# Numerical Simulation of Polymer Flow in Microfluidic Devices *

Bakytzhan Kallemov† Gregory H. Miller‡ David Trebotich§

**Abstract**

We present simulation results from a computational model of polymer flow in microfluidic devices. This work is important because computational models are needed to design miniaturized biomedical devices which leverage microfluidics technology for many significant applications including pathogen detection as well as continuous monitoring and drug delivery involving the processing of polymer molecules such as DNA. Currently, advanced algorithms in design tools are non-existent but necessary to understand the complex fluid and polymer dynamics involved in biological flow at small scales. Our model is based on a fully coupled (including reverse coupling from particle to fluid) fluid-particle numerical algorithm with both stochastic and deterministic components in a bead-rod polymer representation. The particle method is strong second-order accurate, as is the CFD solver. The latter provides a high performance computing platform based on adaptive, embedded boundary methods for these computationally intensive problems with multiple scales. We demonstrate our method on the test problem of flow of DNA molecules in a 2D entropic trap, the square well geometry of which is fundamental component in microfluidic processing yet complicated enough to elicit complex flow features relevant to design.

## 1 Background and Motivation

Understanding complex biological flows through advanced algorithmic modeling is critical to many biomedical applications of significance in an array of industries such as targeted drug delivery in pharmaceuticals, continuous monitoring and diagnostics in biotechnology, and fuel cells in energy. These applications will leverage state-of-the-art miniaturized technology, development which requires understanding of the fundamental physics and chemistry of biological fluids at much smaller than normal scales to design and optimize trustworthy working devices, and to get them to market more quickly and with less cost.

Micro Electro-Mechanical Systems (MEMS) technologies are at the forefront of engineering practice for the design of integrated fluidic control and (bio)chemical sensing devices. Microscale fluidic processors allow for portability, networking, low power and minimal reagent consumption and faster chemical reactions. However, design and fabrication cycles are lengthy because trial-and-error design is time consuming. Design platforms will require predictive capabilities that incorporate advanced modeling to understand the fundamental physical processes of complex fluids in these devices and to predict their behavior.

Modeling complex biological fluids is a challenge because their non-Newtonian constitutive behavior is not easily represented. For example, the presence of long-chain polymers or macromolecules in a Newtonian solvent (e.g., Boger fluid, DNA) can cause a viscous fluid to demonstrate elastic behavior even at micromolar concentrations [1]. Furthermore, the introduction of macromolecules to a solvent can introduce a shear-rate dependence to the viscosity and cause what is known as shear-thinning. In either constitutive case the velocity field in flows through a simple planar channel or axisymmetric tube is altered from the classical parabolic Newtonian flow profile due to change in pressure and evolution of significant secondary flows [2].

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/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., [3]). 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)

*This work was funded by the DOE OASCR Multiscale Mathematics Program.

†University of California, Davis

‡University of California, Davis

§Lawrence Berkeley National Laboratory, Corresponding author

can occur as a result [2]. Discrete representation of particles suspended in a fluid is needed in this case to predict the fate of individual molecules. Furthermore, the processes of interest involve physical phenomena not accounted for in conventional continuum formulations alone. Examples include the effects of flow on conformation of DNA, and the reciprocal effects of DNA conformation on flow [4, 5], as well as the effects of shear on orientation of globular proteins. There is strong experimental evidence in support of the hypothesis that these molecular-scale processes have substantial system-level (engineering device scale) effects.

