A Brownian dynamics-finite element method for simulating DNA electrophoresis in nonhomogeneous electric fields

Ju Min Kim and Patrick S. Doyle

Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

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The objective of this work is to develop a numerical method to simulate DNA electrophoresis in complicated geometries. The proposed numerical scheme is composed of three parts: (1) a bead-spring Brownian dynamics (BD) simulation, (2) an iterative solver-enhanced finite element method (FEM) for the electric field, and (3) the connection algorithm between BD and FEM. A target-induced searching algorithm is developed to quickly address the electric field in the complex geometry which is discretized into unstructured finite element meshes. We also develop a method to use the hard-sphere interaction algorithm proposed by Heyes and Melrose [J. Non-Newtonian Fluid Mech. 46, 1 (1993)] in FEM. To verify the accuracy of our numerical schemes, our method is applied to the problem of λ-DNA deformation around an isolated cylindrical obstacle for which the analytical solution of the electric field is available and experimental data exist. We compare our schemes with an analytical approach and there is a good agreement between the two. We expect that the present numerical method will be useful for the design of future microfluidic devices to stretch and/or separate DNA.

I. INTRODUCTION

Recently, DNA dynamics has attracted much attention due to its important role in understanding fundamental polymer physics, rheology, biophysics in nature, and its widespread use in laboratory on chip devices where it must be mixed, separated, and deformed. DNA is large enough to directly observe with standard fluorescence microscopy in contrast to most synthetic polymers. Furthermore, since DNA’s molecular weight is monodisperse, it can be considered as an ideal model polymer for theoretical research without complexities arising from polydispersity seen in synthetic polymer systems. Many theoretical issues such as coil-stretch hysteresis, electrodynamic equivalence, and electrohydrodynamic equivalence have been established from studies using DNA. Meanwhile, Brownian dynamics (BD) has rapidly developed and can now predict DNA dynamics in homogenous flows.

In microfluidic devices, manipulating biopolymers such as DNA is ubiquitous in diagnostics, size-based separations, and production of new materials. Biopolymers are often charged and can be transported via hydrodynamic or electrical forces. The latter is called electrophoresis. The microfluidic unit processes, such as separation, are typically composed of obstacle arrays and contraction/expansion regions, which have been incorporated for several novel separation schemes (microfabricated postarrays, “ratched” asymmetric obstacles, entropic traps, self-assembled magnetic colloidal post arrays, lateral displacement by the asymmetric bifurcation around obstacles, and quartz nanopillar chips) or stretching devices for genomic mapping. When using electric fields, a nonuniform field is generated around obstacles and in contraction/expansion regions. Moreover, the stretching of DNA is now a key feature of a new genomic mapping device. Thus, understanding DNA deformation in nonuniform electric fields is now an important engineering step for the design of high performance microfluidic devices.

Recently, Randall and Doyle showed in experiments that DNA is deformed by the disturbed electrophoretic field around insulated cylindrical obstacles. They investigated DNA motion around various sizes of cylinders comparable with the radius of gyration of DNA and larger, and showed that the probability of hooking DNA around an insulating obstacle in a hairpin formation is strongly dependent on the nonhomogeneity of the electric field. They also discovered the interesting phenomenon that DNA is stretched postcollision on the back side of large obstacles, especially at high Deborah number (relaxation time × strain rate). They concluded that the nonuniform field due to a finite size insulated obstacle cannot be overlooked in obstacle studies. Randall et al. also fabricated a hyperbolic microfluidic device to stretch a DNA and showed that the DNA stretching can be greatly enhanced by “the preconditioning of initial configuration,” which was realized by introducing a gel region just before hyperbolic region.

Using BD simulations, Panwar and Kumar explored DNA stretching and transport phenomena in electroosmotic flows generated using a spatially periodic wall charge distribution, which also involves a nonuniform velocity field. They showed that there are complex dynamics due to competition of electrophoresis and electroosmosis, which affect the trapping of DNA at the stagnation point. Later, they studied bead-rod polymer translocation through a nanochannel.
and entropic trap with BD and uniform and nonuniform fields. They showed with their BD simulation that the speed of DNA translocation and its dependence upon molecular weight related to three events: approaching, activation, and crossing. With respect to the entropic trap, in addition to conventional “hernia” hypothesis, Streek et al. proposed a new size-dependent separation mechanism suggesting that smaller DNA is more easily trapped in the corner region. Since the entropic trap involved a nonuniform electric field, the authors incorporated a coupled method which combined BD for DNA dynamics and finite element method (FEM) or finite difference method (FDM) for the electric field. Tessier et al. used Monte Carlo (MC) simulation for DNA dynamics and FDM for the electric field. In the literature, the methods to employ nonuniform fields in BD or MC simulations are divided into analytical or numerical solution schemes. In this work, we focus on the numerical solution-based schemes since most engineering problems involve complicated geometries.

As we reviewed, several numerical solution-based schemes have already been developed to simulate DNA in complex electric fields. However, the previous methods have some limitations. There are two issues in incorporating numerical solution-based schemes: one is the tractability of arbitrary geometries and the other is the ability to address the field value at specific coordinate locations according to the spatial movement of each bead. The latter is not problematic in regular FDM grids since we can easily link coordinates with grid points and we can determine local fields. However, in irregular meshes typically used in FEM to describe complicated geometries, addressing fields at arbitrary coordinates is not straightforward. Thus, though FDM-based schemes are well suited to the entropic trap problem since it is composed of several rectilinear parts and a regular rectangular grid system is available, it would not be straightforward to apply to more complicated geometries. For FEM, there is no geometrical constraint. However, it is not clear if the previous method of Streek et al. can be applied to more general geometries since they used regular meshes to solve the entropic trap problem and there was no difference from FDM in the electric field searching algorithm. Thus, the present work is motivated by the necessity to build up a more general framework to analyze DNA deformation in nonhomogeneous electric fields seen in complex microfluidic geometries.

In this work, we develop a more flexible BD-FEM simulation method that can be applied to DNA electrophoresis in arbitrary geometries. We develop an efficient scheme to determine the electric field at bead locations, an essential and potentially time-consuming step in a BD-FEM simulation. The hard-sphere interaction method developed by Heyes and Melrose is extended to work with boundaries described by a FEM. For verification purposes, we simulate λ-DNA deformation around a cylindrical obstacle which was experimentally surveyed by Randall and Doyle. The analytical solution for the electric field in this problem is known and, thus, a direct comparison between the analytical and numerical approach is possible. We also compare our results with experimental results and investigate the physics in more detail since this problem has not yet been examined with numerical simulation. Finally, we predict DNA deformation in a constrained geometry to show the capability of our method.

II. DESCRIPTION OF SIMULATION METHOD

A. Problem geometry

First, we will briefly describe DNA deformation around a single cylinder in an unbounded domain before we go through methodologies. Readers can also be referred to more discussion about kinematics of DNA deformation around a single cylindrical obstacle in Randall and Doyle’s article. We present a schematic diagram in Fig. 1(a) and the corresponding side view is shown in Fig. 1(b). Electrophoretic velocity field (\(\mu E\)) of DNA is defined as the reverse direction of electric field (\(E\)) for convenience since this is the direction DNA moves, where \(\mu\) denotes the mobility of DNA. In Fig. 1, λ-DNA moves from right to left direction, the radius of cylinder is 10 \(\mu m\), and channel height is 2 \(\mu m\). The electrophoretic velocity field around an insulating obstacle in an unbounded domain is defined in Cartesian coordinates as follows:

\[
\mu E(x, y, z) = \mu E_0 \left[ \frac{R_{obs}^2}{(x^2 - y^2)^2} \right] \frac{e_x}{e_y} + \frac{\mu E_0}{(x^2 + y^2)^2} \frac{e_y}{e_z} + 0e_z,
\]

where \(\mu E_0\) is an electrophoretic velocity in an unperturbed region and \(R_{obs}\) stands for the radius of cylindrical obstacle. We stress that \(\mu E\) is not a hydrodynamic velocity field, but is the local velocity of a non-Brownian point charge with mobility \(\mu\) in an electric field. The characteristics of an electrophoretic field are quite different from its counterpart in hy-
ter hydrodynamic flow. That is, as shown in Eq. (1), there is no $z$-direction dependence as long as the channel height is constant. The electrophoretic velocity is also shear-free and disturbances due to insulating obstacles decay as $O(1/r^2)$ compared with $O(1/r)$ decay in low Reynolds number hydrodynamic flow.\(^{32,33}\)

