Big Physics in Small Spaces

MODELING what happens to a particle-laden fluid as it travels through the complex channels of a microdevice is not an easy computational task. The dimensions of the device components, such as channel widths, can be nearly as small as the particles themselves. Yet, the details of this fluid flow are important for such applications as designing drug delivery systems, optimizing biosensors, and even determining blood flow.

The difficulties of modeling these flows in confined spaces are a reflection of the scales involved. Several approaches to modeling particle-laden fluid flow exist, depending on the scale to be resolved. For example, continuum models can adequately simulate macroscale properties such as velocity and pressure, while particle methods can simulate individual molecules on the microscale. However, it is difficult to capture both scales in one algorithm that reflects the physics and chemistry of these scales and that runs in a reasonable amount of time—even on a supercomputer.

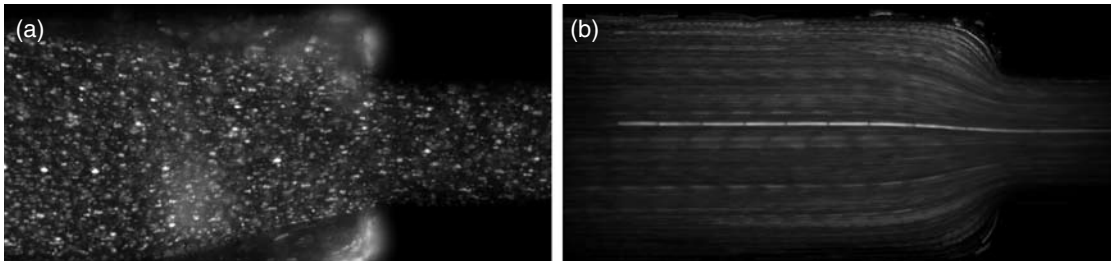
Livermore computational scientist David Trebotich from the Center for Applied Scientific Computing and professor Greg Miller from the University of California (UC) at Davis's Department of Applied Science, along with researchers from Lawrence Berkeley National Laboratory's Applied Numerical Algorithms Group, have developed a multiscale algorithm to better model particle-laden fluid flows. The algorithm can be used to model flow through microscale structures, such as arrays of posts and other complex channels and components inside centimeter-long devices, as well as interactions in biological materials, such as a DNA molecule.

Tiny Flows with Impact

The modeling effort grew out of Trebotich's postdoctoral work at UC Berkeley on microfluidics, in which he explored the fundamental physics of complex flows through microelectromechanical systems (MEMS) devices used in biosensors and drug delivery systems. Trebotich says, "We needed new physical models and advanced numerical algorithms that could accurately simulate the flow of complex fluids containing high densities of biological particles such as DNA in microenvironments."

Livermore's Laboratory Directed Research and Development Program funded Trebotich's project to create a computational design tool for microdevices and components such as those used in pathogen detection systems. "These systems introduce a new flow regime in an already complex biological flow that is not well understood," says Trebotich. "Also, the design and fabrication of bioMEMS devices have been largely a trial-and-error approach. The early devices were certainly not optimal. This project gave us the opportunity to create a computational design tool that would provide critical understanding of the fundamental flow physics in this mostly unexplored regime and provide a predictive capability for designing more advanced microfluidic systems."

Researchers from UC Berkeley's Bioengineering Department performed key validation experiments and proved the hypothesis that a fluid containing even small amounts of long-chain polymers, such as DNA, exhibits both viscous and elastic behavior. "Viscoelasticity is a phenomenon that complicates fluid flow, in general. The difficulty in trying to remove a speck of eggshell from raw egg whites is a practical example of viscoelastic behavior. The eggshell sort of bounces away unless you slowly nudge it toward a surface where there is no flow. If one applies this to macromolecular flow in microdevices where the lengths of the molecules approach those of the flow channels, the behavior becomes even more nonintuitive compared to, say, that of water," says Trebotich. "For instance, if a flow channel contracts sharply, large recirculation zones will appear in the salient corners." If a molecule is caught in such a vortex, it could degrade or possibly break. When the molecule



(a) Experiments show that fluids laden with DNA act in unusual ways when flowing, such as creating large vortices in corners. (b) These behaviors do not occur with plain water. (Images courtesy of Shelly Gulati, University of California at Berkeley.)

reenters the flow near a sensor downstream, it may no longer be identifiable as the original molecule.

The experiments also show that DNA migrates away from regions of high shear, such as close to channel walls, and toward regions of low shear, such as a channel's center. In addition, these molecules stretch out in accelerating flow regions and recoil in decelerating flow or stagnant regions. "This behavior can affect the assumed performance of a biosensor," notes Trebotich. "It's important to be able to not only predict these dynamics in a device for which the objective is to control a biological fluid but also to manipulate and detect biological species in the fluid. Fulfilling these objectives requires using both continuum models to capture bulk properties for flow control and particle methods to represent coarse-grained molecular transport."

