Classical to Path-Integral Adaptive Resolution in Molecular Simulation: Towards a Smooth Quantum-Classical Coupling

A. B. Poma and L. Delle Site

Max-Planck Institute for Polymer Research, Ackermannweg 10, D 55021 Mainz Germany
(Received 22 February 2010; published 22 June 2010)

Simulations that couple different molecular models in an adaptive way by changing resolution on the fly allow us to identify the relevant degrees of freedom of a system. This, in turn, leads to a detailed understanding of the essential physics which characterizes a system. While the delicate process of transition from one model to another is well understood for the adaptivity between classical molecular models the same cannot be said for the quantum-classical adaptivity. The main reason for this is the difficulty in describing a continuous transition between two different kinds of physical principles: probabilistic for the quantum and deterministic for the classical. Here we report the basic principles of an algorithm that allows for a continuous and smooth transition by employing the path integral description of atoms.

Introduction.—The identification of the minimum number of degrees of freedom necessary to properly describe a physical or chemical process is a key to understanding the essential underlying physics of a system. In particular there are numerous cases where the interesting physics or chemistry occurs in a small subregion which then requires high resolution while the rest of the system can be treated at a coarser level; still the equilibrium between the two regions must be assured by free flux of particles; otherwise, density fluctuations are arbitrarily suppressed and thus create physical artifacts. An illustrative example is that of the solvation of a molecule in water. Around the solute, a solvation shell is formed where the hydrogen bonds must be explicitly described since the bonding network uniquely characterizes the solvation properties. Away from the very first solvation shells, bulk water plays the role of a thermodynamic bath and thus can be described with simpler models (e.g., spheres or continuum [1–3]). However, if a proper open boundary between the high and low resolution region is not defined then there would not be a proper exchange of molecules between the two regions and the solvation process would be biased by the methodological artifact of a rigid boundary. Simulation schemes which allow one to adjust the resolution locally on demand and at the same time keep the equilibrium with the whole system are powerful tools for the problems above; in these approaches the space is partitioned in regions characterized by different molecular resolutions where molecules can freely diffuse changing their representation according to the region where they are instantaneously located. In the last few years several approaches have been presented and they are characterized by different levels of theoretical sophistication and computational complexity [4–9]. However, while the adaptive process can be described in a reasonable way according to the basic principles of classical dynamics and thermodynamics, the same cannot be said when quantum mechanics enters into the game. The practical importance of including quantum mechanics can

be illustrated by the problem of solvation in water discussed before. The question in this case is how much quantum mechanics is needed to properly describe the hydrogen bonding structure of the solvation shells around the solute keeping the rest at a classical or coarse-grained level and allowing for particle exchange. The peculiar quantum nature of the hydrogen leads to a hydrogen bonding network which in a quantum regime is by far more flexible and deformable than that of a classical description. At the same time it plays a key role in the direct solute-water hydrogen bonding with the possibility of proton exchange that often has the key role in water mediated processes, above all for biomolecules [10]. Thus understanding how to adaptively couple a quantum description with a coarser classical one is indeed a central problem in physics. In general, the proper coupling of quantum and classical mechanics is known to be a non trivial (and open) problem (see e.g. [11]) and here the adaptive character adds up as a further major difficulty [12]. In this work we aim to develop an approach where the idea of coupling a classical and quantum molecular model in an adaptive fashion can be made in a way that the "probabilistic-deterministic" discontinuity is removed and yet the adaptivity takes place in a smooth controlled numerical way.