As a practical example, the biochemical nature of pathogen detection requires microprocessing of large molecules such as DNA or proteins. Bacterial DNA is approximately 1-2 mm long when stretched out in solution. In a standard amplification/sequencing microprocessor, $10^{10}$ molecules will have to pass through channels with characteristic length scales of 10-100 $\mu$m. The large molecules in the flow will not only affect the fluid dynamics and performance of the device, but the fluid forces can damage (break) the biomolecules required for the bioassay. This dynamic can be beneficial in a DNA amplification device but detrimental in a drug delivery system. (While protein molecules are significantly smaller than DNA molecules and do not exhibit all of the conformational changes of DNA, there are strong indications that protein molecules do not survive flow in micro-environments unscathed, possibly as a result of interactions with channel surfaces.) We have also applied discrete polymer models to the problem of DNA extraction in a polymerase chain reaction (PCR) chamber as part of a pathogen detection system. One of the primary extraction techniques being pursued by industry is a packed bed reactor, which is essentially a small tube packed with microscale glass beads. The physical model presents a three-dimensional (3D) multiscale problem where DNA molecules must be resolved along with the flow geometry. A second extraction design is a pillar chip which is an array of cylindrical obstructions in a shallow microchannel. Though a 3D problem, this latter design lends itself to 2D models. The restriction to 2D is useful and can be reduced to model a single molecule traveling through a smaller section of the array. This is the model problem where we have honed the algorithm development to model relevant physics of the flow for the full 3D problem [8, 9].

In this paper we consider flow of a long-chain polymer in a 2D "entropic trap". An entropic trap is a microchannel that is composed of a number of square wells in series. This configuration has been shown to be more efficient for size separation of long-chain polymers such as DNA over the standard technique of gel electrophoresis [7]. Though a simple geometry an entropic trap contains enough features (expansion and contraction sections of a channel) to serve as an appropriate testbed for advanced algorithm development as far as polymer flow is concerned. More advanced configurations, and, ultimately, a full device simulation, would be the next step in this current work.

## 2 Technical Approach

In our model we will consider discrete polymers suspended in an incompressible viscous solvent. We use a hybrid continuum-particle based on the fluid-polymer coupling algorithm of Kallemov et al. [14, 9, 8] for incompressible polymer-laden flows in irregular microscale geometries. Polymers are represented as beads and rods, that is, a collection of point masses connected by constrained interparticle spacing. Each particle is subject to a hydrodynamic drag force from the fluid, and Brownian motion. The fluid in turn responds to the effect of the particles via a cloud-in-cell model of the discrete Dirac delta function. We note that the effect of the backward coupling is not that large in the dilute limit due to the atomic nature of the particles (small mass). However, if the solution is more concentrated or the particle masses are heavier then the force on the Newtonian solution is apparent. We will demonstrate this behavior. Irregular geometry boundaries are treated with an embedded boundary, or cut-cell, Cartesian grid method [10, 9]. Incompressibility is enforced and velocity and pressure evolved by a projection method [11].

The equations of motion for our model are incompressible Navier-Stokes equations coupled to Langevin particle dynamics through an extra stress or source term in the momentum equation:

$$\frac{\partial \mathbf{u}}{\partial t} + (\mathbf{u}\cdot\nabla)\mathbf{u} + \frac{1}{\rho}\nabla P = \nu\Delta\mathbf{u} + \frac{1}{\rho}\mathbf{F} \tag{2.1}$$

$$\nabla\cdot\mathbf{u} = 0. \tag{2.2}$$

These equations describe an incompressible fluid of density $\rho$, pressure $P$, velocity $\mathbf{u}$, and Newtonian viscosity $\nu$, subject to an additional body force $\mathbf{F}$. On the domain boundary $\delta\Omega$ we have the no-slip boundary condition $\mathbf{u} = 0$.

The polymer solute is represented as a collection of point masses each subject to Newton's second law of motion

$$m_\alpha \frac{d^2\mathbf{x}_\alpha}{dt^2} = m_\alpha \frac{d\mathbf{v}_\alpha}{dt} = \mathbf{f}_\alpha. \tag{2.3}$$

Here $m_\alpha$ is the mass of the $\alpha^{\text{th}}$ particle, $\mathbf{x}_\alpha$ is its coordinate, and $\mathbf{v}_\alpha$ is its velocity. The particle is subject

to a force $\mathbf{f}_\alpha$ which combines a Stokes drag term with a stochastic (Brownian) perturbation,

$$\mathbf{f}_\alpha = m_\alpha\gamma(\mathbf{u}(\mathbf{x}_\alpha) - \mathbf{v}_\alpha) + \mathcal{F}_{\mathbf{B}\alpha}. \tag{2.4}$$