Cookie Cutters, Rods, and Beads

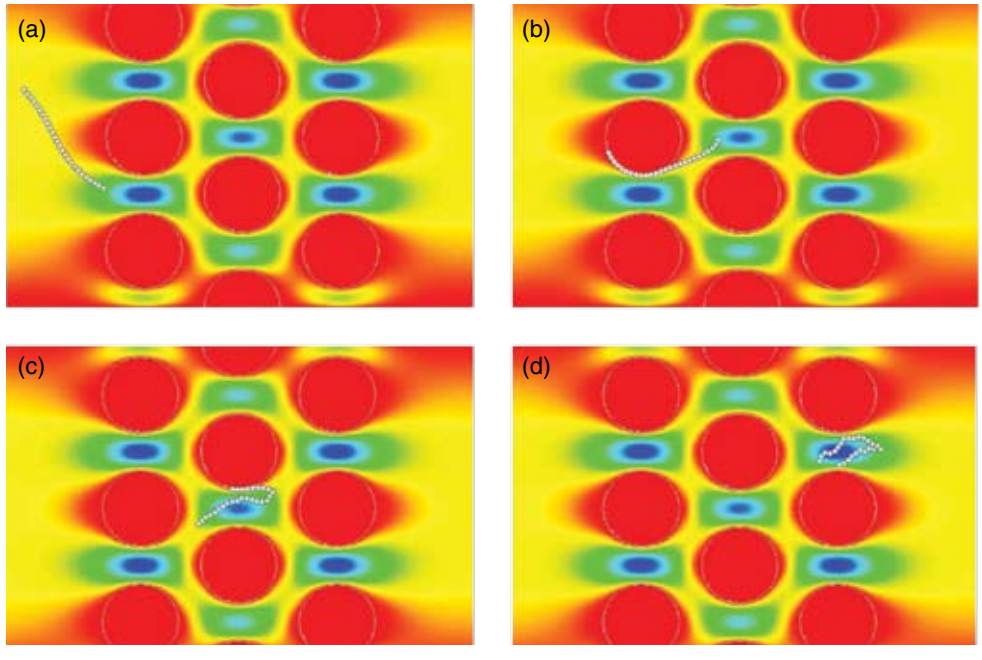
To model the behavior of these unusual flows, Trebotich and Miller created a hybrid fluid–particle numerical algorithm that embraces most scales of interest—from the device scale down to the smallest scale of interparticle interactions. The algorithm is based on discretization of an incompressible Newtonian fluid, such as water, using a high-resolution, finite-difference method. An embedded boundary volume-of-fluid formulation is used near boundaries where the fluid meets structures.

Trebotich and his colleagues chose a finite-difference method on a structured grid because of its simplicity and known numerical properties. However, they found that geometries represented with just squares and rectangles are limited. They then turned to the embedded boundary method, which allows irregular geometries to be represented by overlaying the problem domain on a structured Cartesian grid. In this approach, the irregular boundary of the problem domain cuts through the affected squares on the grid.

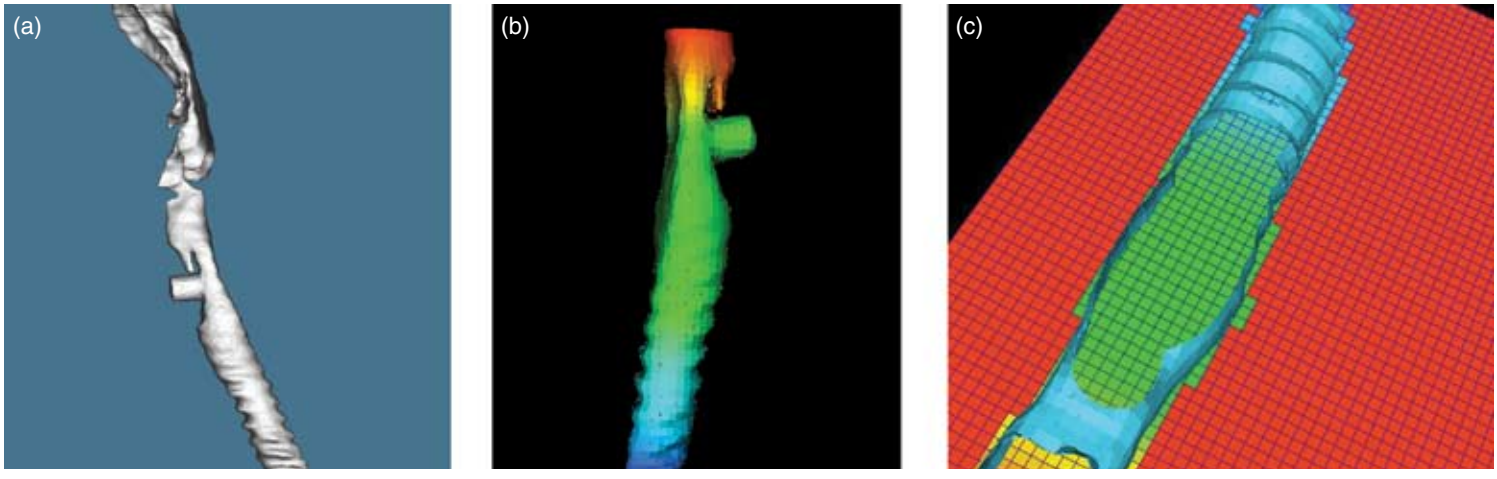
"Think of it," says Trebotich, "as a cookie-cutter approach with the dough spread out on the counter representing a rectangular fluid-flow channel. To represent an obstruction in the flow, such as a post in an array channel, one simply cuts a circle shape out of the dough or domain." The regular grid cells can then be solved with finite-difference methods, and the cut cell can be handled conservatively with a volume-of-fluid approach.