Path integral-polymer ring representation of atoms and molecules.—In this work our quantum systems are composed by atoms described within the path integral formalism by now a standard tool in molecular dynamics (see, e.g., [13]). The important aspect of the path integral approach for this work is that an atom, which is usually represented as a sphere in classical force fields, becomes, within the path integral formalism, a classical "polymer ring" so that the interaction site is delocalized into the beads of such a polymer, each bead of the polymer is linked to its next neighbors along the chain by a harmonic potential. The elastic constant depends on the temperature, T, of the system and the number of beads, n, used to represent each atom, $k = \frac{mn(K_BT)^2}{\hbar^2}$, with k_B being , as usual, the

Boltzmann constant, m the mass of the atom, $\hbar$ Planck's constant. Such a delocalization characterizes the quantum nature of the atom and, given a force field, the nuclear motion is treated in a quantum mechanical way [14–19] (see also the supplementary material [20]). It must be noticed that this is only one way to do path integral and alternative approaches are available (see, e.g., [21]); however, for the development of our idea the polymer ring formalism is what is needed. In fact for the adaptive process the classical polymer representation of atoms has far-reaching consequences, because it translates the quantum-classical *adaptive* coupling into the coupling of two effective classical regions characterized by a different number of (as a matter of fact) "classical" degrees of freedom, so that a molecule passing from one region to another acquires or loses only classical degrees of freedom; thus the whole machinery of classical adaptive methods would apply straightforwardly. This leads to the *relevant* consequence that one can realize the passage from a quantum description to classical one and vice versa within a rather rigorous conceptual framework by simply employing the equilibrium conditions of a classical adaptive scheme. This work represents the numerical proof of the concept above. It must be noticed that this approach applies only to problems where it is sufficient that atoms have quantal nuclear dynamics and not to those problems which require that also electrons must be explicitly treated [22]. Finally, a general problem that our method cannot currently solve is that the coupling of a quantum subsystem to a classical one causes decoherence in the quantum part [25] (see also the supplementary material [20]).

The adaptive scheme.—Regarding the adaptive scheme for the classical case, the basic requirement is a controlled procedure of changing the number of degrees of freedom based on solid physical principles and consistent with the thermodynamic equilibrium of the overall system [26–28]. In this respect the AdResS method meets the requirements above in a (extensively tested) satisfactory way [1,2,29–31]. For this reason in this work the coupling between the polymer rings and the classical particles will be done within the AdResS framework. Below we introduce the basic features of AdResS relevant for this work. In the classical AdResS method the atomistic (high resolution) and the coarse-grained (low resolution) regime are coupled via a force interpolation (see, e.g., [4,12]): $\mathbf{F}_{\alpha\beta} = w(X_\alpha)w(X_\beta)\mathbf{F}^{\mathrm{atom}}_{\alpha\beta} + [1 - w(X_\alpha)w(X_\beta)]\mathbf{F}^{\mathrm{cg}}_{\alpha\beta}$, where α and β indicates two molecules, $\mathbf{F}^{\mathrm{atom}}$ is the force derived from the atomistic force field and $\mathbf{F}^{\mathrm{cg}}$ from the corresponding coarse-grained potential, X is the x coordinate of the center of mass of the molecule and w is an interpolating function which smoothly goes from 0 to 1 (or vice versa) in a transition region (Δ) where the lower resolution is then slowly transformed (according to w) in the high resolution (or vice versa), as illustrated in Fig. 1 (see also the supplementary material [20]). An additional locally acting thermostat is employed to assure the overall thermodynamic
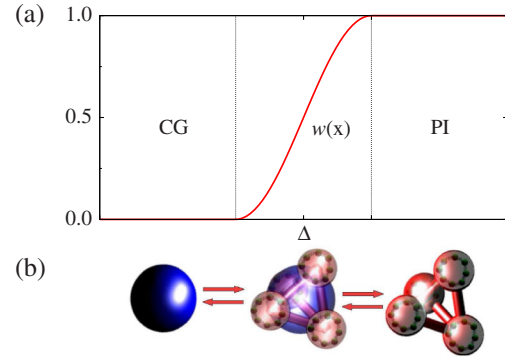

FIG. 1 (color online).   Pictorial representation of the adaptive box and molecular representation. The region on the left, indicated by *CG*, is the low resolution region (coarse-grained), the central part is the transition (hybrid) region Δ, where the switching function $w(x)$ is defined, and the region on the right, indicated by *PI* is the high resolution region (full path integral region).

