UNDERSTANDING THE ROLE OF HYDRODYNAMIC FLUCTUATIONS IN BIOMACROMOLECULAR DYNAMICS THROUGH THE DEVELOPMENT OF HYBRID ATOMISTIC-CONTINUUM SIMULATION

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EXECUTIVE SUMMARY

Biological macromolecules are nanoscale structures that largely exist in ionic aqueous conditions. Proteins, in particular, are biopolymers that fold into functional 3D structures that—under the right solvent conditions and, possibly, lipid environment—can perform mechanicochemical work, and whose dynamics span femtosecond timescales (i.e., covalent bond oscillations) to beyond the millisecond regime (e.g., glucose transport across a lipid membrane). Explicit-solvent, atomistic molecular dynamics (MD) is necessary to fully capture solute-solvent interactions but is currently limited to microsecond timescales—orders of magnitude shorter than the timescale range of most processes of biophysical interest, including even the fastest conformational transitions (tens of microseconds). We are developing a hybrid atomistic-continuum (HAC) method—with a view toward biomolecular simulation—coupling an MD engine to a novel discontinuous-Galerkin-based fluctuating hydrodynamics (FHD) solver; our current focus is to develop an FHD model capturing transport phenomena in dense fluids (e.g., water) arising at subnanometer scales.

RESEARCH CHALLENGE

There is growing interest in hybrid multi-physics simulations, where MD is used in a restricted subdomain requiring atomistic resolution, while an efficient FHD model replaces some, or all, of the solvent [1,2]. Nearly all HAC methods employ Landau–Lifschitz Navier–Stokes (LLNS), a system of stochastic equations describing mass, momentum, and energy transport subject to thermal fluctuations in the viscous stress tensor and heat flux vector [3]. LLNS assumes linear constitutive relations: Newton's law of viscosity (stress is proportional to velocity gradients) and Fourier's law (heat flux is proportional to the temperature gradient). Substituting the constitutive relations into the momentum and energy equations leads to second-order spatial derivatives—the LLNS system is semiparabolic—implying, for example, an infinite speed of heat conduction; physically, however, we expect a finite transport speed. Though LLNS has proven a powerful approach to modeling many nanoflows, we expect the aforementioned assumptions to break down for dense fluids when simulation grid cells approach subnanometer dimensions (i.e., a water molecule) and hydrodynamic timescales of interest are comparable to collision times.

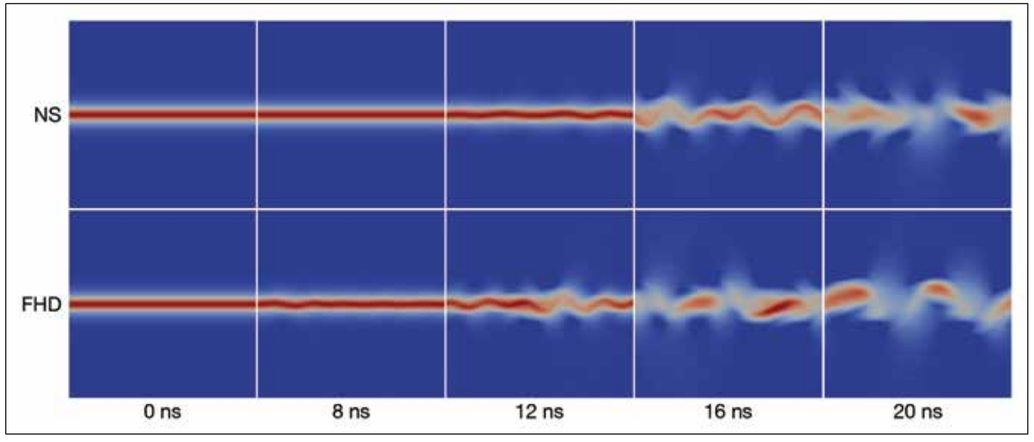

Figure 1: Comparison of rightward horizontal velocities for a simple fluid around water density at STP for: Navier–Stokes (top) and fluctuating hydrodynamics (bottom) over 20 nanoseconds. Blue (red) corresponds to small (large) velocities (0–100 nm/ns). Simulation measures 300 nm per side (30^2 cells) using four-element linear quadrature and second-order Runge–Kutta integration.

