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BEYOND NAVIER–STOKES AND MOLECULAR DYNAMICS: UNDERSTANDING BIOMACROMOLECULAR DYNAMICS THROUGH THE DEVELOPMENT OF MULTISCALE HYBRID AND HYDRODYNAMIC SIMULATION

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EXECUTIVE SUMMARY

Proteins are nanomachines that perform mechanical and/or chemical work dynamics spanning femtosecond timescales (i.e., covalent bond oscillations) to beyond the millisecond regime (e.g., glucose transport across a lipid membrane). All-atom molecular dynamics (MD) can fully capture solute–solvent interactions but is currently limited to microsecond timescales—orders of magnitude short of many biophysical timescales of interest. One viable means of overcoming this timescale problem is the hybrid atomistic–continuum (HAC) method where, for example, MD is used in a subdomain requiring atomistic detail while a hydrodynamic representation elsewhere captures solvent dynamics.

We developed a numerical fluctuating hydrodynamics (FHD) model to extend the regime of applicability of the Landau–Lifschitz Navier–Stokes equations—popular in contemporary HAC methods. Our model can capture nonlinear transport phenomena—e.g., viscoelasticity, thermoacoustic effects, and anomalous transport—that emerge at the nanoscale in liquid water and may be necessary to explain the emergence of collective phenomena in so-called active matter systems.

RESEARCH CHALLENGE

At nanoscale, the behavior of soft-matter is dominated by nonequilibrium dynamics where thermal and sometimes active fluctuations inject energy at the smallest scales. So-called active matter systems, which include collectively swimming bacteria and suspensions of energized colloidal particles [1,2] often exhibit unintuitive behavior such as anomalous (non-Brownian) transport [3,4], flocking [1], or even active turbulence [5]. Active turbulence, for instance, arises in systems at near-zero Reynolds number and is characterized by an inverse cascade of energy upward toward larger spatiotemporal scales (where directed flows emerge spontaneously). Subcellular biology harbors many examples of active matter—e.g., zipping of DNA/RNA hairpins, intracellular transport via molecular motors, and enzyme catalysis—and exhibits collective organization that can span the entire spatial extent of a cell [4,6,7].

The role of fluctuations and transport is essential to the description of active matter, though surprisingly little is known about precisely how such systems produce emergent behavior [3,6,7]. Our long-term goal is to develop a multiscale hybrid simulation method that can bridge the atomistic–continuum gap by combining an MD and efficient FHD (solvent) model that extends the range of phenomena that may be feasibly studied [8,9]. However, our foremost efforts have been devoted to carefully extending hydrodynamic theory and accompanying numerical models to the nanoscale with the idea that our methods may eventually be incorporated in hybrid simulations.

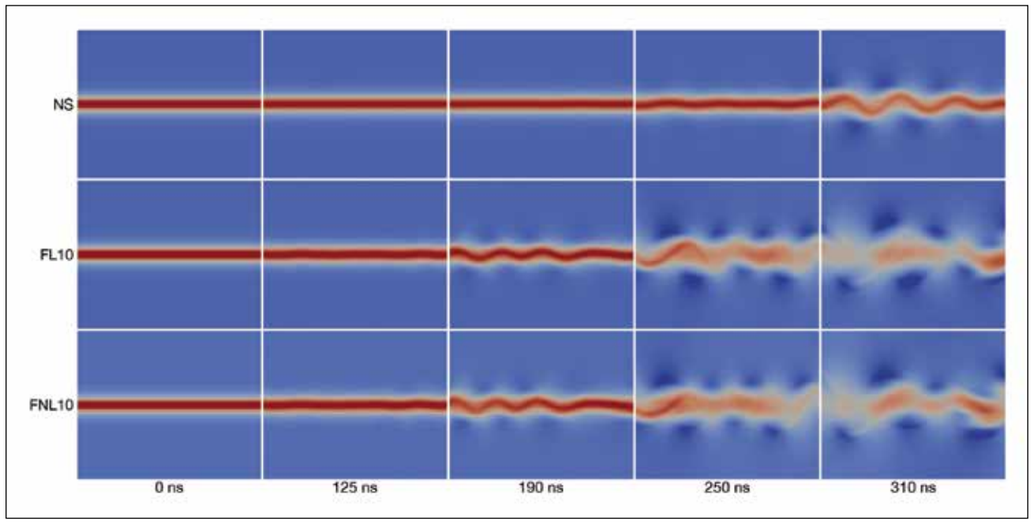

Figure 1: Nanojet comparison for liquid argon (1 bar, 80 K): Navier–Stokes (top), linearized 10-moment FHD (middle), full 10-moment FHD (bottom). Blue (red) corresponds to small (large) velocities (0–100 nm/ns); domain measures 500 μm/side (80 cells). The 10-moment models differ only slightly, while Navier–Stokes takes longer to produce jet breakup.