Here, $1/\gamma$ is a phenomenological relaxation time ($m\gamma = 6\pi\mu b$ for a Stokes sphere of radius $b$) , and $\mathcal{F}_\mathbf{B}$ is the stochastic force

$$\langle \mathcal{F}_{\mathbf{B}\alpha}(t)\rangle = 0 \tag{2.5}$$

$$\langle \mathcal{F}_{\mathbf{B}\alpha}(t)\mathcal{F}_{\mathbf{B}\alpha}(t')\rangle = \sigma_\alpha^2 I\delta(t-t'), \tag{2.6}$$

where $\sigma_\alpha = \sqrt{2m_\alpha\gamma k_B T}$ with $k_B$ being Boltzmann's constant and $T$ the temperature.

The force $\mathbf{F}$ acting on the fluid is

$$\mathbf{F}(\mathbf{x}) = -\sum_\alpha \mathbf{f}_\alpha\delta_\epsilon(\mathbf{x} - \mathbf{x}_\alpha), \tag{2.7}$$

where $\delta_\epsilon$ represents a smoothed Dirac delta function with length scale $\epsilon$.

In addition to the incompressibility condition (2.2) we have three additional constraints on the particles: (i) interparticle spacing is constant

$$\|\mathbf{x}_\alpha - \mathbf{x}_\beta\| = a \tag{2.8}$$

if particles $\alpha$ and $\beta$ represent adjacent nodes in a bead-rod polymer representation; (ii) particles cannot pass through a physical boundary;

$$\mathbf{x}_\alpha \in \Omega, \tag{2.9}$$

and (iii) rods cannot cross.

We use the method of Trebotich et al. [9, 8] to advance the fluid and particles forward in time. For the fluid solver we use the high performance adaptive, embedded boundary method of [10]. The algorithm is a second-order predictor-corrector method based on the projection method [11] with higher-order treatment of the advection terms [12, 13]. Particle advancement is accomplished by folding in a new strong second-order method [14, 15] into the fluid-predictor-corrector as in [9]. The particle timestep is optimized using the technique of Miller and Trebotich [17] such that its magnitude is on the order of the fluid timestep which is only limited by the advective Courant-Friedrichs-Lewy (CFL) condition.

## 3 Results

We demonstrate our method on the flow of a dilute polymer fluid in an entropic trap. An entropic trap is essentially a series of square wells that can be used to separate long-chain polymers of different lengths in biochemical processing. This type of separation is critical to the success of advanced single-molecule detection devices. Though not a full device the entropic trap test problem is a canonical one for modeling microscale flows of complex fluids. Specifically, it is a mechanical technique for size separation of polymers in the absence of chemistry and electrokinetics. It contains geometric singularities which can elicit singularities in solution, a known challenge to numerical modeling. We also note that it is our goal to model full devices and that the results presented here are a step in that direction.

We consider flow of 2 polymer strands in a square well microchannel. We use an operating Reynolds number of one, which is typical of a real flow-through device such as a pathogen detection system [18]. Sample calculations for the 45-node polymer approximation are displayed in Figs. 1-4. Each polymer node is subjected to drag force from the fluid and stochastic Brownian motion according to Eq. 2.4. The interparticle spacing, $a$, is taken to be the so-called Kuhn length, after [16], which is the related to the flexibility of the chain. The Kuhn length can be experimentally measured, e.g., by light scattering [20], NMR spin relaxation [21], or even single-molecule atomic force microscopy [19]. For DNA, the measure is $\approx$ 100nm. In our preliminary results we do resolve this scale. The timestep for each iteration is subjected to the CFL condition, so time intervals between each screenshot is not necessarily equal. Although it is more natural to consider initial polymer configuration as a random coil we chose simple initial polymer configurations for demonstration purposes. The background color of the figures is the horizontal fluid velocity where blue is the maximum value as seen in regions of fluid acceleration and red is 0, or slightly less as in the recirculation zones.

Fig. 1 demonstrates the dynamics of two polymers introduced into a square well channel. In this flow scenario, neither strand gets trapped. Fig. 2 demonstrates the trapping of a single polymer due to fluid forces while the other escapes the channel. We were also able to simulate two polymers in an entropic trap with two wells whose configuration is similar to that in [7]. These results were obtained for fictitious polymer parameters for demonstration purposes (Fig. 3).