However, there is more complexity in DNA dynamics due to its flexibility, elasticity, and Brownian motion. When a “centerline” collision is considered (here, centerline collision means that the y coordinate of center of mass of DNA is nearly identical to the y coordinate of the center of the cylinder when DNA impacts the cylinder, we present a precise definition in Sec. II). Randall and Doyle\(^{35}\) recognized that the above electric field kinematics around an isolated insulating cylinder can result in DNA deformation comprising three stages: “preimpact” stretching in front of a cylinder, the rotation of principal axes for the directions of stretching and compression along the cylinder wall, and “postimpact” stretching leaving a cylinder. Thus, DNA initially starts to stretch in front of cylinder, then compresses in the back side region of the cylinder, and finally restretches leaving the cylinder. In this work, we define preimpact as a period until the leading edge of DNA goes over the rightmost part of the cylinder ($x = 10 \mu m$) and postimpact as a period after the rightmost part of DNA passes the leftmost part of the cylinder ($x = -10 \mu m$). Since we consider a centerline collision, DNA moves along the cylinder wall, which coincided with one of the field lines, as shown in Fig. 1. When part of a DNA passes $x = 0$, DNA starts to compress since the principal axis of compression starts to more closely align with the field line on the cylinder.\(^{33}\)

Though the above analytical electrophoretic velocity field can be directly incorporated into a BD simulation,\(^{32}\) here we develop more general methodologies applicable to complicated geometries. The above analytical expression of electric field around a single obstacle in an unbounded domain will be used to verify our FEM.

### B. Brownian dynamics simulation and parameters

#### 1. Bead-spring model

We model the DNA as $N_b$ beads connected by $N_s = (N_b - 1)$ springs. The velocity for bead $i$ is

$$\frac{d\mathbf{r}_i}{dt} = \mu^b \mathbf{E}(\mathbf{r}_i) + \frac{1}{\kappa} [\mathbf{F}^b_i(t) + \mathbf{F}^S_i(t) + \mathbf{F}^F_i(t) + \mathbf{F}^{\text{EV}}_i(t) + \mathbf{F}^{\text{EV,wall}}_i(t)],$$

where $\mu^b$ is the mobility of bead and $\kappa$ the bead drag coefficient, $\mathbf{F}^b_i$ the Brownian force, $\mathbf{F}^S_i$ the net spring force on the bead, and $\mathbf{F}^{\text{EV}}_i$ denotes the force due to excluded volume interaction with other beads. Bead interactions with boundaries (bounding walls or the obstacle) $\mathbf{F}^{\text{EV,wall}}_i$ are treated with a hard-sphere algorithm discussed below. We track DNA dynamics with evolving bead positions $\{\mathbf{r}_i\}$. In this work, hydrodynamic interaction (HI) is not included due to the large computational cost. However, HI is screened in free solution electrophoresis because of the counterion movement\(^{43}\) to compensate for the charged bead and HI due to nonelectrical forces is diminished in thin slits.\(^{44,45}\) We consider electrophoresis of linear DNA in which the phosphate backbone is uniformly negatively charged and the Debye length ($\kappa^{-1}$) is smaller than the persistence length of DNA ($\lambda_p$) in sufficiently concentrated salt solution (typically $\kappa^{-1}$ is approximately in nanometers\(^{44,45}\)). Thus, DNA globally behaves like a neutral polyelectrolyte\(^{14}\) and the electric field is governed by Laplace’s equation since local electric field disturbance by movement of a DNA monomer is screened over the Debye length.\(^{14}\) In this work, the smallest confined region is the radius of gyration of $\alpha$-DNA ($0.7 \mu m$), which is still quite larger than the Debye length scale. Thus, our assumption is still relevant. However, if a confined region is comparable with the Debye length scale, the electric field disturbance by DNA movement will not be negligible. Finally, we comment that it is assumed that electroosmotic flow is not present. Electroosmotic flow was eliminated in experiments by producing an absorbed polymer layer on the walls.\(^{32,33,34}\) The Brownian force $\mathbf{F}^b_i$ models thermal kicks from solvent molecules and is chosen to satisfy the following:\(^{46}\)

\begin{equation}
\langle \mathbf{F}^b_i(t) \rangle = 0,
\end{equation}

\begin{equation}
\langle \mathbf{F}^b_i(t_1) \mathbf{F}^b_i(t_2) \rangle = 2k_BT\delta_{t_1-t_2}\delta_{ij}\frac{2k_BT\zeta_0}{\delta t} \mathbf{I},
\end{equation}

where $k_B$ stands for Boltzmann’s constant, $T$ the absolute temperature, $\mathbf{I}$ unit tensor, $\delta_{ij}$ Kronecker delta, $\delta(t_1-t_2)$ delta function, and $\delta t$ denotes the time step. $\mathbf{F}^F_i(t)$ is the sum of spring forces adjacent to bead $i$,

\begin{equation}
\mathbf{F}^F_i = \begin{cases} 
\mathbf{f}^S_{i,N_b-1}, & i = N_b \\
\mathbf{f}^S_{i,i+1} + \mathbf{f}^S_{i-1,i}, & 1 < i < N_b \\
\mathbf{f}^S_{i,2}, & i = 1,
\end{cases}
\end{equation}

where $\mathbf{f}^S_{i,j}(t)$ denotes the spring between beads $i$ and $j$. We use a Marko-Siggia (MS) spring\(^{16,48}\) with effective persistence length\(^{16,48}\) as follows:

\begin{equation}
f_{ij}^S = k_BT \left[ \frac{r_{ij} - r_i}{l} - \frac{1}{4} + \frac{1}{4(1-r_{ij}/l)^2} \right] \mathbf{r}_{ij},
\end{equation}

where $A_{eff}$ is an effective persistence length, $l$ stands for the maximum extensible spring length ($=L/N_s$), and $r_{ij}$ denotes the distance between $\mathbf{r}_i$ and $\mathbf{r}_j$. Underhill and Doyle\(^{48}\) devised a systematic way to determine the effective persistence length such that the mean extension of a spring subject to a constant force matches that of the wormlike chain model. Following Underhill and Doyle,\(^{48}\) we select the low-force criterion such that

\begin{equation}
\langle R^2 \rangle = \frac{\int_0^L dr r^4 \exp[-U_{eff}(r)/k_BT]}{\int_0^L dr r^2 \exp[-U_{eff}(r)/k_BT]} = 2lA_p,
\end{equation}

where $A_p$ is the true persistence and $U_{eff}(r)$ is the energy of wormlike chain model with effective persistence length as follows:
Using the above equations, we can easily obtain the ratio \( \lambda = A_p \ell / A_p \) for given \( \nu \), where \( \nu \) denotes the number of persistence length per each spring (=\(1/\ell_A\)) and \( 1/A_p \) is equivalent to \( \nu/\lambda \). We set the contour length \( L \) of DNA to 20.5 \( \mu \)m, which was chosen to match the contour length of \( \lambda \)-DNA stained by TOTO-1 (4.71 bp/dye molecule). In this work, we set the persistence length \( A_p \) at 0.053 \( \mu \)m [that of unstained DNA (Ref. 49)] since there is still uncertainty about the persistence length of stained DNA. We model \( \lambda \)-DNA with 19 beads and thus, 18 springs such that \( \nu = 21.488 \) and we obtain \( \lambda = 1.386 \) and, therefore, \( A_p \) computed to be \( -0.0735 \mu \)m using Eq. (7) with given parameters. We employ the excluded volume effect with the soft potential devised by Jendrejak et al. (19,21,50) and will show the performance of each method.

