# A coupled molecular-continuum hybrid model for the simulation of macromolecular dynamics

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We describe a hybrid simulation method that captures the combined effects of molecular and hydrodynamic forces which influence macromolecules in solution. In this method, the solvent contribution is accounted for implicitly as the Navier-Stokes equations are solved on a grid using a finite volume method, while we use coarse-grained molecular dynamics to describe the macromolecule. The two systems are coupled by a dissipative Stokesian force. We show that our method correctly captures the hydrodynamically enhanced self-diffusion of a single monomer for different fluids and grid sizes. Moreover, the monomer diffusion does not depend on the monomer mass for the mass range used, as postulated by polymer dynamics theories. We also show that the dynamical properties of the chain do not depend on the grid size $a$ when the chain radius of gyration $R_g \gg a$.

*Keywords*: Macromolecular dynamics; simulation; hybrid coupled models

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## 1. Introduction

Understanding the dynamics of macromolecules in solution is a prerequisite in order to unveil and comprehend the properties and mechanisms that regulate a wide variety of physical systems (polymers, liquid crystals, self assembled structures, etc.), which are commonly referred to as soft-matter. In fact, for such systems, macroscopic properties are affected and sometimes dictated by underlying microscopic, molecular processes[1]. This not only poses the difficult theoretical problem of linking the microscopic behaviour to macroscopic quantities, but also presents a real challenge when simulating such systems, as the time and space scales involved can

easily span a range between femtoseconds and microseconds or more, i.e. at least nine orders of magnitude.

For the case of macromolecules in solution, the greater part of the computational time is spent simulating the less interesting part of the system, i.e. the solvent molecules, which mediate long range hydrodynamic interactions. Therefore, fully atomistic simulations of such systems, when possible, are bound to be computationally very expensive. However, on one hand theoretical work has provided a simple description of macromolecules, as it is demonstrated that for a wide range of dynamical properties at the physical scales we are interested in, the dynamical description is not affected by chemical details (i.e. it is "universal")[2], effectively eliminating many atomistic degrees of freedom for a wide class of systems and physical scales[2]. On the other hand, hybrid models can reduce the computational cost of the solvent. Ahlrichs and Dünweg [3] coupled the dynamics of a polymer chain to a lattice Boltzmann hydrodynamic solver which allowed an implicit solvent description able to retain the hydrodynamic interactions. The same objective was obtained by Padding and Louis[4] who investigated colloidal suspensions using Stochastic Rotational Dynamics (SRD).

In this work, we present an implicit solvent method based on the approach of Ahlrichs and Dünweg[3] but using a solver for the fluctuating hydrodynamics equations. This model allows the simulation of the dynamics of macromolecules in solution at larger scales because the solvent is accounted for implicitly. The fluctuating hydrodynamics equations are solved on a grid using a finite volume method[5], and the resulting velocity field coupled with the dynamics of the macromolecule[6], which is computed using standard MD techniques. This leads to a simulation speed increase of up to an order of magnitude, depending on the system studied and on the method employed to resolve the velocity field.

This approach can be used to study a variety of physical systems, such as semiflexible polymers, copolymer, dendrimers and so on. The computational cost of solving the hydrodynamic equations is largely dependent on the fluid mesh size but care must be taken in order to calculate the dynamics without introducing spurious effects[3]. The present paper also elucidates this procedure. The paper is organized as follows: in Section 2 we describe the model and provide details of the simulation parameters used, in Section 3 we discuss some results obtained from simulation performed on fully flexible polymers and Section 4 contains our conclusions.

## 2. The model

We integrate the fluctuating hydrodynamics (FH) equations [7] for an athermal compressible fluid over a cubic lattice using a finite volume discretization method as proposed by De Fabritiis et al. [5] for the FH equations

$$
\begin{aligned}
\partial_t \rho &= -\partial_\beta g_\beta, \\
\partial_t g_\alpha &= -\partial_\beta \left( g_\beta v_\alpha + \Pi_{\alpha\beta} + \widetilde{\Pi}_{\alpha\beta} \right),
\end{aligned}
\tag{1}
$$