As a proof-of-concept for full (reverse) coupling we performed calculations for an unrealistic "massive" polymer so that the contribution from the force acting on the fluid is discernible. The result is presented in the Fig. 4 where the surrounding fluid velocity is highly disturbed. This effect is important to model in more concentrated polymer fluids where large numbers of molecular masses can have an effect the fluid.

## 4 Conclusions

We have demonstrated a simulation capability for modeling flow of polymer-laden fluids such as DNA in microscale environments. A higher-order particle method has been coupled to an adaptive incompressible flow solver in complex geometry which has been optimized for high performance. This coupling is done through source terms for extra stress in the momentum equation and at no expense to the fluid timestep which enables long time simulation to access experimental timescales for validation. We have demonstrated the trapping of a polymer in two square well microchannel configurations. These "entropic trap" type devices are not complete industrial devices but are canonical components that are typical of channels in lab-on-a-chip microprocessors. Also, we have chosen polymer parameters, such as interparticle spacing, that are not completely realistic (cf. Kuhn length of DNA) but sufficient for demonstration purposes. More importantly, we have for the first time shown the reverse coupling effect of particles on surrounding fluid by simulating fictitious massive particles. The success of the full coupling will be important in future applications of this capability in real devices where the polymer concentrations are much larger than the dilute limit considered here. With that, comparisons can be made with continuum viscoelastic representations of polymer constitutive behavior, and a hierarchical approach to modeling these complex fluids can be formulated.

## References


[1] B. M Baumert and S. J. Muller, *Flow visualization of the elastic Taylor-Couette instability in Boger fluids*, Rheol. acta, 34 (1995) pp. 147–159.

[2] R. B. Bird and R. C. Armstrong and O. Hassager, *Dynamics of Polymeric Liquids*, Wiley, New York, 1977.

[3] D. Trebotich, G. H. Miller and P. Colella, *A stable and convergent scheme for viscoelastic flow in contraction channels*, J. Comput. Phys., 205 (2005) pp. 315–342.

[4] P. Shrewsbury and S. J. Muller and D. Liepmann, *Concentration effects of a biopolymer in a microfluidic device*, Biomed. Microdevices, 3, (2001) pp. 225–238.

[5] T. Kwan and N. Woo and E. S. G Shaqfeh, *An Experimental and Simulation Study of Dilute Polymer Solutions in Exponential Shear Flow: Comparison to Uniaxial and Planar Extensional Flows*, J. Rheol., 45 (2001) pp. 321–349.

[6] A. Nonaka, S. Gulati, D. Trebotich, G. H. Miller, S. Muller and D. Liepmann, *A computational model with experimental validation for DNA flow in microchannels, Technical Proceedings of the 2005 NSTI Nanotechnology Conference and Trade Show*, Anaheim, CA, May 8-12, Vol. 3, (2005) pp. 712–715.

[7] J. Han and H.G. Craighead, *Separation of Long DNA Molecules in a Microfabricated Entropic Trap Array*, Science, 288, (2000) pp. 1026–1029.

[8] D. Trebotich and G. H. Miller, *A tightly coupled particle-fluid model for DNA-laden flows in complex microscale geometries*, in Computational Fluid and Solid Mechanics, (2005) pp. 1018–1022.

[9] D. Trebotich, G. H. Miller and M. D. Bybee, *A Penalty Method to Model Particle Interactions in DNA-laden Flows*, J. Nanosci. Nanotechnol. 8 (2008) pp. 3749–3756.

[10] D. Trebotich, B. Van Straalen, D. T. Graves, and P. Colella, *Performance of Embedded Boundary Methods for CFD with Complex Geometry*, J. Phys.: Conf. Ser., 125 (2008), 012083.

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

[12] P. Colella *Multidimensional Upwind Methods for Hyperbolic Conservation Laws* J. Comp. Phys., 87 (1990) pp. 171–200.

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

[14] B. Kallemov, G. H. Miller and D. Trebotich, *A Duhamel approach for the Langevin equations with holonomic constraints*, Molecular Simulation, 35 (2008) pp. 440–447.