\[
\begin{align*}
U_{\text{eff}}(r) &= k_BT \left( \frac{1}{A_{\text{eff}}} \right) \left( \frac{(r/l)^2}{2} \frac{(r/l)}{4} - \frac{1}{4(1-r/l)} \right). \\
&= \frac{1}{A_{\text{eff}}} \left( \frac{k_BT}{4} \right) \left( \frac{(r/l)^2}{2} \frac{(r/l)}{4} - \frac{1}{4(1-r/l)} \right).
\end{align*}
\]  

(8)

2. Time-stepping scheme

We use Eq. (12) to generate DNA trajectories. We use a first-order explicit Euler time forwarding scheme except for the spring force as follows:

\[
\begin{align*}
\mathbf{r}_i^{n+1} &= \mathbf{r}_i^n + \langle \mathbf{F}_i^{s} \rangle \delta t + \langle \mathbf{F}_i^{\text{EV}} \rangle \delta t + \langle \mathbf{F}_i^{\text{EV,wall}} \rangle \delta t, \\
\mathbf{F}_i^{s} &= \mathbf{f}_i(r_0), \\
\mathbf{F}_i^{\text{EV}} &= -\sum_{j=1}^{N_b} \frac{9}{2} \frac{2}{v_{ij}^{\text{EV,p}}} \left( \frac{3}{4 \pi} \right) v^{\beta/2} \exp \left[ -\frac{9}{4} \frac{r_{ij}^2}{v_{ij}^{\text{EV,p}}} \right] \mathbf{f}_j - \mathbf{f}_i.
\end{align*}
\]  

(9)

where \( \mathbf{r}_i^{n+1} \) and \( \mathbf{r}_i^n \) stand for intermediate time steps while a time step is forwarding from \( n \) to \( n+1 \). During computation of Eq. (18), if spring overstretching is encountered (i.e., non-dimensional bead separation is greater than 1), the spring force in Eq. (18) is implicitly treated as \( \mathbf{F}_i^{\text{**}} = \mathbf{f}_i^{\text{**}} + \mathbf{F}_i^{\text{EV,wall}} \). The nonlinear equations are linearized with Newton-Raphson method, and algebraic equations are solved with an iterative solution method. We also consider other three different variants. One is to consistently use explicit Euler, another is to always use implicit Euler scheme, and the last one is to adaptively evaluate Eq. (18) as explained. We will call those schemes by “explicit,” “implicit,” and “adaptive” schemes in turn. In the explicit method, if overstretching is encountered, the calculation cannot go further in contrast to the other two schemes. On the other hand, the computational time at each time step is relatively large due to Newton-Raphson/iterative method when the implicit scheme is used. Our implicit scheme is similar to that used by Jendrejak et al. (19,21,50). The adaptive scheme is incorporated to reduce computational time to overcome the disadvantages of both explicit and implicit methods. This “adaptive algorithm” is different from a “rejection” algorithm which was implemented by Somasi et al. (51). In a rejection algorithm, the time forwarding is reattempted with a different random number whenever overstretching is encountered and this can lead to non-negligible errors. We studied all three time forwarding schemes (explicit, implicit, and adaptive) and will show the performance of each method.

3. Bead-wall interactions

The equation of motion [Eq. (18)] does not prevent a bead from passing through a solid boundary (i.e., an obstacle or wall). A potential energy barrier could be devised to prevent penetration of beads through solid walls, that is to say, an explicit form for \( \mathbf{F}_i^{\text{EV,wall}} \) in Eq. (12) can be devised. However, if the potential is steep near a wall, such as that of
Lennard-Jones, a very small time step should be used to avoid numerical instability. On the other hand, in the case of soft potential, a bead can sometimes penetrate through a wall. Jendrejack et al.\textsuperscript{30} devised a potential barrier for bead-wall interactions which is harder than the Gaussian soft potential used for bead-bead interaction and softer than typical Lennard-Jones potential. However, it is not clear that this approach can be universally applied irrespective of field kinematics since it is not obvious that this potential is sufficiently steep so that a bead is completely prohibited from penetrating through a wall but yet is not steep enough that numerical instability is avoidable. We adopted a “potential-free” algorithm developed by Heyes and Melrose\textsuperscript{42} to mimic the hard-sphere interaction between two beads, which has been widely used in colloid simulation.\textsuperscript{42,52,53} Practically, it is implemented such that a bead is repositioned to the nearest wall whenever it penetrates through the wall during a time step, as shown in Fig. 2.

\[
\Delta \hat{r}_i^{HM} = \Delta \hat{p}_i \hat{H}(\Delta p_i),
\]

where \(\Delta \hat{r}_i^{HM}\) is the displacement vector by Heyes and Melrose’s algorithm and \(\Delta p_i\) denotes the minimum distance from boundary. \(\Delta \hat{p}_i\) is a vector connecting a bead and the boundary point where the distance between a bead center and boundary point is minimum. The Heaviside step function is used to consider only the penetrated beads.\textsuperscript{42} After the computation of Eq. (18), Eq. (19) is applied to each bead and the final location is as follows:

\[
\hat{r}_i(\hat{t} + \delta t) = \hat{r}_i^{**} + \Delta \hat{r}_i^{HS}.
\]

In our simulation, we reposition the center of a bead onto the boundary. Physically, this corresponds to saying the bead has a negligible radius and acts like a point. Other possible choices for the bead radius might be half the DNA width (∼2 nm) or the spring radius of gyration (∼0.14 μm). Both of these are much smaller than other length scales of interest (e.g., DNA stretch of microns). We chose to simplify the modeling by reducing the bead to a point and thus the bead radius never appears as a length scale. The present model works well with guaranteeing numerical stability and no penetration of beads through walls. One potential problem is that overstretching of a spring can occur when a DNA moves along a convex boundary in a highly stretched state with large time stepping. However, when implicit or adaptive time stepping is used, an overstretched spring returns within the maximum extensible length after the evaluation of Eq. (18) at the next time step.

4. Parameters

We define the Deborah number (De) as\textsuperscript{33}

\[
De = \tilde{e}^d \tau,
\]

where \(\tilde{e}^d\) denotes the electrophoretic strain rate at the front stagnation point and \(\tau\) is the relaxation time of the polymer. For the unbounded cylinder problem, the strain rate is \(2\mu E_0 / R_{obs}\), and \(De = 2\mu E_0 / R_{obs}\). However, the strain rate was numerically computed for the problem of a cylinder with lateral confining walls. The parameter for excluded volume was determined by matching the experimentally measured radius of gyration (0.69 μm).\textsuperscript{54} The computed radius of gyration (using 300 independent trajectories) is 0.7±0.01 μm when \(\tilde{e}^V\),\(\rho = 0.0004 \mu m^2\). We obtained the relaxation time in the 2 μm height channel by fitting chain relaxation to the following single exponential function:\textsuperscript{16}

\[
\langle x(t)^2 \rangle = A \exp(-t/\tau) + \langle x^2 \rangle_0,
\]

where \(\langle x(t)^2 \rangle\) denotes the difference between the upstream-most and downstream-most parts of DNA at each instance \(t\), \(\langle x^2 \rangle_0\) denotes the corresponding mean square difference between the upstream-most and downstream-most parts at equilibrium, and \(A\) is a fitting parameter. An ensemble of 500 DNA chains was initially placed in the middle of channel and linearly stretched to the initial relative extension \(\langle x/L \rangle_0 = 0.7\). Equation (22) was fitted to the data in the region \(x/L < 0.3\), as was done in the previous experiments.\textsuperscript{33} The nondimensional relaxation time \(\hat{\tau}\) was 0.53.

C. Finite element method

The electric field is computed from the electric potential with the relationship \(\mathbf{E} = -\nabla \Phi\) in an arbitrary domain, where \(\Phi\) denotes electric potential. We consider electrophoresis in a microfluidic device with a constant gap height and insulating boundaries. Thus, due to the natural boundary condition on the insulating wall, the problem scale is reduced to two dimensions (2D). As noted by Randall and Doyle,\textsuperscript{33} the electric field is harmonic in contrast to the biharmonicity of Stokes equation which is typically applied to the pressure-driven flow analysis in a microfluidic channel. Thus, the gradient of the electrophoretic velocity is steeper around an obstacle than the corresponding hydrodynamic problem, which means that the domain around an obstacle should be more finely discretized than in the the hydrodynamic flow counterpart.