"This approach is an efficient way to solve the problem," says Trebotich. "It uses less computational time than a body-fitted grid approach, particularly when the grid or mesh is moving. The embedded boundary technique itself is specifically intended to enhance parallel scalability and to facilitate adaptive mesh refinement, which focuses computations in areas of interest in the domain. All in all, this approach provides a powerful tool for multiscale, multiphysics computational fluid dynamics."

To represent the DNA and other polymerlike molecules in the fluid, Trebotich and his colleagues use a model of beads connected in a chain by rods or springs. The polymer is then coupled to the fluid through forces representing hydrodynamic drag and stochastic thermal fluctuations. "In this model, the fluid can 'feel' the effects of the polymer molecules, a reverse-coupling mechanism that could prove to be important in simulating more concentrated polymer flows," says Trebotich.



A newly developed algorithm is tested in this simulation of a DNA strand as it flows through an array of posts in a microchannel. (a) The strand begins to wrap around a post. It then is (b) loosened by Brownian and hydrodynamic forces and (c–d) swept through the flow field. Colors show the underlying velocity flow fields: fast (blue) and slow or reversed (red).



(a) A human trachea is shown in this computed tomography scan. (b) Livermore researchers developed a computational tool that uses embedded boundary grids to model fluid flow through a trachea. (c) In this close-up of a three-dimensional simulation, geometric detail is shown in cut cells of a two-dimensional slice.

To increase the realism of the model, the researchers added algorithms that keep the simulated polymers from crossing or "passing through" each other in an unrealistic, ghostlike fashion. "Noncrossing is a constraint frequently ignored in other bead-rod models," says Trebotich. The team developed a novel technique in which the rods elastically bounce off one another without the small time steps typical of particle methods. In a similar way, the model also treats interactions between polymers and surfaces as elastic. "The ability to advance the particles at time steps on the order of the fluid timescale allows us to perform system-level modeling for engineering-scale problems involving particle-laden fluids," adds Trebotich.

Re-creating the Real Thing

The researchers tested their model by simulating a DNA molecule flowing through two microdevice configurations—a microchannel with an array of posts and a small tube packed with microspheres resembling a porous medium. These configurations are similar to those used for extracting DNA in microfluidic-based devices that contain a polymerase chain reaction component. The team used a simple post-array microchannel to hone their algorithm development, model short-range interactions between particles and solid surfaces, and simulate how the rods interact.

"Ultimately, we want to determine if one configuration is better than the other for extracting a molecule," says Trebotich. "In flow-through devices, we want at least one strand of DNA to adhere to a structure so the DNA can be amplified for better signal detection. If the flow rate is too high, the DNA molecule will pass through without being captured. If it's too low, the DNA might not have enough momentum to arrive at the capture point. This effort is an example of how we can help engineers design devices optimized for their purposes."

The algorithms that the team developed are multipurpose. With researchers at Lawrence Berkeley and UC San Francisco, the team examined how realistically its model re-creates flow in a human trachea, which has an intricate anatomical geometry. They used the embedded boundary method to successfully model a trachea from a patient's computed tomography scan, down to the detailed ribbing, where flows can be complex. "The smallest geometric irregularities can alter the flow, causing flow perturbations that other models will not capture if the geometry and mesh obtained from the medical image do not contain enough detail," says Trebotich. "Fluid dynamics can become very complicated when we get down to the details—that is, the smaller scale features." The details are important in certain situations, for example, when a physician needs to know how a tracheotomy procedure could affect the flow of air in a damaged trachea or how a partial blockage in an artery could affect blood flow.

The team's goal is to develop methods to simulate the physics that occur at multiple scales for a variety of flow problems in a time frame that is useful for engineers, physicians, and practitioners in other fields. Trebotich says, "It's an end-to-end endeavor, from model to simulation to analysis, and one that draws on experts in multiple disciplines from throughout the UC system."

—Ann Parker

Key Words: algorithm, biosensor, continuum model, DNA, fluid flow, microchannel, microfluidic device, multiscale computational fluid dynamics, particle model, post array, viscoelastic fluid.

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