[15] B. Kallemov and G. H. Miller, *A Strong Second Order Duhamel Method for the Langevin Equations with Holonomic Constraints*, SIAM J. Sci. Comput., submitted.

[16] W. Kuhn, *Relationship between molecular size, static molecular shape and elastic characteristics of high polymer materials*, Kolloid Zeit., 76 (1936) pp. 258–271.

[17] G. H. Miller and D. Trebotich, *Toward a Mesoscale Model for the Dynamics of Polymer Solutions*, J. Comput. Theoret. Nanosci. 4, (2007) pp. 797–801

[18] F. P. Milanovich, J. Dzenitis, B. J. Hindson, A. J. Makarewicz, M. T. McBride and B. W. Colston, *APDS, A network-ready, broad-spectrum , environmental pathogen detection system*, Defense against Bioterror: Detection Technologies, Implementation Strategies and Commercial Opportunities, 1 (2006) pp. 67–75

[19] M. Rief, F. Oesterhelt, B. Heymann, and H. E. Gaub, *Single molecule force spectroscopy on polysaccharides by atomic force microscopy*, Science, 275 (1997), pp. 1295–1297.

[20] H. U. Termeer and W. Burchard, *Determination of chain flexibility by light-scattering*, Polymer Comm., 26 (1985), pp. 273–275.

[21] D. W. Woessner, *NMR relaxation of spin-3/2 nuclei: effects of structure, order, and dynamics in aqueous heterogeneous systems*, Concepts Magnetic Resonance, 13 (2001), pp. 294–325.

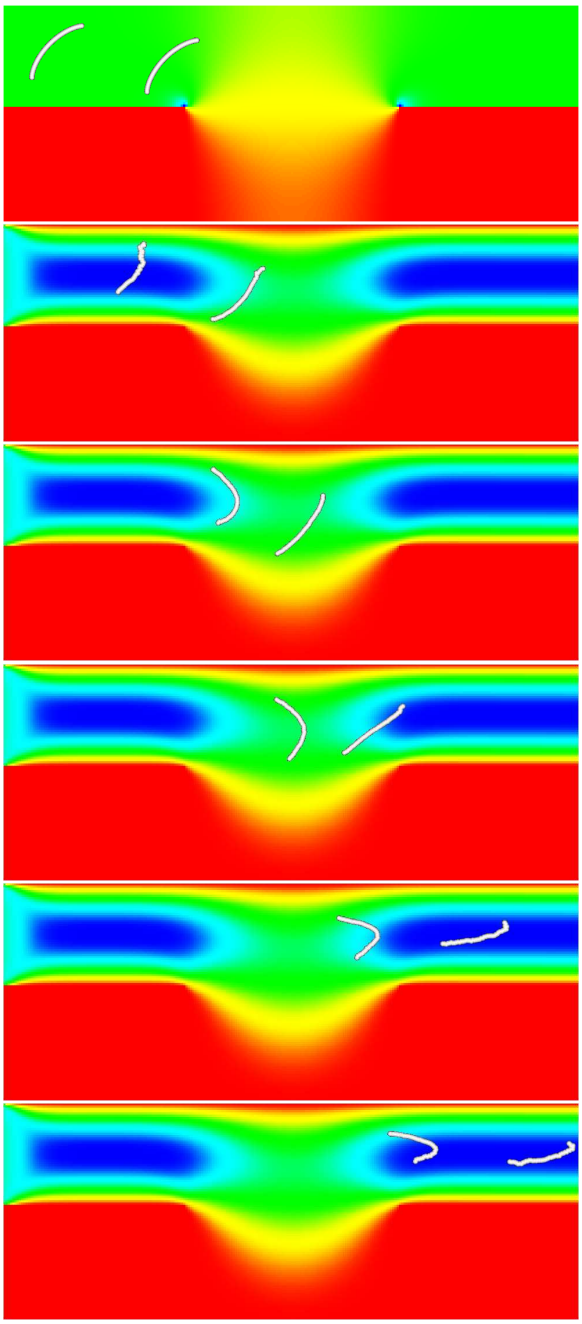

Figure 1: Two polymers flowing over a square well in a microchannel. $N_{nodes} = 45$, $m = 1$, constraint length $= 6 \cdot 10^{-4}$, $\gamma = 10^2$, $\sigma = 1$. Time: 0, 0.235, 0.496, 0.757, 1.017, 1.174. Background color is horizontal velocity, blue (max), red (min).