With increasing complexity of geometry, it becomes necessary to use a numerical method for the field equation. In this work, we use the Galerkin finite element method as a spatial discretization scheme for the governing equation, in which the interpolation in each finite element can be easily
performed using the same framework as solution scheme. We begin with the governing equation for the electrostatic potential,
\[ \nabla^2 \Phi = 0 \quad \text{in } \Omega, \]
where Eq. (24) denotes boundary conditions on boundary \( \partial \Omega \) and \( \mathbf{n} \) denotes the normal vector along boundary. There are several types of boundary conditions in a typical electric potential problem. However, in this work, only two boundary conditions are considered. One is an essential boundary condition which corresponds to inlet and outlet conditions such that the potential is explicitly prescribed. The other is the natural boundary condition at an insulating solid wall. In the experimental system, the channel walls and obstacles are made of poly(dimethylsiloxane) (PDMS) and we will treat PDMS as a perfect insulator. In FEM, the domain \( \Omega \) is divided into a discretized space \( \Omega^e \) such that \( \Omega^e = \bigcup \Omega_e \) and \( \bigcap \Omega_e = \emptyset \). In this work, \( \Omega_e \) are finite element elements and in 2D FEM, triangular or quadrilateral element is typically used and hybrid of triangular and quadrilateral meshes is also possible. In this work, a triangular mesh is adopted since a complicated geometry is easily discretized with the well-known Delaunay triangulation method, and when the electric field is interpolated with triangular linear shape function, the mapping of local coordinates onto master element coordinates is unique with a linear relationship,
\[ \Phi = \sum \Phi_i \Psi_i, \]
where \( \Psi_i \) is six-node \( P_0^3 \) shape function and we obtain the weak formulation of Eq. (24) after weighted residual and integration by parts,
\[ \langle \nabla \Phi, \nabla \Psi \rangle = \left\langle \frac{\partial \Phi}{\partial \mathbf{n}}, \Psi \right\rangle \quad \text{in } \Omega^e, \]
where \( \langle \cdot \rangle \) stands for a domain integral and \( \langle \cdot, \cdot \rangle \) denotes a boundary integral. Equations (26) and (24) yield a complete set of algebraic equations to solve for electric potential. In Eq. (26), we know that the insulating boundary condition can be easily imposed by setting the right-hand side to 0. This simple way to impose the boundary condition in FEM is another merit compared with the FDM. Since the unknowns for electric potential amount to \( O(10^5 \sim 10^6) \), the dense memory format is practically impossible to store data in in-core memory. We use ILU(0) preconditioner and general-purpose BiCGSTAB solver \(^{56}\) as solution scheme, which was previously used for viscoelastic flow analysis. We set the error tolerance in the iterative solver to \( \| L_i \| \leq 10^{-8} \). Once electric potential is obtained, \( E \) is simply computed from \( E = -\nabla \Phi \), where \( E \) is interpolated with three-node \( P_1^0 \) shape functions and the calculated electric field is stored in a database. Then, we normalize the electric field with the unperturbed electric field \( (E_0) \) in the upstream and the length scale is normalized with \( l \).

\[ E_x = \sum_{i=1}^{3} E_{x_i} \hat{y}_f, \quad E_y = \sum_{i=1}^{3} E_{y_i} \hat{x}_f, \]

\( x, y \) coordinates of the element are also expressed by isoparametric mapping as shown in Fig. 3.

D. Connection algorithm between BD and FEM

In our simulation, the BD algorithm addresses the electric field at each bead’s position from a database which was made with the previously explained method. In the literature, we could not find a BD-FEM computation in which irregular meshes were used. This can be attributed to difficulty in addressing the local electric field in irregular meshes. On the other hand, addressing the electric field is relatively straightforward in regular meshes. For example, consider a simple rectangular box geometry \((x_b, y_b)\). The box can be uniformly divided into rectangular meshes with \( N_x \times N_y \) nodes, that is, \((N_x - 1) \times (N_y - 1) \) meshes. Thus, each mesh size is \( \delta x \times \delta y \), where \( \delta x \) is \( x_b/(N_x - 1) \) and \( \delta y \) corresponds to \( y_b/(N_y - 1) \). Then, we can easily find what mesh includes a bead coordinate \((x_b, y_b)\) by integer commands [for example, in FORTRAN77 \( \text{INT}(x_b/\delta x) \) and \( \text{INT}(y_b/\delta y) \)]. Then, we can interpolate the electric field using the electric field values at nodes of the mesh. However, in irregular meshes, which are essential for most engineering problems, there is no simple one-to-one mapping rule between coordinates and electric field as used in regular meshes.

Though the interpolation used in FEM is well established,\(^{58,59}\) we briefly present the concept to elucidate the issue related to the present work. On each triangular finite element, electric field is interpolated by linear shape functions as follows:

\[ E_{x_i} = \sum_{i=1}^{3} E_{x_i}^e \hat{y}_f, \quad E_{y_i} = \sum_{i=1}^{3} E_{y_i}^e \hat{x}_f, \]
Therefore, once it is known what element includes the target bead, local coordinates are changed into master element coordinates \((\xi^e, \eta^e)\) and then the electric field can be easily computed with Eq. \((28)\). However, to find out what element surrounds the specific bead is not straightforward in nonuniform finite elements for an arbitrary geometry. Unless the addressing scheme is efficient, the computation is not possible since the BD computation is composed of so many time steps (in this work, \(10^4 \sim 10^5\)) and many ensembles \((\sim 10^3)\). We first consider a naive approach which scans all finite elements to find out what element includes the target bead, where the method scans from element 1 to the final element until the element that includes the bead is encountered. Since the excluded volume effect is implemented in our BD algorithm, the operation count (neglecting the searching algorithm) at each time step is \(O(N_e^2)\), however, the number of elements in this work amounts to \(\sim 10^3\) and, therefore, the operation count for the searching algorithm would be \(O(N_b \times 10^5)\), which would be the dominant operation count in the BD computation. Thus, this naive scheme does not work for the present problem which contains many elements. On the other hand, in previous works, which considered a nonhomogeneous electric field, to access the element in FEM or the points surrounding a bead in FDM can be quickly performed with simple mapping rules since all the geometries are composed of simple rectilinear shapes. However, these geometries are just topologically special cases.

In this work, we present a more general method applicable to arbitrary geometries. As shown in Fig. 4, the finite element meshes constitute a kind of network composed of many nodes (vertices) and edges, or assembly of elements. Thus, the present problem is equivalent to searching a specific element on the network. Since Euler’s famous solution for Königsberg bridges problem, the property of the network has become an important issue in mathematics and engineering. Graph theory is a mathematical language to treat the property of a network. In graph theory, a network is represented with a “graph” and Saad has used the graph concept to analyze FEM structure. We represent the FEM as a network of elements since the importance exists in finding a specific element in the graph. Graph \(G\) is composed of two sets. One is a set of elements,

\[ E = \{e_1, e_2, e_3, \ldots, e_{n, \text{elem}}\}. \]

The other set \(C\) contains pointers to denote connection \(e_i\) and \(e_j\) such that \(C \subseteq E \times E\) and graph \(G = (E, C)\). \(G\) is undirected and each element \(e_i\) is a loop composed of three nodes \((n_{i,j}^e, j = 1, 2, 3)\) or three lines \((l_{i,j}^e, j = 1, 2, 3)\) which can be naturally extracted at the preprocessing step. Thus, the present problem is defined as

\[ \text{find } e : e \supseteq (x^e, y^e) \quad \text{for } e \in E \in G. \]

In this work, we assume that a bead is located at the position \(O\) in element \(I\) as shown in Fig. 4 and the bead moves to the location \(T\) in element \(F\) at the next time step.

\[ x^e = \sum_{i=1}^{3} x_i^e \hat{\phi}_i, \quad y^e = \sum_{i=1}^{3} y_i^e \hat{\phi}_i. \]
searching algorithm returns to $E^T$. Among the three elements adjacent to $E^T$, the element is chosen which is neither $E^W$ nor a previously passed element to reach $E^P$ ($L(E^P)$).