equilibrium. The coarse-grained potential is obtained from a reference all atom simulation at the given thermodynamic condition via an iterative inverse Boltzmann procedure employing the molecular center of mass radial distribution [32]. For the case of the path integral description we have exactly the same procedure as for the classical case but with the difference that instead of a classical atomistic representation of the molecule we have a molecular representation where the atoms are described as polymer rings in a path integral approach (see Fig. 1). Note that here the corresponding coarse-grained model implicitly contains (in average) "quantum aspects" of the path integral molecule. However the coarse-grained molecule is classical in the sense that does not have the beads delocalization of the path integral description and basically can be seen as an effective, one-site classical force field. However the idea of changing molecular representation is in this case amplified by the very extended reduction of degrees of freedom. A short general discussion about coupling different levels of molecular representation is given in the supplementary material [20]. Given the framework reported above the coupling between the path integral representation and the coarse-grained model occurs via the interpolation according to w between $\mathbf{F}^{\mathrm{pi}}$ acting on the beads of the rings and the $\mathbf{F}^{\mathrm{cg}}$ derived from the coarse-grained potential acting among the centers of mass of the molecules. We tested this idea studying a liquid of tetrahedral molecules whose atomistic model was used in the original development of AdResS [see Fig. 1(b)].

Results of the path integral-coarse-grained adaptive resolution simulation.—We studied a system of a thousand molecules at temperature $T = \frac{T_1}{\sqrt{10}}$, where T_1 is the temperature used in the original work of AdResS and which in the Lennard-Jones units of this Letter (see the note [33] or Ref. [29]) is equal to 1. For the testing purpose we have deliberately chosen the temperature T to be lower than that

employed for the classical simulations in the original
AdResS because it mimics the thermodynamic conditions
of a ''more quantum'' system. We have used $n = 30$ num-
ber of beads which is usually used in simulations with
hydrogen particles (see e.g. [17,34,35]) and thus is a robust
test in the view of later possible applications. Figure 2
reports the radial distribution functions (RDF) and the
density distribution of the AdResS simulation of thousand
molecules compared to a full path integral simulation.
They show that indeed this coupling procedure displays
the desired behavior. In particular, in Fig. 2(b), the com-
parison between the bead-bead radial distribution function
obtained with AdResS in the quantum region and that
obtained from a full path integral simulation shows a
remarkable agreement. This is a very relevant results
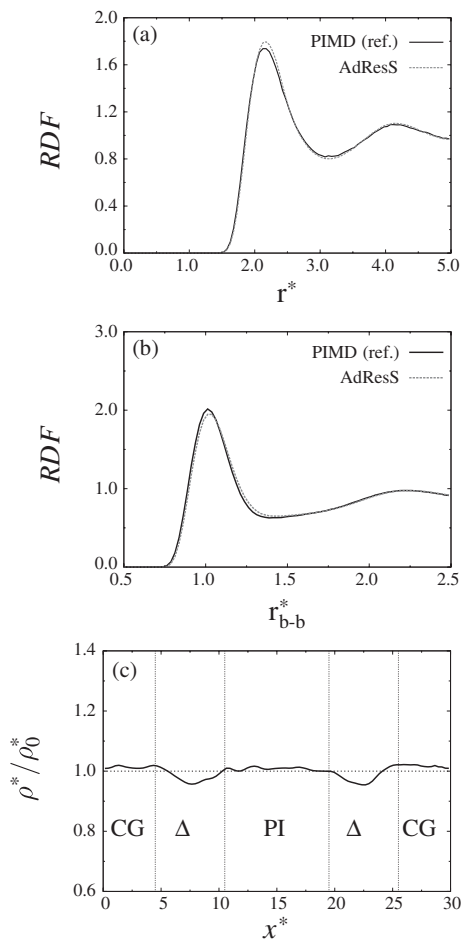from both a conceptual and a technical point of view. In