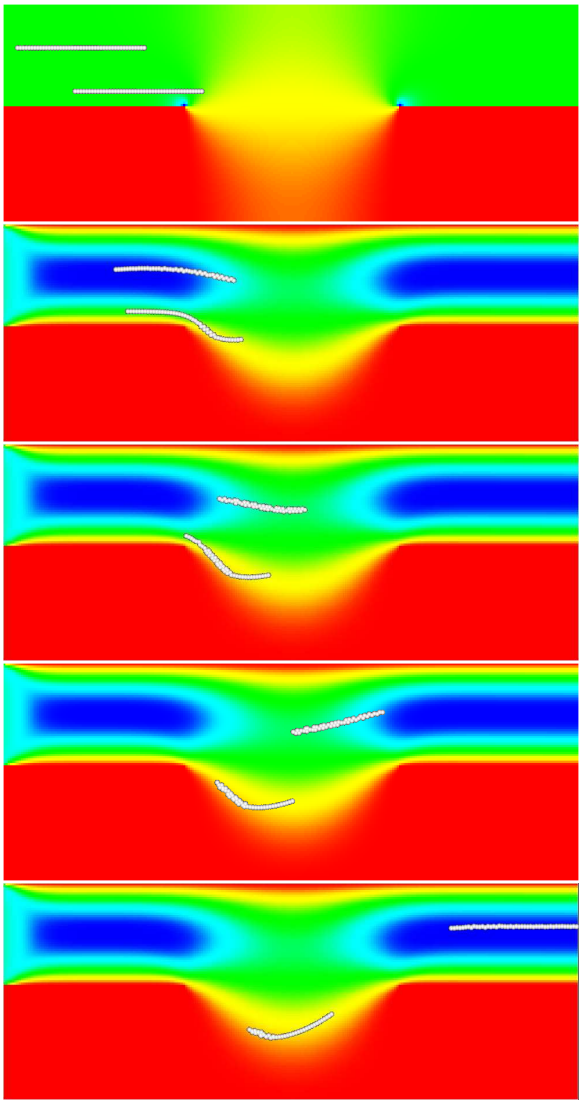

Figure 2: "Trapping" a polymer into the square well. $N_{nodes} = 45$, $m = 1$, constraint length $= 1 \cdot 10^{-2}$, $\gamma = 10^4$, $\sigma = 5$. Time: 0, 0.235, 0.496, 0.758, 1.226. Background color is horizontal velocity, blue (max), red (min).