An example in complicated geometry is presented in Fig. 4, where one end of the line is the centroid of the starting element, and the other end is the target location. The line denotes the trajectory trespassing the centroid of elements. We call this algorithm a target-induced searching algorithm. In real computations, since beads move slowly in graph $G$, the target is typically encountered within hopping over a few elements, except the starting of computation at $t=0$.

III. RESULTS

A. Verifications and comparison with experiments

1. Domain determination and mesh refinement

Randall and Doyle$^{33}$ made 5–10 mm long, 100 $\mu$m wide, and 2 $\mu$m high microchannels with a single cylindrical obstacle with 10 $\mu$m radius. Thus, the channels are confined by sidewalls, and upper and bottom walls. In the simulation, we fixed the gap height between the upper and bottom walls to 2 $\mu$m and also the length to 10 mm. Randall and Doyle$^{33}$ assumed that the sidewall effect (finite channel width) is negligible for the electric field and, thus, the field kinematics is equivalent to the unbounded domain case. However, in a numerical simulation, there should be a more stringent condition such that the sidewall effect is sufficiently eliminated to mimic the unbounded domain. We varied the width of channel and examined the $x$ component of electrophoretic velocity field on the cylinder wall for $-1 < x/R_{obs} < 1$ and along the centerline for $x/R_{obs} > 1$ or $x/R_{obs} < -1$, as shown in Fig. 5. We examine the numerics at $x=0$ for different channel widths, where the deviation is the largest due to sidewalls. The relative error compared with the analytical solution was $\sim 3.4\%$ in the case of a channel width equal to 100 $\mu$m, which might be negligible error for the experiments. We increased the channel width up to 800 $\mu$m to reduce the deviation. Then, the error was reduced to 0.045% at $x=0$ and the whole profile is in good agreement with the analytical solution, as shown Fig. 5(a). Then, we checked the mesh dependence for the 800 $\mu$m channel width. In this work, we considered three different finite elements for a width of 800 $\mu$m (see Table I for details). The value of streamwise velocity at $x=0$ converged to 2.0009 irrespective of mesh. The small difference from the value 2.0 for an unbounded domain can be attributed to the finite width (800 $\mu$m). Though the deviation could be reduced more with a larger channel width, we assume that an 800 $\mu$m width sufficiently mimics the unbounded domain. In this work, we use mesh III for all the computations.

2. DNA properties and initial conditions

We measure several physical quantities of the DNA during a simulation. The chain center of mass $(x_{c.m.}, y_{c.m.})$ is calculated from

\begin{equation}
\begin{aligned}
x_{c.m.} &= \frac{1}{N_b} \sum_{i=1}^{N_b} x_i, \\
y_{c.m.} &= \frac{1}{N_b} \sum_{i=1}^{N_b} y_i,
\end{aligned}
\end{equation}

where $x_i$ and $y_i$ denote the Cartesian coordinates of each bead. Following Ref. 33, the extension of DNA is computed such that after the leftmost, rightmost, topmost, and bottommost points are located, the longest distance among lines connecting any two points is chosen as the extension $x_{c.m.}$. Care must be taken in evaluating stretch near the cylinder. Since we consider centerline collisions, there are two possible regions where DNA significantly stretches: on the cylinder wall and postimpact stretch (downstream from the cylinder). We consider that a DNA is “on the cylinder” when the stretch of DNA is larger than 5 $\mu$m and the $x$ component of the rightmost bead in a chain is greater than $-10 \mu$m. The latter criterion was used to preclude the postimpact stretch region. This criterion is very similar to that used previously in analyzing experimental data.$^{33}$ We then compute the DNA stretch using the end-to-end arc length when a DNA is on the

<table>
<thead>
<tr>
<th>No. of vertices</th>
<th>No. of nodes</th>
<th>No. of elements</th>
<th>Characteristic mesh size at front stagnation point $(\Delta x/R_{obs}, \Delta y/R_{obs})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesh I</td>
<td>91 264</td>
<td>362 288</td>
<td>179 760</td>
</tr>
<tr>
<td>Mesh II</td>
<td>173 554</td>
<td>690 244</td>
<td>343 136</td>
</tr>
<tr>
<td>Mesh III</td>
<td>304 932</td>
<td>1 214 008</td>
<td>604 144</td>
</tr>
</tbody>
</table>

TABLE I. Detailed information about the meshes used for the DNA deformation around a single cylinder in an unbounded domain.
cylinder. The strain accumulated by a chain during a trajectory is computed as follows.\textsuperscript{33}

\[ \epsilon(r(t')) = \sum_{i=1}^{n} \epsilon(r(t)) \delta t, \]  

(32)

where \( \delta t \) is time step and \( \epsilon(r(t)) \) is the strain rate for the given location \( r(t) \), which can be analytically defined for the cylinder problem in unbounded domain.\textsuperscript{33} However, this value should be numerically computed using eigenvalues of the electrophoretic velocity gradient tensor for the cylinder confined by sidewalls. For an unbounded cylinder, we made sure that the strain obtained using the numerically computed strain rate was equivalent to the analytical value.

Saville and Sevick\textsuperscript{60} defined the parameter \( b \) as the \( y \) offset between DNA's center of mass and the obstacle center in their BD simulation. Randall and Doyle\textsuperscript{33} analyzed the centerline collisions only with \( |b| < 1 \) \( \mu \)m when DNA passes \( x_{c.m.}=2R_{obs}+R_g \). In this work, we also considered the centerline collisions with \( |b| < 1 \) \( \mu \)m at \( 2R_{obs}+R_g \). In experiments, DNA is randomly distributed along the channel width and approaches a cylinder from a reservoir. DNA is selected for analysis when the offset is within \( |b| < 1 \) \( \mu \)m at the checkpoint. In our numerical simulation, to directly replicate experimental conditions is too exhaustive. We select the starting point of DNA movement as \( x=5R_{obs} \) from the center of cylinder. Stretching of the chain in the region \( x \gg 5R_{obs} \) is assumed to be negligible since \( \epsilon(5R_{obs})=f_{x=5R_{obs}}^{x=K_{obs}} \epsilon(r) / \mu E(r) dr \sim 0.04 \) and \( \epsilon(5R_{obs}) \times \tau \ll 1 \).

We preserve a uniform center of mass distribution of DNA in the \( y \) direction within \( |b| < 1 \) \( \mu \)m at \( x=2R_{obs}+R_g \) by widening the region where DNA is initially distributed (5\( R_{obs} \)). That is to say, if we naively distribute DNA just within \( |b| < 1 \) \( \mu \)m at 5\( R_{obs} \), the distribution of DNA at 2\( R_{obs}+R_g \) will be skewed towards the center by lateral diffusion. The initially uniform distribution \( P(y_0) = 1/H \) for \( y_0 \in [-H/2,H/2] \), where \( H \) denotes a width at \( x=5R_{obs} \), will be diffused to \( P(y) \) for \( y \in [-1,1,1] \mu \)m, 

\[ P(y) = \frac{1}{H} \int_{-H/2}^{H/2} \exp(-y-y_0)^2/4Dty_0, \]  

(33)

where \( t \) is the convective time computed by dividing the distance between 5\( R_{obs} \) and 2\( R_{obs}+R_g \) by the electrophoretic velocity in the unperturbed region (\( \mu E_0 \)) and the DNA diffusivity \( D = k_BT/2N_a \). The chosen criterion (\( P(0 \) \( \mu \)m) - \( P(1 \) \( \mu \)m))/\( P(0 \) \( \mu \)m) < 0.01) should be satisfied to obtain the uniform distribution at \( x=2R_{obs}+R_g \). For the given parameters at \( De=2 \), we obtain \( H > 4.3 \mu m \) using the above criterion. We use \( H=5 \mu m \) at \( De=2 \) since there is a gradual decrease in the \( x \) component of electrophoretic velocity during the movement between 5\( R_{obs} \) and 2\( R_{obs}+R_g \). In brevity, the initial uniform distribution of the center of mass of DNA in \( \pm 2.5 \mu m \) width around \( y=0 \) at \( x=5R_{obs} \) will guarantee a uniform distribution within \( \pm 1 \mu m \) width around \( y=0 \) at \( x=2R_{obs}+R_g \). The increased with (e.g., 3 \( \mu m \) in the case of \( De=2 \)) to compensate for lateral diffusion scales as \( -1/\sqrt{De} \). We used 2000–3000 DNA chains. Initially 1000 configurations without excluded volume are generated by choosing spring length from a Boltzmann distribution and having random orientations. We reject configurations penetrating the bounding walls. We then run BD simulations for over 10\( \tau \) including the excluded volume effect to obtain equilibrium configurations in the channel. Then we successively prepared additional initial configurations by running BD simulation for over 2\( \tau \) using the 1000 equilibrated DNA configurations as initial conditions.