where summation is implied over repeated indices, $\rho(\mathbf{r}, t)$ is the density field of the fluid, $v_\alpha(\mathbf{r}, t)$ is the continuous velocity field in the component $\alpha$ and $g_\beta(\mathbf{r}, t) = \rho(\mathbf{r}, t) v_\beta(\mathbf{r}, t)$ is the momentum field. $\Pi_{\alpha\beta}(\mathbf{r}, t)$ and $\widetilde{\Pi}_{\alpha\beta}(\mathbf{r}, t)$ are respectively the average (Navier-Stokes) and fluctuating stress tensor fields. The average stress tensor is defined as

$$\mathbf{\Pi} = (p + \pi)\mathbf{1} + \overline{\mathbf{\Pi}}, \tag{2}$$

where $p$ is the thermodynamic pressure given by the equation of state for the fluid, $\pi = -\zeta \partial_\gamma v_\gamma$ and $\overline{\Pi}_{\alpha\beta} = -\eta \left( \partial_\alpha v_\beta + \partial_\beta v_\alpha - 2D^{-1} \partial_\gamma v_\gamma \delta_{\alpha\beta} \right)$ where $\eta$ and $\zeta$ are the shear and bulk viscosity respectively and $D$ is the spatial dimensionality. The fluctuating stress tensor field $\widetilde{\Pi}_{\alpha\beta}(\mathbf{r}, t)$ is a random Gaussian matrix with zero mean and correlations given by

$$\langle \widetilde{\Pi}_{\alpha\beta}(\mathbf{r}_1, t_1) \widetilde{\Pi}_{\delta\gamma}(\mathbf{r}_2, t_2) \rangle = 2k_B T C_{\alpha\beta\gamma\delta} \delta(t_1 - t_2) \delta(\mathbf{r}_1 - \mathbf{r}_2), \tag{3}$$

where $C_{\alpha\beta\gamma\delta} = \left[ \eta(\delta_{\alpha\delta}\delta_{\beta\gamma} + \delta_{\alpha\gamma}\delta_{\beta\delta} + (\zeta - \frac{2}{D}\eta)\delta_{\alpha\beta}\delta_{\delta\gamma} \right]$, $k_B$ is the Boltzmann constant and $T$ is the temperature. his method allows us to impose an equation of state for the fluid and boundary conditions such as a Couette and Poiseulle flow, which are necessary in order to study rheological properties of complex fluids such as mixtures of fluids and macromolecules (i.e. polymers in a solvent). Fluctuations are included according to the Landau formalism and are thermodynamically consistent. Moreover, transport coefficients such as shear and bulk viscosities, which heavily influence macromolecular dynamics, are input parameters. This permits us to investigate the dynamics of macromolecules over a wide range of viscosities. All quantities are reported in $[l] = \text{Å}$, $[\text{m}] = g/mol$, $[\text{T}] = \text{Kelvin}$ and $[\text{E}] = Kcal/mol$ unless otherwise stated. We note that the time unit is a derived quantity and is equal to 48.8 femtoseconds. For water at $T = 300K$ and $p = 1$ atm, we set shear and bulk viscosities to $\eta = 2.6$, $\zeta = 6.2$ respectively for water solvent and use periodic boundary conditions[8].

We focus here on the dynamics of fully flexible polymers modelled as a set of Lennard-Jones (LJ) monomers

$$V_{LJ}(r) = \begin{cases} 4\epsilon[(\frac{\sigma}{r})^{12} - (\frac{\sigma}{r})^6 + \frac{1}{4}] \ r \le r_{cut}; \\ 0 \ r > r_{cut} \end{cases} \tag{4}$$

where $\sigma$ and $\epsilon$ are respectively LJ length and energy units. $V_{LJ}(r)$ is truncated at a cutoff radius $r_{cut}$, depending on the solvent quality modelled, and is shifted by a factor $1/4$ to avoid an energy discontinuity when $r_{cut}$ equals the potential minimum[9]. We set $r_{cut}$ to $V_{LJ}(r)$ minimum ($r_{cut} = 2^{1/6}\sigma$) when mimicking good solvent conditions, i.e. the potential is only repulsive, whereas an attractive tail is added when simulating poor solvent conditions.

A spring potential is introduced to model chain connectivity

$$V_b(r) = \frac{1}{2} K_b (r - b)^2 \tag{5}$$

where the spring constant $K_b = 0.8$ is chosen large enough to limit the fluctuations in the polymer radius of gyration to less than 20 per cent. The bond length $b = 0.6\sigma$ is chosen to match the static scaling exponent $\nu = 0.588$[10].

