Institute of Physics Publishing Journal of Physics: Conference Series **46** (2006) 316–321
doi:10.1088/1742-6596/46/1/044 SciDAC 2006

Modeling complex biological flows in multi-scale systems using the APDEC framework

David Trebotich

Center for Applied Scientific Computing, Lawrence Livermore National Laboratory, Livermore, CA

E-mail: trebotich1@llnl.gov

Abstract. We have developed advanced numerical algorithms to model biological fluids in multiscale flow environments using the software framework developed under the SciDAC APDEC ISIC. The foundation of our computational effort is an approach for modeling DNA-laden fluids as "bead-rod" polymers whose dynamics are fully coupled to an incompressible viscous solvent. The method is capable of modeling short range forces and interactions between particles using soft potentials and rigid constraints. Our methods are based on higher-order finite difference methods in complex geometry with adaptivity, leveraging algorithms and solvers in the APDEC Framework. Our Cartesian grid embedded boundary approach to incompressible viscous flow in irregular geometries has also been interfaced to a fast and accurate level-sets method within the APDEC Framework for extracting surfaces from volume renderings of medical image data and used to simulate cardio-vascular and pulmonary flows in critical anatomies.

1. Introduction

Modeling biological flows such as DNA in solution or blood *in vivo* is a challenge because their constitutive behavior is not easily represented due to the presence of macromolecules in the fluid. For example, a highly concentrated solution of suspended polymer molecules such as DNA may be represented at the system level with a continuum viscoelastic constitutive model. Blood, on the other hand, has been long understood to be "shear-thinning" over a wide range of shear rates, but this understanding becomes tenuous at the microscale when shear rates are large, in which case the fluid is practically Newtonian. Furthermore, when geometry length scales are comparable to the inter-polymer spacing, a continuum approximation is no longer appropriate, but, rather, a discrete particle representation coupled to the continuum fluid is needed. However, fluid-particle methods are not without their issues as stochastic, diffusive and advective processes can result in disparate time scales which make stability difficult to determine while capturing all the relevant physics and electro-chemistry.

CFD methods have been used extensively for modeling flow conditions in idealized representations of vascular structures. Recently, there has been a greater effort to base these predictions on patient-specific conditions. This requires extraction of lumenal surfaces from imaging data, and determination of flow velocities *in vivo*. Methods of surface extraction are limited in their ability to recover the geometry of complex objects like tubular branching structures in real time. Moreover, it is necessary to convert the surface extracted by image processing techniques into a computational domain appropriate for the CFD solver, involving the construction of a mesh on the surface and in the 3D domain that it encloses. Valuable information can be lost during this

construction due to limitations of the CFD solvers with respect to the properties of the surface mesh. It is often the case, for example, that the surface needs to be smoothed in order to build a finite-element mesh necessary to some CFD codes. Failing that, irregular surfaces must be approximated by a large number of small mesh elements, pushing the limits of computer memory. The result in this and other cases is a compromise in the level of accuracy of the surface extraction method.

In this paper we discuss computational solutions to these biological flow problems by leveraging solver and algorithmic capabilities developed in *An Algorithmic and Software Framework for Applied Partial Differential Equations* (APDEC), a SciDAC Integrated Software Infrastructure Center.

2. Technical Approach

Our numerical approach to computational fluid dynamics is high-resolution finite difference methods on adaptive, structured grids with complex geometry capability via embedded boundary / volume-of-fluid methods. The APDEC Framework provides software infrastructure, solvers and exemplary physics algorithms for this methodology as well as support for particles and parallel computing. This CFD strategy provides a powerful high-resolution tool for modeling multi-scale fluid dynamics in complex geometry.

2.1. Modeling of DNA-laden flows

We have taken two approaches to modeling DNA-laden flows in microfluidic devices. Our first approach considered DNA as a long-chain polymer in solution, like a Boger fluid; thus, we modeled it at the continuum level as a viscoelastic fluid described by the Oldroyd-B constitutive equation. This is an acceptable scale to model from a device design perspective as bulk fluid velocities and pressure drops are the key parameters for flow control. We developed a new semi-implicit method based on Lax-Wendroff, with a projection method to enforce incompressibility [1] and a continuous splitting of the viscoelastic terms using Duhamel's formula [6]. The algorithm is convergent and stable for a single CFL condition for the full range of elastic flows, including the benchmark "high Weissenberg number" problem of steady-state viscoelastic flow in 4:1 abrupt contractions, where all other methods have failed for the past 30 years. With this method we were able to perform preliminary validation studies involving low concentration solutions [4].