3. Performance of time forwarding schemes

We first compared the three different time forwarding schemes explained previously with the analytical electric field [Eq. (1)] and analytical circle equation to define the cylinder region (for the bead-wall interaction calculation). In the case of explicit Euler scheme, we chose the time step as large as possible, but such that overstretching does not occur. We compared the ensemble-averaged fractional extension (\( \langle x_{eq} \rangle /L \)) versus strain at \( De=9 \). The simulations start with an ensemble of 2000 chains of which 42%–45% of the chains are selected at the checkpoint \( x=2R_{obs}+R_g \) with \( |b| < 1 \) \( \mu m \) criterion and were involved in the computation of ensemble averages. We show the details of each time forwarding scheme in Table II. Implicit scheme with analytical electric field solution and analytical description of cylinder region (anal./anal.) is represented by case 1. Adaptive and explicit schemes with the same methods for electric field and cylinder domain as case 1 are called by case 2 and case 3, respectively. As shown in Table II, the difference of time step between case 3, and case 1 and case 2 schemes is 100-fold. As shown in Fig. 6(a), the difference among results from three different methods is quite small and this difference can be attributed to statistical error. However, as shown in Table II, the total computational time is decreased as time step increases. The difference of total computational times be-
between the case 1 and the case 2 methods is twofold, where the total number of computations is slightly different even for the same $\delta t$ since we do not proceed the computation for a DNA which is out of range at the checkpoint. Thus, we chose the adaptive scheme as the time forwarding scheme since it is the most efficient with the reliable accuracy as we compared three different time forwarding schemes at $De=9$.

We fixed $\delta t=10^{-3}$ at $De=9$ and the time step size for larger $De$ scales as $1/De$. However, for small $De$, the maximum time step is restricted to $4 \times 10^{-3}$ to preserve the convergence in obtaining the spring force. Jendrejack et al.\(^\text{19}\) chose a time step equal to 0.1 multiplied by whichever is smaller between the bead diffusion time scale (using the spring $R_g$ as the length scale) and the inverse of strain rate. In terms of our parameters, their criterion is $\delta t=0.1 \times \min\{(z^2/k_BT)/3, 1/\dot{\varepsilon}^{1/3}\}$ or $\delta t=0.1 \times \min\{0.02, 0.54/De\}$. Thus, for $De=9$ our $\delta t$ is smaller than that used by Jendrejack et al.,\(^\text{19}\) whereas our maximum time step is approximately twice that of Jendrejack et al.\(^\text{19}\) at lower $De$.

As previously explained, the analytical solution of electric field around a cylinder in an unbounded domain is available and the cylinder edge can be explicitly defined with a circle equation. However, we also solve this problem with numerical-based schemes based on FEM and a target-induced searching algorithm to validate our algorithm and benchmark the performance. In addition to the previously explained numerical schemes (FEM and target-induced searching algorithm), another numerical scheme is necessary to deal with events occurring around boundaries, which is related to Heyes and Melrose’s algorithm\(^\text{42}\) for hard-sphere excluded volume interactions. As shown in Fig. 2, a bead is repositioned onto the nearest boundary point from the bead if a bead is outside the domain. When a bead penetrates through a top or bottom plate, $z$ coordinate of the bead is repositioned onto the $z$ coordinate of the plate. For a cylindrical boundary, the nearest point can be analytically determined.

When using arbitrary boundary geometries, a more general method must be developed. We define the boundary as the set of segments (lines) connecting boundary nodes of finite element meshes. Thus, the domain is represented by a polygon. First, we should confirm whether a bead is in the domain or not. We use the ACM112 algorithm\(^\text{61}\) to confirm the position of a bead relative to the polygon. ACM112 is a general-purpose algorithm that checks whether a point is in a polygon or not. Then, we search for the point nearest to a bead which is out of the domain by scanning all the boundary line segments. However, to use ACM112 algorithm for all beads at each time step is computationally too exhaustive since this procedure involves the investigation of all the boundary segments ($O(10^3)$). Since the event that a bead is out of the domain is relatively rare, we call the ACM112 algorithm only after the target-induced searching algorithm has failed to locate the target bead with 100 steps. We then use ACM112 to make sure that a bead is out of the domain since the prescribed number of searching steps might be not sufficient. However, at least for the present problem, the prescribed number 100 was sufficient.

We implemented two different numerical-based algorithms: one is to incorporate the numerical electric field obtained with FEM and analytical treatment of cylindrical boundary, and the other is to use both numerical electrical field and numerical treatment of boundary. We denote the former as case 4 and case 5 corresponds to the latter. The details for each case are given in Table II. The adaptive time forwarding scheme is used and the time step was set to $\delta t=10^{-3}$. In Fig. 6(b), we compare the ensemble-averaged extension versus strain for cases 2, 4, and 5 at $De=9$. Case 2 was inserted for comparison since it analytically treats both the electric field and excluded volume interaction. As shown in Fig. 6, the difference between the results for the various methods is negligible and, therefore, we can confirm the accuracy of the FEM treatment of both the electric field and boundary interactions. Favorable agreement between the methods was also confirmed at other $De$. We present the computational times for each numerical scheme in Table II. Comparing case 4 to case 2, we see that treating the electric field using FEM increases the total computational time 35% relative to the analytical treatment. When purely numerical method-based algorithms (case 5) are used, the total computational time is increased to 2.4 times the purely analytical approach (case 2). The increase of total computational time.
is mainly due to the numerical treatment of a bead which passes through a boundary. We expect that a heuristic algorithm would be helpful to reduce computational time due to boundary searching, for example, a hybrid analytical-numerical method, or domain decomposition into several blocks to reduce the number of boundary segments to be investigated. Such studies will be investigated in the future. However, the current algorithm is robust and the total computational time is still modest. For the remainder of the results presented here, we treat both the field and obstacle boundary numerically (case 5).

4. Comparison with experimental results

We turn now to the direct comparison of numerical simulation and experimental data. In previous research, BD has given promising results in that its predictions are in good agreement with experimental data in both qualitative and quantitative aspects.6–19,21,30,62

As shown in experiments,33 the deformation of DNA around cylindrical obstacles shows rich physics due to nonhomogeneities of field kinematics and the elasticity of DNA. Moreover, the diversity of chain dynamics due to “molecular individualism” results in a complex system. Thus, the question that BD is still useful in nonhomogeneous electric fields should be determined. Keeping these facts in mind, we compare experimental and numerical data.