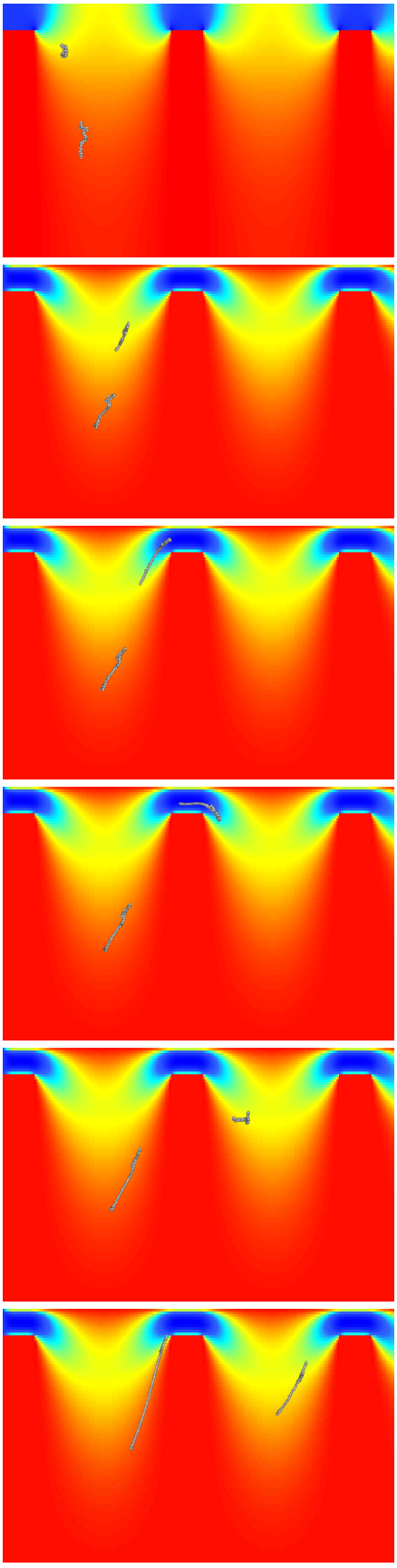

Figure 3: Two polymers flowing through two square wells, similar to entropic trap device in [7]. $N_{nodes} = 45, m = 1$, constraint length $= 5 \cdot 10^{-3}$, $\gamma = 10^4$, $\sigma = 5$. Time: 0, 1.35, 1.91, 2.16, 2.70, 4.04. Background color is horizontal velocity, blue (max), red (min).

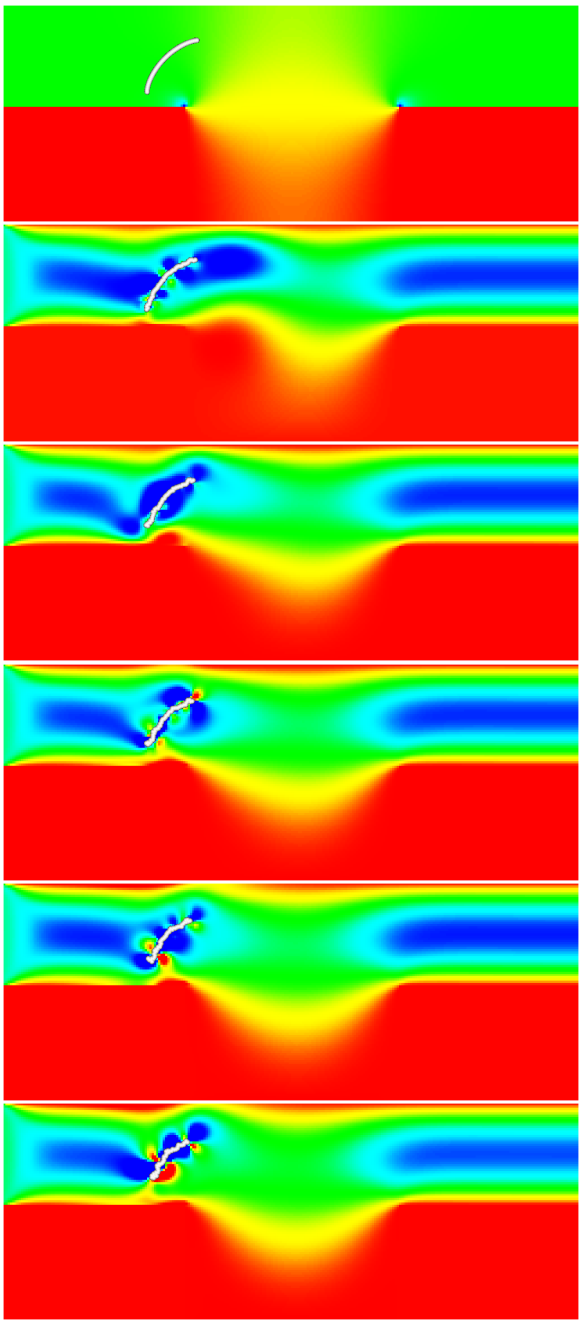

Figure 4: Velocity field for a fictitiously heavy polymer flowing in a square well microchannel demonstrating reverse coupling effect. $N_{nodes} = 45$, $m = 10^3$, constraint length $= 6 \cdot 10^{-4}$, $\gamma = 1$, $\sigma = 5$. Time: 0, 0.01, 0.016, 0.021, 0.029, 0.041. Background color is horizontal velocity, blue (max), red (min).