FIG. 2.   Results for the adaptive simulation of the liquid of
tetrahedral molecules. Top (a), the molecular center of mass-
center of mass radial distribution function obtained with AdResS
is compared with that obtained from the full path integral
reference system,. Middle (b), the bead-bead radial distribution
function obtained with AdResS in the quantum region compared
with that of the full path integral reference system. Bottom (c),
the particle density in AdResS compared with the reference
system. The density is equal to $0.1\sigma^{-3}$ in the units reported in
the note [33].

fact the reduction of degrees of freedom when the molecule
pass from a quantum to a classical description is from 120
to 3 per molecule (and vice versa for acquiring degrees of
freedom), this means that indeed the physical principles
defining the boundary where the molecule change repre-
sentation, and their numerical implementation, are solid
enough to keep the correct quantum behavior in the quan-
tum region and the overall equilibrium in the rest of the
system. Regarding the density in Fig. 2(c), the deviations
with respect to the reference value (above all in the tran-
sition region) are the same obtained in the classical case
[29]. As for the classical AdResS case, one must be sure
that indeed there is exchange of molecules between the two
regimes. In fact it may occur situations where the two
regimes are in equilibrium because some barriers, artifact
of the method, would hinder the free exchange so that the
molecules are reflected back at the transition region.
Figure 3 shows that this is not the case and the molecules
diffuse between the two regions in a proper way.

   Conclusions.—Having proved the validity of the con-
ceptual aspects, it remains to address the question of why
such an approach may be useful for applications and not a
mere conceptual exercise. In part this was discussed before
for the case of water as a solvent and water mediated
process and indeed this is already a rather ample field
[36–40]. However, in general, there is a large amount of
problems in soft condensed matter where relevant proper-
ties are the results of the interconnection between the local
bonding and the larger scale molecular packing. In such
cases classical models may give a satisfactory description
of the large scale packing but are not sufficient for the high
resolution required locally and the path integral description
becomes crucial [41]. For instance, the central question of
diffusion of small additives in polymer matrices. In this
case local cages formed by entangled polymers capture the
additive molecule for a certain amount of time. The knowl-
edge of the physical principles regarding the forming and
rupture of these cages and their average lifetime is essential
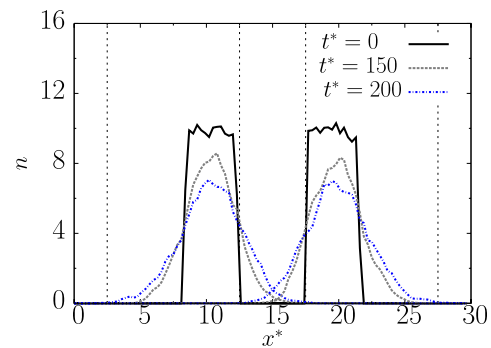to understand the material properties (additives make pol-

FIG. 3 (color online).   Diffusion profile for the molecules mov-
ing from the path integral region to the coarse-grained one and
for molecules moving in the opposite direction. The picture
shows that no barriers, due to possible artifacts of the algorithm,
hinder the diffusion process.

ymeric systems softer). While the overall conformational properties of a polymer system can be rather well described by bead and spring coarse-grained models, the formation of a local cage (similarly to the case of a molecule solvated in water) must be done with explicit chemical details. However, classical atomistic models cannot describe the full flexibility of the additive-polymer and polymer-polymer bonds and thus can give only a very partial description of the cage effects, missing the (most likely) crucial quantum effects. In this case the scheme proposed here would be ideal. In general, as for the classical case of AdResS, the proof of validity of the concept (i.e. this work) is the most important step towards the realization of the applicative studies mentioned above, in any case it is needless to say that this is only a first step towards the development of a generic scheme for *adaptive* quantum-classical coupling and serve also as a basis for further work regarding the conceptual aspects.

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