Since DNA deformation in elongational flows is strongly sensitive to initial configurations, DNA deformation looks chaotic. However, we observe two representative modes as shown in Fig. 7, where we present two independent trajectories in the same figure for comparison. The trajectories were independently computed at De=2 using the same conditions (i.e., the same numerical methods and parameters are used) except for the initial configuration and random number sequence. In Fig. 7, the trajectory following the upper half of the cylinder (we denote DNA0) shows negligible deformation while passing the cylinder region, whereas the other DNA moving along the lower half of the cylinder (denoted as DNA1) experiences significant stretching. One might suspect that this difference is due to differing residence times and hence accumulated strain; however, they have very similar strains (6.5 and 6.4 for DNA0 and DNA1, respectively, as they pass the rear stagnation point). This means that individual DNA dynamics are quite different even when the molecules experience similar strains. The present observations clearly show molecular individualism in a nonhomogeneous electric field, which also supports the previous experimental results.33

When De is increased to 9, we observe an interesting phenomenon, as shown in Fig. 8. The DNA initially begins to stretch as it moves along the cylinder and then begins to compress after passing x=0. The DNA continues to compress and has the minimum size near the rear stagnation point (x=−10 µm and y=0 µm). The deformation history of DNA up to this point is similar to the DNA1 case in Fig. 7. However, the DNA in Fig. 8 shows a significant postimpact stretching, as shown in Figs. 8(g) and 8(h), responding to a local strain rate near the rear stagnation point, where the principal axis of stretching aligns with the centerline (y=0 µm).33 The simulation poststretch results reproduce the experimental observations.33 When DNA0 leaves the obstacle, as shown in Fig. 7, we can also observe some postimpact stretching in spite of no significant front-side stretching. All these qualitative trends are consistent with experiments.33

We show 30 sample trajectories for De=1, 2, and 9 in Fig. 9 for comparison with experiments, where strains are integrated following each DNA’s center of mass trajectory. Overall, simulations reproduce the trend observed in experiments, where the deformation history of each DNA is individually very different, which is the hallmark of molecular

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**FIG. 7.** (Color online) Sample images (top view) of two representative modes at De=2. A DNA moving along the upper half of the cylinder (green; gray) shows an example of negligible deformation (“roll-off”), whereas a DNA moving the lower part of the cylinder (black) experiences significant stretching. The trajectories of these two DNAs were sampled from the whole trajectory set. Each configuration in the same figure was captured at the same time. Time between successive images is 0.75µs.

**FIG. 8.** (Color online) Sample images (top view) of λ-DNA collision at De=9. Time between successive images is 0.28µs for (a)–(c) and 0.09µs for (c)–(g), and 0.19µs for (g) and (h).
individualism. However, it is obvious that there are three stages: initial stretching, compression, and stretching in both simulation and experiments. Here, we mention that the equilibrium stretch in experiments is shown to be larger than numerical simulation, which is mainly due to the blooming effect when visualizing small objects with fluorescence microscopy. For example, the computed equilibrium stretch \((x_{eq})_{eq}/L\) was 0.08 whereas it was experimentally measured to be 0.13. In Fig. 9, we see that the level of stretch overall increases with increasing De in simulation data [Figs. 9(b), 9(d), and 9(f)]. However, this trend is not obvious in experimental data when De = 2 and 9 cases are compared [Figs. 9(c) and 9(e)], whereas it seems that the stretch level at De = 2 and 9 is higher than the De = 1 case [Fig. 9(a)]. We attribute this nonmonotocity of experimental data to the small number of ensembles, that is, a statistical problem.

Finally, we compared the normalized stretch \((\langle x_{eq}^2 \rangle - \langle x_{eq} \rangle^2)/L^2\) in the downstream region of the cylinder (\(x < 0\)). Following the previous study, 33 we reset \(l/\tau\) to 0 when a stretched DNA is compressed to \(x_{eq}/L = 0.3\). In the absence of an applied field, the decay of the normalized stretch will be proportional to \(\exp(-l/\tau)\) for \(x_{eq}/L < 0.3\). Faster relaxation can occur in the present problem due to the compressive nature of the field kinematics in the region \(x < 0\). As shown in Fig. 10, the numerical simulation predicts well the experimental data except that the predicted stretching postimpact is slightly lower than the experimental data. In the experiments, the local minimum of compression before postimpact stretch at De = 9 is increased compared with the De = 2 case. This trend is also numerically observed and the simulation accurately predicts the position and the value of local minimum. Thus overall the simulation accurately predicts DNA deformation in nonhomogeneous electric fields.

5. Comparison with conductive obstacles

Saville and Sevick 60 studied polymer dynamics around conductive cylindrical obstacles for various sizes and strengths of electric fields (Péclet numbers) using BD simulations. They assumed a uniform electric field around the cylindrical obstacle. It is difficult to quantitatively compare our results with their results since the details of the BD schemes and numerical parameters used in the studies are rather different. For example, they used a Hookean spring model in their bead-spring model and modeled the bead-obstacle interaction using a soft repulsive potential. Also, our main dimensionless parameter is De, whereas their analysis was based on Péclet numbers (“dimensionless field strength”). Nevertheless, it is interesting to survey how different electrical properties of an obstacle affect DNA dynamics at least even on a qualitative level.

The present 10 \(\mu\)m radius cylinder for \(\lambda\)-DNA corresponds to the “large cylinder” case considered by Saville and Sevick 60 (the ratio of the cylinder radius to the radius of gyration, \(\gamma_c\) of \(\lambda\)-DNA is \(\approx 14\) in this work). They showed that for large \(\gamma_c\) when DNA experiences a direct impact (this corresponds to the centerline impact of the present work), two distinct modes are observed when the DNA leaves the obstacle highly stretched state from chain unraveling at the front of the obstacle or unperturbed “roll-off” chains. The roll-off observed by Saville and Sevick 60 may be coincident with the DNA” case of Fig. 7. However, the origin of the other stretched state is quite different from our works. The unraveled chains in front of an obstacle unhook by a kind of “rope-over-pulley” mechanism 63 and then, this state is preserved in the case of a conductive obstacle until a DNA is
thermally relaxed. However, in this work, as shown in Fig. 7, the stretched DNA compresses near the rear stagnation point. That is to say, it is not probable to preserve the front-side stretching due to the back-side compression. Instead, as shown in Fig. 8, the observed stretch when a DNA leaves an obstacle originates from the postimpact stretch near the rear stagnation point.

The other interesting difference is the lateral movement (y direction) of center of mass seen in the conductive obstacle case when a DNA is doing a centerline collision. As shown in Fig. 1, when we consider the centerline collision (direct impact) around an insulating cylinder, the field line will be symmetric around \( x=0 \). Thus, the \( y \) coordinate of center of mass of DNA when the DNA leaves the cylinder is not so different from centerline. However, in the case of a conductive obstacle, as soon as a bead passes \( x=0 \) the field is no longer pushing it into the obstacle and so it will tend to convect in the field direction (x direction). This leads to a substantial displacement of the \( y \) component of the center of mass after a collision with a conductive obstacle.

Though a conductive obstacle is not in principle impossible,\(^6\) we expect that our results would be more relevant for practically more important insulating obstacle cases which are often made in PDMS using soft lithography.\(^6^4\) The uniform electric field is applicable to an obstacle of which the electrical conductivity is ideally matched with that of the DNA buffer solution. The present discussion shows that DNA dynamics is strongly dependent upon the electrical property of an obstacle and considering field nonhomogeneities is essential to accurately predict DNA dynamics around an insulating obstacle since polymer dynamics are sensitive to local kinematics.

**B. Deformation around a cylinder at various Deborah numbers**

In this section, we present results from parametric studies of DNA deformation around a single cylindrical obstacle. The DNA experiments are quite tedious due to the overwhelming amount of data measurement and processing.\(^6^5\) Numerical simulations are more feasible for large parametric studies. We first show results for the stretching around a single cylinder in an unbounded domain, which corresponds to the experimental research by Randall and Doyle.\(^3^3\)

In Fig. 11, we present ensemble-averaged deformation histories versus strain for various De. There are three distinct stages as strain increases. It is observed that DNA stretching occurs within strain less than 4 and compression occurs at slightly higher strain. Finally, there is a flat region for strain > 6 where the level of chain extension gradually increases with increasing De. The initial stretching (strain < 4) and compression (4 < strain < 6) modes can obviously be linked with the front-side stretching and back-side compression. When we examine the deformation history versus the strain for individual DNA in Fig. 9, some DNA molecules are still compressing while others start to experience postimpact stretching for strain > 6. Thus, the ensemble-averaged stretch versus strain for strain > 6 looks somewhat flat. We also present the deformation histories versus the x component of the center of mass in Fig. 14 for comparison to a confined geometry which will be presented in the next section.