Due to the hybrid nature of this model, it is convenient to use the same units for MD and FH. Therefore, we must choose appropriate MD mass, length and time parameters according to our units system. This requires a deeper understanding of the coarse graining procedure that allows macromolecules to be modelled as a collection of LJ-interacting beads connected by a spring[11]. We use the chemical formula of a standard polymer, polyethylene, to coarse-grain $3 - 4$ repeat units as a single bead, which we refer to as a "monomer". Atomistic MD forcefields like CHARMM are used to estimate an excluded volume parameter for such a monomer. We therefore choose $\sigma = 15\mathring{A}$, and $m = 50 - 100$ a.m.u. The same estimates can be found in the literature[12]. We set $\epsilon = 1.2 k_b T$ where $k_b T = 0.6 Kcal/mol$ at 300 K. The equations of motion are integrated using the velocity Verlet algorithm. It is important to stress that the timestep used to integrate the fluctuating hydrodynamics equations can differ from $\delta t$. Here, we set the two integration timesteps $\delta t = 10$ femtoseconds.

Finally, the coupling between MD and FH is implemented following the model of Ahlrichs and Dünweg[6]. Each monomer is a point-like object which interacts with the fluid via a friction term to represent the viscous force $\vec{F}_i$ exerted by the fluid on monomer $i$

$$\vec{F}_i = -\zeta_b [\vec{v}_i(\vec{r}) - \vec{u}_f(\vec{r})] + \vec{f}, \tag{6}$$

where $\zeta_b$ is the "bare" friction coefficient, $\vec{v}_i(\vec{r})$ and $\vec{u}_f(\vec{r})$ are respectively the velocity of the monomer and the fluid at position $\vec{r}$ and $\vec{f}$ is a stochastic force [6]. The fluid velocity at position $\vec{r}$, $\vec{v}_i(\vec{r})$ is calculated using linear interpolation of grid point velocities[3]. The same interpolation scheme is used to transfer the same force from the monomer to the fluid, so ensuring the conservation of total momentum in the system.

A key parameter in the model is the grid spacing size $a$, for the following reasons.

1) $a$ influences the effective diffusion of a monomer coupled to the fluid, as the effective monomer friction is[3]

$$\frac{1}{\zeta_{eff}} = \frac{1}{\zeta_{bare}} + \frac{1}{g\eta a} \tag{7}$$

where the factor $g$ takes into account the grid geometry[3]. In other words, the effective friction is the sum of a (first) term related to the Brownian motion due to uncorrelated collisions with fluid particles, and a (second) term which takes into account the hydrodynamic velocity field. One goal of the present paper is to measure the factor $g$ once and for all. Eq.7 can also be considered as a first check on the correct implementation of the method.

2) $a$ is also the minimum scale at which hydrodynamic interactions can be resolved. The Navier-Stokes equations cannot realistically be expected to extend to grid cells which contain only a few tens of water molecules. On the other hand the

dynamical modes of macromolecules can extend down to very small, monomeric, length scales. In order to investigate the influence of hydrodynamic interactions on the dynamics of macromolecules it is therefore necessary to strike a balance between these two conflicting considerations. Ahlrichs and Dünweg choose[3] $\sigma = b = a$, Padding and Louis[4] $\sigma = 2a$ (for stochastic rotation dynamics simulations of colloids). Here we show that, at least for polymer dynamics, a less conservative $a = k\sigma$, $k \sim 2$ definition can be safely adopted for long chains.
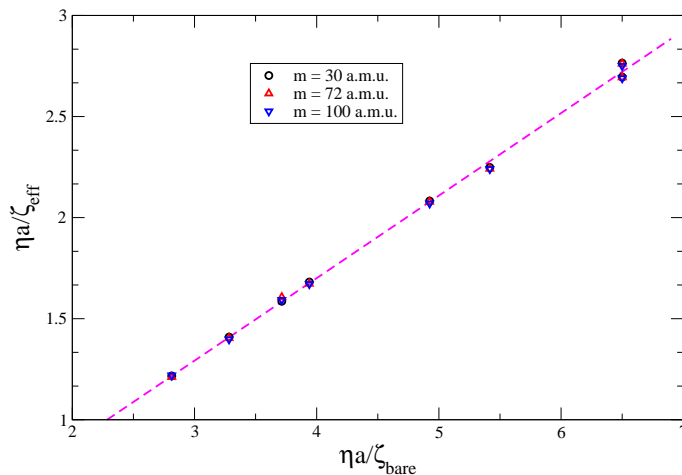
## 3. Results



Fig. 1.   Plot of nondimensional bare (effective) monomer diffusivity versus dimensionless viscosity. We use different viscosities ($\eta = 0.27, 2.6$) and grid sizes ($a = 15, 20, 25\text{Å}$) to test eq. 7 . The agreement with eq. 7 is remarkable with $g = 45$.