For the purposes of this paper we focus on a hybrid fluid-particle model that can be used to predict the transport of a discrete molecule like DNA in dynamic fluid environment. Our approach here was to model "bead-rod" polymers whose dynamics are fully coupled to an incompressible viscous solvent [8]. In this algorithm, long chain polymers such as DNA are represented as a chain of nodes separated by fictitious rigid rods. The nodes are subject to forces by the fluid–both viscous Stokes drag and stochastic (thermal, Brownian motion); and the solvent experiences equal and opposite body forces. It is in this sense of obeying Newton's third law of motion that we consider the dynamics to be "tightly coupled". Additionally, the polymer nodes may experience elastic collisions with domain boundaries. With this numerical algorithm, we have been able to simulate polymer-boundary interactions which occur in size-separation and extraction devices (Figure 1). This algorithm promises to demonstrate for the first time the effect of a semi-dilute or concentrated solution of discretized particles on a fluid.

In the freely-jointed ball-rod model we initially implemented, as with many other current implementations, crossing of rod sections is allowed. The resulting behavior has a strong theoretical foundation and is therefore important for algorithm validation, but does not respect the correct non-crossing physical behavior of real molecules. Furthermore, macromolecules like DNA are charged, and chemically active. They interact through screened Coulombic interactions

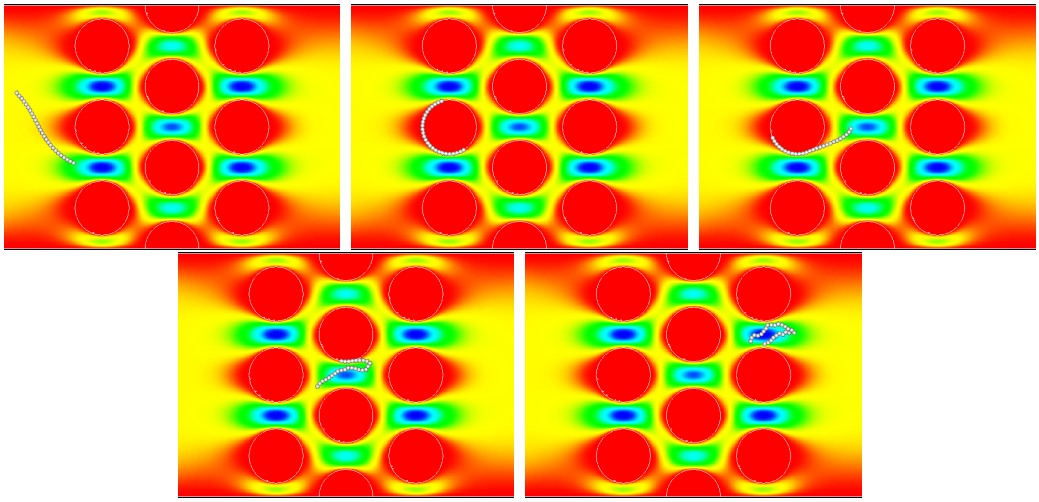

Figure 1. Fluid-particle simulation of genomic DNA in a microfluidic extraction device. DNA molecule enters from left in frame 1, then wraps around post in frame 2, is loosened by hydrodynamic and Brownian forces in frame 3 and is swept out of the chamber by the flow field in frames 4 and 5. Color map indicates underlying flow field, horizontal component of velocity.

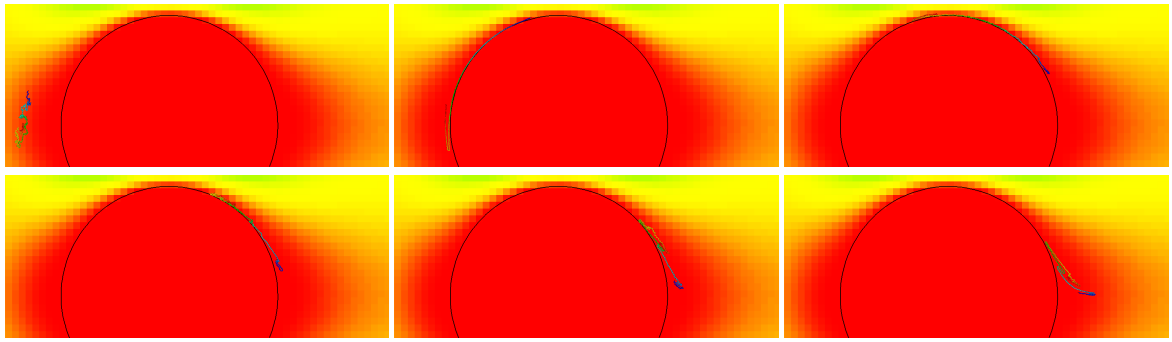

Figure 2. Time sequence of 200-bead polymer model of DNA flowing past a cylinder in 2D demonstrating intra-polymer and polymer-structure interactions using smooth potential. (a) Nearly entangled polymer. (b) Short-range polymer-surface interaction. (c) Acceleration around pillar due to Brownian perturbation and hydrodynamic drag. (d) More acceleration of the tail and slowing of the head in stagnation region in wake of pillar. (e) Accelerated tail catching up with stagnated head. (f) Re-entanglement in wake with multiple intra-polymer interactions.