METHODS & CODES

Our HAC method currently uses the LAMMPS MD engine and is being developed in concert with a novel FHD model that extends LLNS. Development is currently focused on our FHD implementation, called HERMESHD (Hyperbolic Equations and Relaxation Model for Extended Systems of HydroDynamics), which is based on Grad's 13-moment (G13) approximation [4]. G13 includes additional equations describing time-dependent transport of viscous stresses (tensorial, symmetric/traceless—five equations) and heat flux (vectorial—three equations). Fluctuating terms can be incorporated either as stochastic fluxes in the momentum and energy equations, or as stochastic sources in the stress and heat flux equations. HERMESHD uses a discontinuous Galerkin (DG) spatial discretization of G13 with stochastic sampling performed on a per-cell basis (i.e., not individual DG Gaussian quadrature points). For temporal integration, we leverage FG13's (fluctuating G13) hyperbolic structure to form a split-level, semi-implicit scheme: explicit time advance is carried out with a second- or third-order strong-stability preserving (SSP) Runge–Kutta method, while a locally implicit relaxation method is used to step over the time step constraint imposed by stiff source terms [5,6].

RESULTS & IMPACT

The additional equations in G13 generate hysteresis in stress and heat flux transport, leading to viscoelastic behavior on small spatiotemporal scales; in fluctuating G13 (FG13), stress and heat flux fluctuations, modeled as white Gaussian noise, are thus also subject to memory effects and give rise to colored Gaussian noise. For nanoscale FHD and HAC simulations of dense fluids like water, we expect FG13 to produce transport phenomena that are neglected by LLNS, such as finite-speed thermoacoustic waves, which may have consequences for protein dynamics, especially as recent experiments have demonstrated a connection between heat released during enzyme catalysis and enhancement of diffusion [7].

As a first test of G13-based FHD, we augmented a linearized version of G13 (L13), with appropriate stochastic terms, to construct a fluctuating L13 (FL13) system. The numerical FL13 model was examined for qualitative correctness in the large collision frequency limit (i.e., solutions should relax to ordinary LLNS); Fig. 1 compares simulations with and without the fluctuating terms of an unstable nanoscale hydrodynamic jet for viscous, compressible, isothermal flow. The jet was initialized in a periodic domain with small, random velocity perturbations throughout and simulated until instability occurred. As expected, the jet went unstable in the FHD simulation first, though we have yet to quantify differences in the manner of jet breakup or in the overall flow fields between the two models. This comparison will soon be extended to include FL13 results for moderate collision frequency, and a complete comparison with the full FG13 system is being planned.

HERMESHD has a Python-wrapped library interface to facilitate rapid prototyping, Pythonic data manipulation, and simplified communication with external codes. Our HAC method employs a Python-based driver code to couple HERMESHD to the LAMMPS MD engine, though minimizing MD/FHD code interdependence is a priority. We plan to release the HERMESHD code under the GPLv3 license on Github.

WHY BLUE WATERS

We must verify that our G13-based FHD models reduce to LLNS when appropriate limits are taken and also pass common computational hydrodynamic benchmarks. Blue Waters enables these benchmarks—especially high-resolution 3D simulations that would otherwise create long turnaround times—to be executed quickly without hampering the development process. FHD and HAC model validation requires examining their correspondence to numerical experiments using gold-standard atomistic MD, necessitating large microcanonical ensemble simulations in order to avoid spurious effects introduced by thermo-/baro-statting, to mitigate long-range spatial correlations across periodic boundaries, and to obtain adequate statistical sampling. Furthermore, HAC simulations require matching the continuum region to the atomistic domain through empirical constitutive relations and equations of state, which must be calculated numerically from MD simulations of bulk fluids [8]. The multifaceted nature of our project requires running custom and existing codes as well as post-processing and visualizing diverse data, making access to Blue Waters staff and resources essential.

Sean L. Seyler, a fifth-year Ph.D. student in physics at Arizona State University, is working under the direction of Oliver Beckstein. He expects to receive his Ph.D. in December 2017.