Polymer Simulation for Single Molecule Detection in Microdevices

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ABSTRACT

We have developed a novel algorithm for the simulation of polymer-laden flows in microfluidic devices. Our algorithm is based on a hybridization of high-order accurate continuum and particle methods. The continuum algorithm provides the basic framework for high performance computations to resolve device length and time scales. It is coupled to a new particle method with an optimized treatment of particle interactions such that the time step is on the level of the fluid continuum. We demonstrate our simulation capability on the flow of DNA molecules in a contraction microchannel used for single molecule detection.

Keywords: polymer simulation, microfluidics

1 INTRODUCTION

Understanding complex biological flows through advanced algorithmic modeling is critical to several important biomedical applications such as targeted drug delivery or continuous monitoring and diagnostics. These applications will leverage miniaturized technology based on advancements in microfluidics and nanofluidics. In order for this development to continue toward the design of optimized trustworthy working devices, advanced modeling and simulation tools are needed to understand the fundamental physics and chemistry of biological fluids at much smaller than normal scales. This will enable shorter design and fabrication cycles and ultimately get devices to market more quickly and with less cost.

Modeling complex biological fluids is a challenge because their non-Newtonian constitutive behavior is not easily represented. The problem is further complicated when the flow of biological fluids is restricted to the small length scales of state-of-the-art biomedical devices. At these scales new fluid mechanical and modeling issues arise because (1) surface-to-volume ratios are extremely large; and (2) characteristic lengths of the macromolecules or cells approach those of the flow geometry. For example, a highly concentrated solution of suspended polymer molecules may be represented at large, system-level scales with a continuum viscoelastic constitutive model (e.g., [2]). However, when the geometry length scales are comparable to the inter-polymer spacing a continuum approximation is no longer appropriate, and a discrete molecular approximation is needed. In addition, when the length scale of the geometry is comparable to the length of an individual polymer macromolecule, new physical behavior may be observed near surfaces where velocity and concentration gradients tend to be large and macromolecular shear degradation or even breaking (scission) can occur as a result. This dynamic can be beneficial in a DNA amplification device but detrimental in a drug delivery system. Discrete representation of particles suspended in a fluid is needed in this case to predict the fate of individual molecules.

In this paper we consider a canonical flow that occurs in microfluidic detection devices: flow of individual DNA polymer strands through an abrupt contraction microchannel. In our flow demonstrations we introduce two polymers with DNA parameters in a pressure-driven flow through a sudden contraction microchannel. Abrupt contractions in microchannels are common for the purpose of flow control in a microfluidic device [8]. Here, the abrupt contraction is intended to mimic a single molecule detection component in a larger system (e.g., [1]) where the molecules are threaded through a region for detection using fluid mechanical forces alone. The goal of these simulations is to predict optimal parameters for a flow-through device.

2 RESULTS

We use a hybrid fluid-particle algorithm to simulate polymers represented by a chain of beads and rods coupled to an incompressible viscous solvent [3]–[5], [7]. We perform 2D simulations of two polymers, 150 and 80 nodes, respectively, flowing in an abrupt contraction microchannel at three different Reynolds numbers. The channel section is 10 μm long and the inlet is 3.75 μm wide. The Kuhn length is a measure of the flexibility in the polymer chain. In these simulations we choose the interparticle spacing, or constraint length, to be the Kuhn length for DNA, a = 100 nm; other parameters are the particle mass, m = 1e-19 g, relaxation time, γ = 1e+12 sec and σ = 5e+08 cm/sec$^{3/2}$ (see [3], [7] for definitions).

In Figure 1 the Reynolds number at the inlet of the

channel is 0.000375. The polymers are in an initially coiled state. The advective forces are not strong enough to stretch them out as they proceed through the abrupt contraction where the flow accelerates, which is typical behavior in experimental DNA flows [8]. The low resolution of these simulations is such that the viscous forces, which dominate inertial forces at this very low Reynolds number, are not resolved, and, therefore, do not manipulate the polymer either. This flow scenario is likely not ideal for single molecule detection to occur in the smaller contracted channel.

In Figure 2 the Reynolds number is 0.0375. The stronger inertial flow along with velocity gradients due to viscous forces uncoils the polymers and stretches them out in the accelerated region as if threading the polymers through the contracted channel. These dynamics seem to be ideal for the design of a sensor.

In Figure 3 the Reynolds number is 3.75. The polymer transport is faster and the polymers are stretched out. These could be acceptable parameters for sensor design in this channel, but the flow might be too fast for capture and detection of the molecule to occur. This finding is consistent with detection systems that rely on DNA capture techniques before amplification to ensure a signal[1]. In such systems the typical operating Reynolds number is on the order of one so that individual DNA molecules are not transported too rapidly to avoid capture.