and migrate in response to imposed electric fields. Microfluidic separators have been designed based on the increase of residence time with molecule length in packed bed geometries, or through chemically-mediated residence time enhancement achieved by binding selective proteins to channel surfaces. These physical effects are characterized by intra-polymer, inter-polymer, and polymer-wall interaction potentials which may be long-ranged. We incorporated these Coulombic interactions into our model using a short-range Debye-Hückel potential. Results for intra-polymer and polymer-structure interactions are shown in Figure 2.

2.2. Implementation of CFD solver in APDEC Framework

In order to implement the particle-fluid model using the APDEC Framework we began with available solvers and algorithmic features needed in the context of a projection method for incompressible viscous flow [1]. Starting with an elliptic solver for the heat equation with Neumann boundary conditions we designed a new solver to accommodate viscous flow boundary conditions, namely Dirichlet [5]. This required a new discretization based on a least-squares approach for determining the flux at an embedded boundary where only a Dirichlet condition is prescribed. The other essential algorithmic feature which we needed for the projection method was a technique for treating the hyperbolic part, or convective derivative, of the equations of motion explicitly, that is a higher-order Godunov method to resolve steep gradients and to maximize the CFL-limited timestep [2]. There are other algorithmic features such as pressure gradient operators and coping with regular and irregular cell discretizations. From here we put the algorithmic pieces and solvers together to form an efficient and accurate scheme for incompressible viscous flow. Without further additions to support particles the code developed from this approach served as the CFD solver for complex geometries extracted from patient-specific anatomical images.

2.3. From image data to surface extraction to simulation

In order to treat complex geometries such as those found in anatomical structures we use an embedded boundary / volume-of-fluid representation of the discretized solution near the boundary. In this approach, the surface is represented by its intersection with an underlying rectangular grid, or a cookie-cutter approach. This leads to a natural, finite-volume discretization of the PDE on irregular control volumes adjacent to the boundary. However, the primary unknowns are assumed to live at the centers of the Cartesian grid control volumes, i.e., as if the boundary wasn't there. Such an approach has been shown to give consistent and stable discretizations, even in the case of moving boundaries. One of the principal advantages of the embedded boundary method is that the problem of generating the description of the geometry on the grid starting from surface tessellations produced, for example, by a CAD system has been completely solved. It is also complementary to a fast and accurate level-sets method for surface extraction from 3D image data [3]. This feature makes the embedded boundary method superior to body-fitted unstructured grids used for finite element simulations. Finite element gridding is based on re-meshing which often discards surface details in the approximation of surfaces by NURBS (Non-Uniform Rational B-Spline), the consequence of which is substantial loss of geometric detail. This process also involves much user interaction. In order to retain the details in this type of meshing strategy a large number of mesh elements are required which in turn taxes the computing resources. With the embedded boundary method meshing is more tractable and less expensive computationally, especially in the case of a moving boundary as re-gridding is unnecessary, requiring only a conservative movement of the boundary.

Our approach to complex geometry using embedded boundary methods has been leveraged to simulate cardio-pulmonary flows in realistic anatomies [3, 7]. We have demonstrated this new approach to anatomical flows on a patient-specific carotid artery with stenosis (Figure 3) and a trachea which has undergone tracheostomy (Figure 4). The resolution of geometric detail here is a recent improvement over previous results in the field where surface meshes are a smooth representation of the original geometry, illuminating the advantage of our new approach over the previous state-of-the-art. This capability can ultimately provide clinicians with time-sensitive and accurate information needed to evaluate how pathologies form, how they evolve, and ultimately how they are effectively treated.