We calculate the mean-square displacement $< \vec{r}(t)^2 - \vec{r}(0)^2 >$ of a monomer with different values of the bare friction $\zeta_b$. The monomer is embedded in a $500\text{Å} \times 500\text{Å} \times 500\text{Å}$ fluid box with periodic boundary conditions imposed in all 3 spatial directions. We set temperature $T = 300K$ and pressure $p = 1$ atm and derive the effective friction coeffient $\zeta_{eff}$ via the relation $< \vec{r}(t)^2 - \vec{r}(0)^2 >= \frac{k_b T}{\zeta_{eff}} t$.

We plot in fig. 1 the simulation results for different monomer masses, fluid types (viscosities) and grid size (see caption for details). The agreement with eq. 7 is excellent, leading to a value $g = 45.5$ which is consistent with the result of Ahlrichs and Dünweg[3] and Usta et al.[13], who couple the dynamics of a polymer to a lattice Boltzmann solver. The graph also shows that the effective diffusion does not depend on the monomer mass for the range of masses studied here, in agreement with the situation where the monomer dynamics is primarily influenced by viscous forces.

To estimate the influence of the grid size $a$ on the dynamics of a polymer chain, we plot in fig. 2 the centre of mass diffusion coefficient vs. $a$ for chains with different

degrees of polymerization $N = 30, 50, 100$ embedded in a $125 \times 10^6 \mathring{A}^3$ cubic water simulation box. The graph shows how the dependence of the diffusion coefficient on $a$ decreases as the number of monomers in a chain $N$ increases. It is clear that, for the range of $a$ employed here, the diffusion of chains with $N > 50$ is correctly described also when using the biggest mesh size $a = 25 \mathring{A}$. In our simulations, $b = 15 \mathring{A}, \sigma = 10 \mathring{A}$, therefore for $N > 50$ chains a bigger grid size can be used, $a \sim 2\sigma$. This is because for bigger chains, the high $k$ hydrodynamic modes play a smaller role, at least regarding chain diffusion, as the chain gets bigger. In other words, cutting off the hydrodynamic modes for $\tilde{k}_a \geq \frac{2\pi}{a}$ is equivalent to restricting the modes to a range of $a$ for which $\tilde{k}_a << \frac{2\pi}{R_g}$, where $R_g$ is the polymer radius of gyration. Our results show that this is the case when $R_g > 3a$ at least. Our assessment is consistent with the value of $R_g > 5a$ suggested by Usta et al.[13].
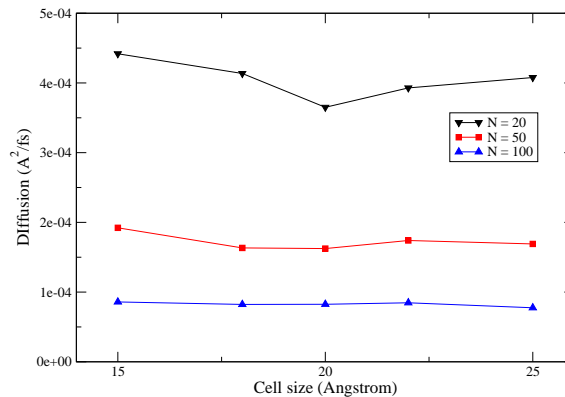


Fig. 2.   The diffusion coefficients for $N = 20, 50, 100$ polymers in a $125 \times 10^6 \mathring{A}^3$ cubic water box for different values of grid spacing $a = 15, 20, 25 \mathring{A}$. The diffusion constants do not depend on $a$ for $N > 50$.