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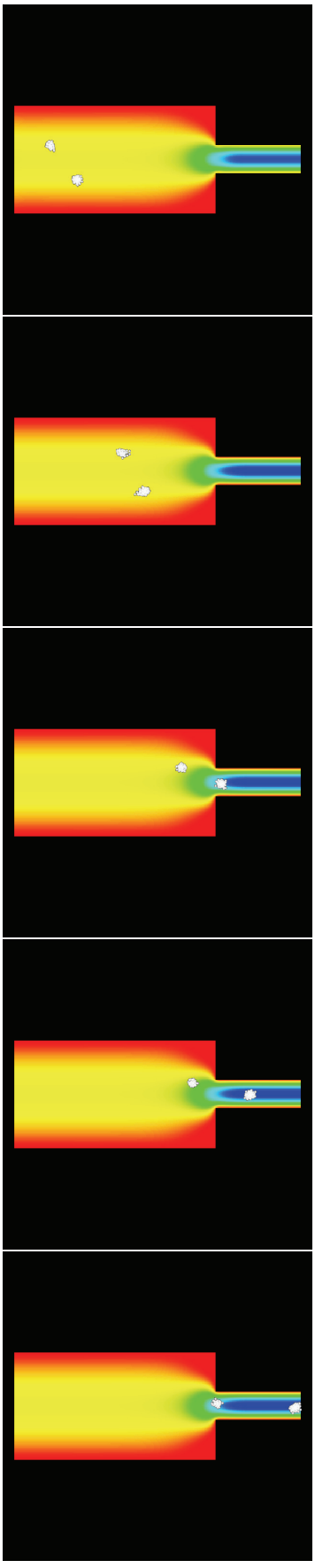

Figure 1: Polymer locations at times 0.00199, 0.01999, 0.03499, 0.03699, 0.03989 seconds for $Re = 0.000375$. Background color is velocity: blue (high), red (low).

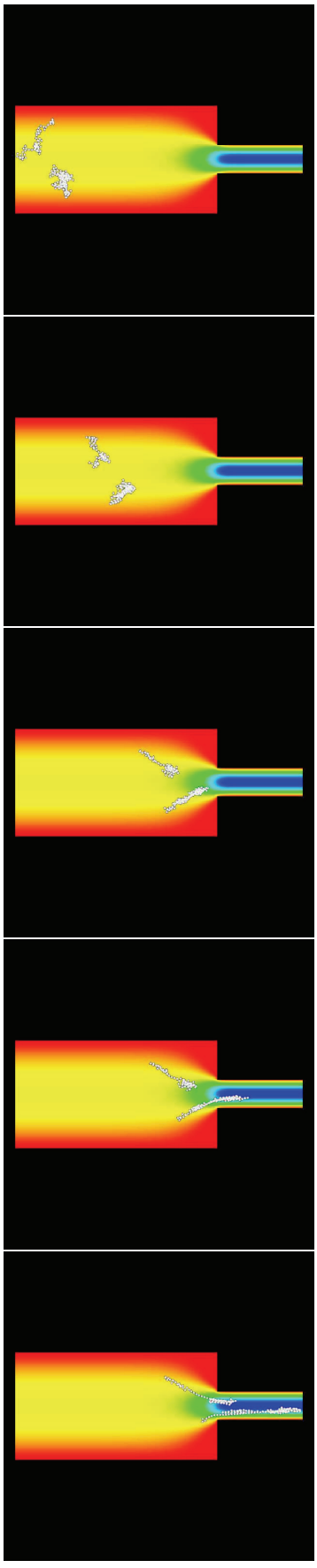

Figure 2: Polymer locations at times 3.3e-06, 0.00017, 0.00034, 0.00038, 0.00042 seconds for $Re = 0.0375$. Background color is velocity: blue (high), red (low).

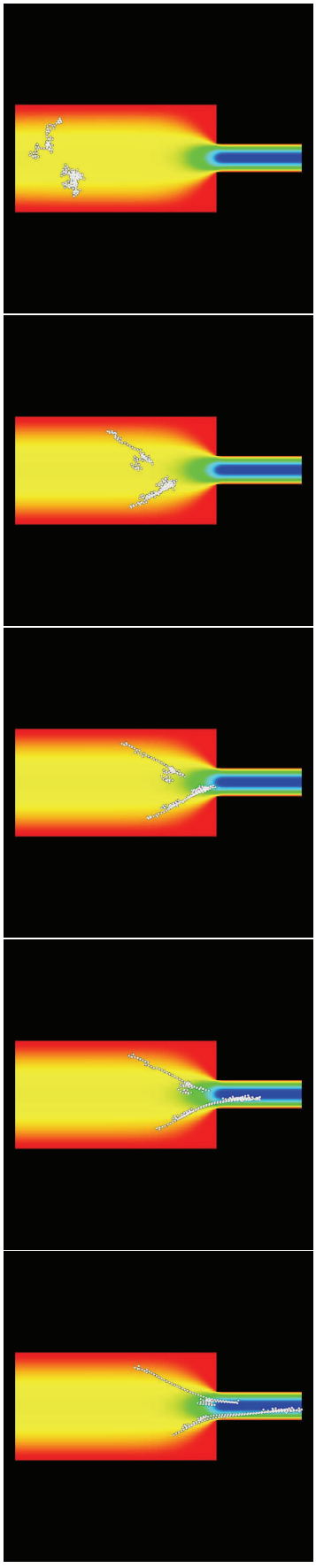

Figure 3: Polymer locations at times 3.4e-07, 2.7e-06, 3.4e-06, 3.8e-06, 4.0e-06 seconds for $Re = 3.75$. Background color is velocity: blue (high), red (low).