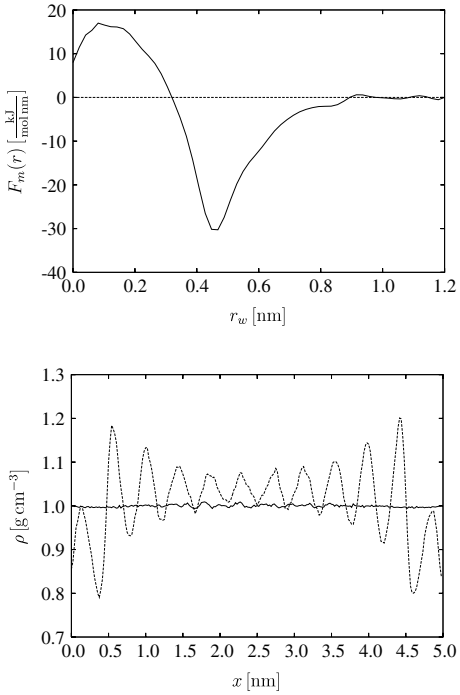

Fig. 2. Top: The resulting external boundary force after applying the control algorithm for a system of bulk liquid CGW at the state point ($T = 300$ K, $\rho = 1.0$ g cm^{-3}). Bottom: The controlled density profile (- - -). The value used for k_p is 2.0 $\frac{\text{nm}^{2.5}\ \text{kJ}}{\text{amu mol}}$ and both the force and density have been sampled over 0.6 ns.

The method has converged [3] approximately after 0.8 ns for a k_p of 2.0 $\frac{\text{nm}^{2.5}\ \text{kJ}}{\text{amu mol}}$ as shown in Fig. 2. The control algorithm eliminates the density disturbances not only close to the boundary but additionally prevents its propagation into the interior of the domain. When periodic boundary conditions are applied, the correspondence between the volume of the domain and the pressure is simple. The density oscillation though due to the incomplete introduction of non-periodic boundary conditions can ruin this relation as it leads to non-bulk properties close to the mesoscopic–continuum interface that could also propagate inside the domain (see Fig. 2). It is therefore more systematic to accomplish the bulk properties on the boundaries accurately when applying non-periodic boundary conditions and avoiding in this way buffer regions [3].

3.2. Validation for the system of lipid bilayer in water

The system (cf. Fig. 3) consists of 26 250 CG water particles (corresponding to $26\,250 \times 4 = 105\,000$ molecules), and 1250 dipalmitoyl phosphatidylcholine (DPPC) molecules. We performed CGMD simulations based on the MARTINI force field. The details on the potential parameters are described in [1]. One CG particle for water correspond to 4 water molecules. One CG DPPC molecular model consists of 12 CG particles, two hydrophilic ones with positive and negative charges, two glycerol ester particles and two hydrophobic chains, each consisting of four CG particles. The system is equilibrated in NPT ensemble using periodic boundary conditions in advance. Here, the Berendsen barostat is applied only in the x direction, i.e., the direction of the membrane thickness. The unit domain lengths in the y and z directions are constant both at 20nm. The resultant system domain configuration is $12 \times 20 \times 20$ nm. The CGW is at the state point ($T = 323$ K and $\rho = 0.97$ g cm^{-3}) in order to be consistent with the simulations presented in [1]. The periodicity is broken in the x direction.

The value of k_p was 4.0 $\frac{\text{nm}^{2.5}\ \text{kJ}}{\text{amu mol}}$ and the control force was updated every 4 ps. In Fig. 4 we show the external boundary force in the controlled and uncontrolled (no external boundary force) cases and the resulting density profiles. After 0.3 ns the method has converged, the controller successfully eliminates the deviations from the target density value and prevents propagation of the oscillation into the interior of the domain.

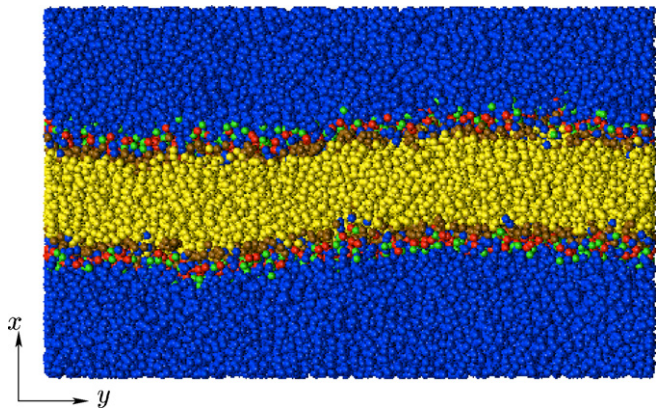

Fig. 3. The DPPC lipid surrounded by CGW.

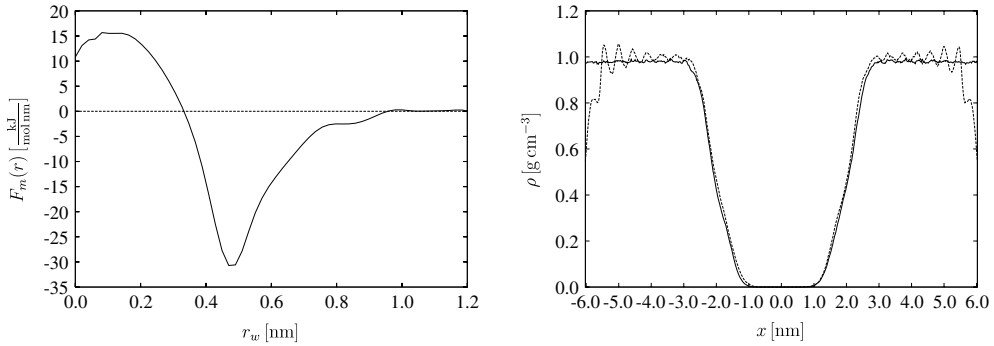

Fig. 4. Here we show the results for the system of the DPPC lipid surrounded by CGW. Left: Zero external boundary force and the resulting one after applying the control algorithm at the state point ($T = 323$ K, $\rho = 1$ g cm^{-3}). Right: The corresponding uncontrolled (—) and controlled density values (- - -). The value used for k_p is 4.0 $\frac{\text{nm}^{2.5}\ \text{kJ}}{\text{amu mol}}$ and both the force and density have been sampled over 0.4 ns.

4. Conclusions

In summary, we have applied a control algorithm [3] to eliminate density fluctuations when conducting non-periodic CGMD simulations of mesoscopic systems. The algorithm is validated for pure CGW at $T = 300$ K at rest and in non-periodic simulations of a DPPC lipid in CGW at $T = 323$ K. The controller eliminates the density perturbations close to the boundary while preserving the structural characteristics of the lipid. The results presented herein demonstrate that the use of the control algorithm seamlessly integrates CGMD and continuum description of complex systems. Current work involves extensive multiscale simulations involving water, fullerenes and lipid bilayers.

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