We provide further evidence by studying the collapse time of a polymer which undergoes a coil to globule transition as a consequence of quenching from good to poor solvent conditions[14]. We plot in fig. 3 (bottom panel) the radius of gyration $R_g$ vs. time for an $N = 300$ polymer which is at equilibrium in good solvent (snapshot A in fig. 3 ) at time $t = 0$. As the solvent quality is changed from good to poor (i.e. $r_{cut}$ is greater than the minimum value of $V_{LJ}(r)$), the radius of gyration decreases with time very rapidly until it is not possible for the polymer to shrink any further (see snapshot in fig. 3). The chain assumes a spherical collapsed state for which all monomers are closely packed at the maximum theoretical density $\rho = \frac{N^3}{4\pi R_g^3}$. We perform different simulations from the same initial configuration, changing the mesh size $a$. In the top panel, we plot the time for total collapse $\tau_c$ (defined as in

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Kikuchi et al.[15])

$$R_g(\tau_c) = \frac{(R_g(0)- <R_g>_{eq})}{100} + <R_g>_{eq} \tag{8}$$

where $<R_g>_{eq}$ is the averaged radius of gyration for the collapsed state. The collapse time for the chain is clearly not affected by the grid sizes we have used ($a = 15, 20, 25\mathring{A}$). So we conclude that it is generally safe to set the grid size $a$ greater than the macromolecule parameters $\sigma$ and $b$ in order to correctly capture the main dynamical features, provided that the radius of gyration of the chain $R_g \gg a$. The $R_g > 3a$ estimate trivially holds here for an $N = 300$ chain. We also want to point out that this simulation method can be applied to different systems and physical processes. In the present case (fig. 3) we focus on the scaling of the collapse time $\tau$ with degree of polymerization $N$, which is a currently debated theoretical problem[12]. In the immediate future, we plan to study less theoretically resolved systems such as semi-flexible polymer chains and dendrimer dynamics. We also want to stress the computational speed-up of this method. For instance, solvating the polymer chain with $N = 300$ requires over a million particles with a much larger computational cost. In order to observe the collapse of the same $N = 300$ polymer chain, we ran a simulation with explicit solvent for 10 nanoseconds. This required 64 processors for around 20 hours, whereas 40 hours on a single CPU were needed to simulate the same system for the same time using this implicit model, i.e. a computational speed up by a factor of 30.
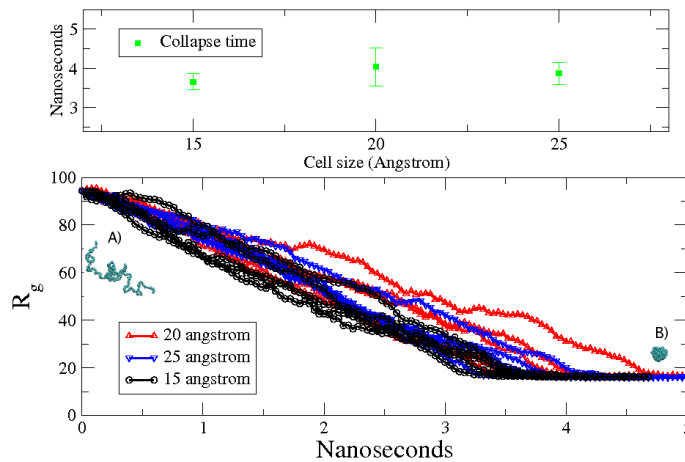


Fig. 3.   (Top) The collapse time $\tau_c$ for an $N = 300$ polymer chain in poor solvent conditions. The collapse time does not depend on the grid size $a = 15, 20, 25\mathring{A}$ used. (Bottom) The radius of gyration $R_g$ vs. time for an $N = 300$ chain undergoing a coil (snapshot A) to globule (snapshot B) transition.

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## 4. Conclusions

In this paper we have introduced a model to simulate the dynamics of macro-molecules in solution. We apply this technique to simulate a fully flexible polymer chain within a solvent. We model the polymer chain as a set of connected coarse-grained monomers, while the solvent is accounted for implicitly by solving the fluctuating hydrodynamics equations on a grid using a finite volume method. The macromolecular dynamics is coupled to the solvent velocity field via a dissipative term. We show that our method correctly captures the hydrodynamically enhanced self diffusion of single monomers for different fluids and continuum fluid mesh sizes. Moreover, the monomer diffusion does not depend on the monomer mass for the mass range we used, as postulated by polymer dynamics theories. We also show that the chain dynamical properties do not depend on $a$ when the chain radius of gyration $R_g$ is much bigger than the mesh size $a$. We propose to use $R_g > 3a$ as a rule of thumb. To demonstrate that the method is well suited for simulation of macromolecular dynamics, we report data for the collapse time for a coil to globule transition of homopolymer in a poor solvent, showing the independence of the collapse time on grid spacing.

## Acknowledgments

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