METHODS & CODES

To construct a HAC method for nanoscale hydrodynamic simulation, it is necessary to augment the Navier–Stokes (NS) equations—a macroscopic hydrodynamic description—with thermal fluctuations [10]. This procedure was first explored by Landau and Lifschitz [11], where stochastic hydrodynamic equations describing mass, momentum, and energy transport were obtained by incorporating fluctuations in the viscous stress tensor and heat flux vector with correlations obeying linear fluctuation–dissipation [8,12,13]. Commonly known as the Landau–Lifschitz Navier–Stokes (LLNS) equations, this model still assumes that hydrodynamic timescales are "long" compared to microscopic collision times, leading to Gaussian white noise fluctuating terms that are spatiotemporally uncorrelated. Though LLNS has proven a powerful approach to modeling many nanoflows, we expect the aforementioned assumptions to break down for dense, inhomogeneous fluids when simulation grid cells approach nanometer dimensions (i.e., several water molecules) and hydrodynamic timescales of interest become comparable to molecular collision times.

We have developed an FHD model that extends the domain of applicability of LLNS. Our implementation is called HERMESHD (Hyperbolic Equations and Relaxation Model for Extended Systems of HydroDynamics) and is inspired by Grad's 13-moment approximation [14]. The principal difference between LLNS and the fluctuating 13-moment (F13) equations is as follows: Whereas LLNS contains the familiar linear constitutive relations of Navier–Stokes—Newton's law of viscosity and Fourier's law (where stresses and heat flux are proportional to, respectively, velocity and temperature gradients)—F13, in effect, promotes these constitutive laws to time-dependent equations describing stress (tensorial, symmetric/traceless—five equations) and heat (vectorial—three equations) transport.

RESULTS & IMPACT

HERMESHD has a Python-wrapped library interface to facilitate rapid prototyping, Pythonic data manipulation, and interfacing with external codes; the code has been made available as open-source code under the MIT license on GitHub. HERMESHD is based on an efficient discontinuous Galerkin spatial discretization and leverages the hyperbolic structure of the F13 equations in a split-level, implicit–explicit scheme: Explicit time advance is carried out with second- or third-order strong-stability preserving (SSP) Runge–Kutta methods, while a locally implicit relaxation method steps over timestep constraints imposed by stiff source terms [15].

Unlike LLNS, the coupling of stress and heat flux equations to the momentum and energy equations in F13 generates memory effects, while thermal fluctuations, modeled as white Gaussian noise, enter through the extended (rather than momentum and energy) equations. As a result of this coupling, F13 naturally gives rise to viscoelasticity, finite-speed thermoacoustic waves, and colored Gaussian noise on small spatiotemporal scales, which may have important consequences for molecular motors and enzyme dynamics; indeed, recent experiments have revealed a connection between heat released during enzyme catalysis and enhancement of diffusion [16].

Previously, HERMESHD had been limited to simulating the 10- and 13-moment linearized equations (with fluctuations); we have since successfully implemented the nonlinear 10-moment equations and are nearing completion of the full (nonlinear) 13-moment model originally proposed by Grad [14] and being developed by others [17,18]. We are currently exploring applications of our numerical models to describing molecular motor efficiency as well as collective protein dynamics.

WHY BLUE WATERS

Proper validation of HERMESHD requires extensive testing against both hydrodynamic test problems and gold-standard atomistic MD simulation, which is particularly computationally expensive in three dimensions. Since HERMESHD uses MPI-based domain decomposition, Blue Waters' nodes facilitate quick execution of such benchmarks. Blue Waters is also ideal for running benchmark MD simulations, which must be sufficiently large microcanonical systems to avoid spurious effects introduced by thermostats and barostats, to mitigate spurious correlations across periodic boundaries, and to obtain adequate statistical sampling. The quality of these data is essential, as empirical relations that enter into FHD simulation must be calculated numerically from MD simulations of bulk fluids [19].

Sean Seyler received a PhD in physics from Arizona State University in December 2017. He worked under the supervision of Oliver Beckstein.