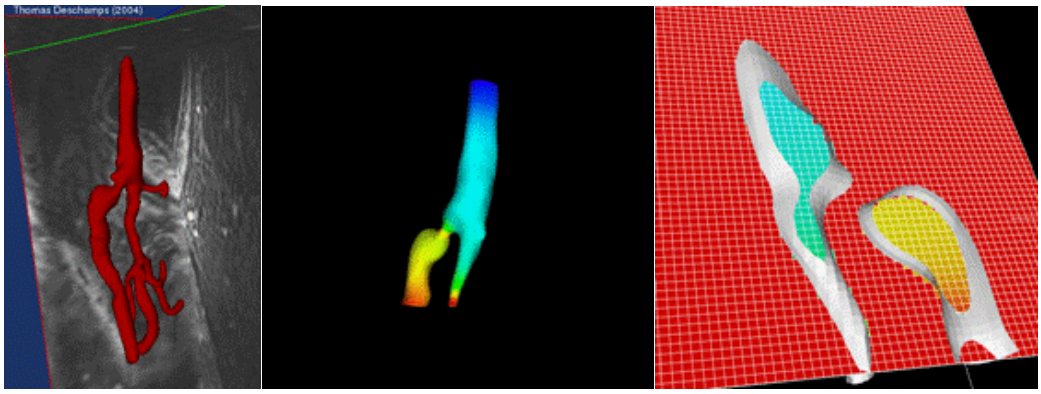

Figure 3. Stenotic carotid artery. (a) Surface rendering from magnetic resonance image. (b) 3D simulation result, pressure. (c) Embedded boundary in mesh showing detail of surface intersecting rectangular grid.

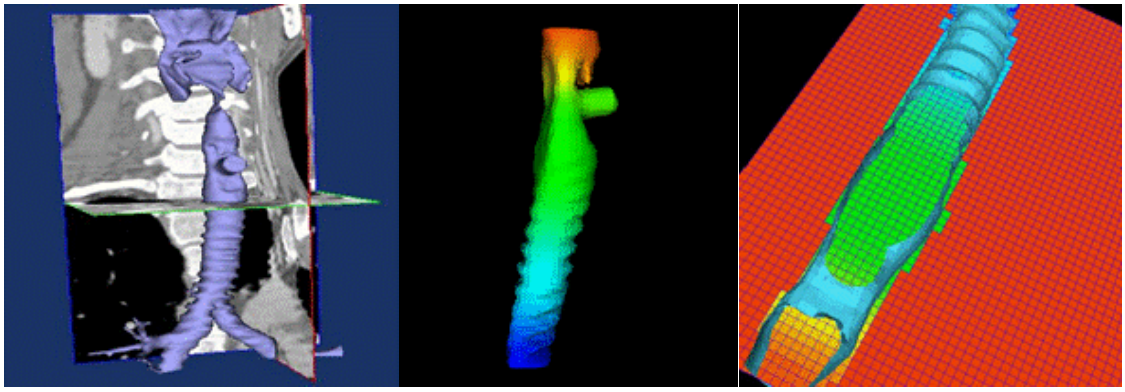

Figure 4. Trachea with tracheostomy. (a) Surface rendering from CT scan. (b) 3D simulation result, pressure. (c) Embedded boundary in mesh showing detail of surface intersecting rectangular grid. Note resolution of detail in trachea ribbing between simulation and surface extraction.

Acknowledgment

This work was performed under the auspices of the U.S. Department of Energy by the University of California, Lawrence Livermore National Laboratory under contract No. W-7405-Eng-48.

References

[1] J. B. Bell, P. Colella, and H. M. Glaz. A second-order projection method for the incompressible Navier-Stokes equations. *J. Comput. Phys.*, 85:257–283, 1989.

[2] P. Colella, D. T. Graves, B. Keen, and D. Modiano. A Cartesian grid embedded boundary method for hyperbolic conservation laws. *J. Comput. Phys.*, 211:347–366, 2006.

[3] T. Deschamps, P. Schwartz, D. Trebotich, P. Colella, D. Saloner, and R. Malladi. Vessel segmentation and blood flow simulation using level-sets and embedded boundary methods. In *International Congress Series*, volume 1268, pages 75–80, June 2004.

[4] A. Nonaka, S. Gulati, D. Trebotich, G. H. Miller, S. J. Muller, and D. Liepmann. A computational model with experimental validation for DNA flow in microchannels. In *Proceedings of the 2005 NSTI Nanotechnology Conference and Trade Show, Anaheim, CA*, 2005.

[5] P. O. Schwartz, M. Barad, P. Colella, and T. J. Ligocki. A Cartesian grid embedded boundary method for the heat equation and Poisson's equation in three dimensions. *J. Comput. Phys.*, 211:531–550, 2006.

[6] D. Trebotich, P. Colella, and G. H. Miller. A stable and convergent scheme for viscoelastic flow in contraction channels. *J. Comp. Phys.*, 205:315–342, 2005.

[7] D. Trebotich, T. Deschamps, and P. Schwartz. Air-flow simulation in realistic models of the trachea. In *Technical Proceedings of the 26th Annual International Conference IEEE Engineering in Medicine and Biology Society*, pages 3933–3936, September 2004.

[8] D. Trebotich, G. H. Miller, P. Colella, D. T. Graves, D. F. Martin, and P. O. Schwartz. A tightly couple particle-fluid model for DNA-laden flows in complex microscale geometries. *Computational Fluid and Solid Mechanics*, pages 1018–1022, 2005.