Though the relative extension of DNA increases gradually with increasing De, the maximum stretch gradually becomes saturated for De > 9. The postimpact stretch (strain > 6) continues to increase for De > 9. From a kinematic viewpoint, the stretching can occur up to \( x=0 \) \( \mu m \). That is DNA moves mainly along a cylinder wall for the centerline collision as shown in Figs. 7 and 8 and thus, each bead’s velocity will correspond to the local circumferential velocity field \( (E_\theta) \) along the cylinder. The stretching can occur up to \( x=0 \), since the circumferential gradient of the circumferential electrophoretic velocity component \( (\partial E_\theta / \partial \theta) \) is positive for \( \theta=0−\pi/2 \) and \( 3\pi/2−2\pi \) [cf. the analytical \( \partial E_\theta / \partial \theta \) is \( 2 \cos \theta R_{obs} \) (Ref. 33) on the cylinder wall].

![FIG. 11. (Color online) Extension-strain curves for various Deborah numbers, where the “adaptive” time forwarding scheme is used and the solutions were obtained with FEM/FEM (electric field solution/cylindrical obstacle description).](image)

In the end, stretching can typically occur in one quadrant and the breadth of arc which can be wrapped by the stretched DNA will be limited to a quarter of the cylinder perimeter \( (2\pi R_{obs}/4) \). For the current study this corresponds to a maximum relative extension of \(-0.8\) which agrees with the data in Fig. 11.

We present the deformation histories occurring on the back side of the cylinder in Fig. 12(a), where Fig. 12(b) shows a magnified view for \( \dot{t}/\dot{\tau}<0.3 \). We also plot the extension versus \( \text{De} \times \dot{t}/\dot{\tau} \) in Figs. 12(c) and 12(d) (the magnified view). Rescaling time in this manner corresponds to a strain computed using the (constant) strain rate at the cylinder wall. We set \( \dot{t}/\dot{\tau} \) to 0 when the relative extension of each molecule \( (x_{ex}/L) \) is reduced to 0.3.\(^3^3\) This value of \( x_{ex}/L \) is
as shown in Fig. 12. The arrow shows the direction of increasing 
De. The solid line corresponds to the affine deformation
based on the strain rate on the cylinder wall ($\omega_0 = 0.3 \exp(-De \times t/\tau)$) and the 
arrow shows the direction of increasing De. (d) The magnified view of (c) 
up to $t/\tau = 3.0$. The solid line corresponds to the affine deformation based on
the strain rate on the cylinder wall. The dash line corresponds to thermal
relaxation at $De=1 (0.3 \exp(-t/2\tau))$ and is plotted to compare the affine
deformation. For clarity, we mention that the $x$ axis can be commonly used
at $De=1$ without any scaling for the thermal relaxation curve and affine
deformation. The slope of thermal relaxation at $De$ higher than 1 is flatter
than the dash line.

FIG. 12. (Color online) Mean relative extension on the back side of a large
obstacle. The label attached to each curve shows the corresponding $De$. (a) 
Relative extension vs $t/\tau$. The arrow denotes the direction of increasing $De$. 
(b) A magnified view of (a) up to $t/\tau = 0.3$. (c) The $x$ coordinate of (a) was
rescaled to $De \times t/\tau$. The principal axis of compression over a rather wide strain scale,
different from the predicted affine deformation with constant
data, it seems that the deformation histories are not so dif-
ferent wall, it is expected that the predicted affine deforma-
tion limit based on the constant principal axis of compression
will be a good approximation that the computed affine deforma-
tion based on the assumption of constant principal axes will be
an upper limit even for a nonhomogeneous field.

When we more closely examine compression at small
times [Fig. 12(d)], we see several interesting trends. First, the
initial slope of compression at $De=1$ is quite different from
those at other $De$. This slow initial compression at $De=1$ is
related to the center of mass location where DNA has
$x_{ex}/L = 0.3$. The ensemble-averaged center of mass $x$ coordi-
nates at which $x_{ex}/L = 0.3$ are $3.1 (3.1) \mu m$, $-4.0
(-4.0) \mu m$, $-8.4 (-7.5) \mu m$, $-11.0 (-7.9) \mu m$, $-13.3
(-8.2) \mu m$, and $-11.4 (-8.5) \mu m$ for $De = 1, 2, 9, 18, 36,$ 
and $72$, respectively. Here, some molecules do not compress be-
low $x_{ex}/L = 0.3$ on the cylinder but start to compress far
downstream due to thermal relaxation and their $x$ coordinates
can have quite large values (sometimes less than $-100 \mu m$).
The values in the parentheses denote ensemble-averaged values
which only include DNA who begin to compress below
$x_{ex}/L = 0.3$ before $x_{cm} = -11 \mu m$. Unlike the data for other
$De$, we find that at $De = 1$ the ensemble-averaged center of
mass $x$ coordinate at which $x_{ex}/L = 0.3$ is on the front side of
the cylinder. For $De = 1$ the DNA is relaxing in region along
the cylinder in which the field line is neither aligned with the
primary axis of extension nor compression. In fact, on the
cylinder at $x = 0 \mu m$ the streamline is at an angle of $\pi/4$ with
respect to either one. This results in negligible deformation
of the DNA by the field and so the relaxation of the DNA is
dominated by thermal effects. In Fig. 12(d), we see that the
initial slope at $De = 1$ is comparable with the slope predicted
due to thermal relaxation. However, the slope of the late
stage at $De = 1$ becomes comparable with $De = 2$ as the DNA
passes over the back side of the cylinder and field effects
become important.

Second, it is obvious that the slope of compression
gradually deviates from the affine deformation for $De > 2$, 
which is in contrast to a priori expectation. This deviation is
due to the field kinematics near the rear stagnation point,
and the finite size of DNA. The principal axis of stretching aligns
with $x$ direction and the compression axis is aligned in the $y$
direction near the rear stagnation point. In this region, the
partial compression and stretching can simultaneously occur
within one DNA molecule since DNA has finite size. That is,
while DNA is approaching the rear stagnation point, a part of
DNA can start to stretch in the downstream direction due to
postimpact stretch while its tail on the cylinder is still comp-
ressing. The DNA can take a shape similar to a rotated “L”
($\bot$) at this stage [e.g., see Figs. 8(d)–8(g)]. This tendency
increases with increasing $De$ since postimpact stretch be-
comes stronger for higher $De$. Thus, the retarded compression
rate in Fig. 12(d) results from the strengthening of
postimpact stretch with increasing $De$.

As shown in Figs. 12(c) and 12(d), the stretch has a local
minimum which corresponds to the rear stagnation point (cf.
Fig. 14). We believe this is due to a change in the strain
experience by the molecules between the location where
$x_{ex}/L = 0.3$ and the rear stagnation point ($x = -10 \mu m$).
Strains experienced are $1.63, 1.06, 0.74, 0.67, and 0.62$ at
$De = 1, 2, 9, 18, 36,$ and $72$, respectively. Since the strain
experienced during the compression is decreased with in-
creasing $De$, the local minimum due to the compression is
gradually increased.

After the compression stage, DNA stretches along the $x$
direction as the molecule leaves the obstacle, where the prin-
cipal axis of extension is coincident with the negative $x$
direction. In Fig. 12, it is obvious that the poststretch mono-
tonically increases as $De$ increases. This tendency was also
experimentally observed in comparing two data sets at De=2 and De=9. We can conclude that our simulation shows that this trend is general over a wide range of De. The postimpact stretch was limited to ~40%, which is in agreement with the estimated value by Randall and Doyle, where they surmised that postimpact stretching would be limited by the affine deformation limit (strain ~1.0–1.5).

C. DNA electrophoresis past a cylinder with tight bounding sidewalls

To highlight the versatility of our method, in this section we consider a channel geometry which does not have an analytical solution for the electric field. This channel is similar to the cases previously presented, except that the sidewalls are close to the cylinder [cf. Fig. 13(a)]. The minimum constriction between the cylinder wall and sidewalls is chosen to be equal to the $R_g$ of λ-DNA (0.7 μm). The corresponding electrophoretic velocity profile [Fig. 13(b)] shows an abrupt increase of velocity in the constriction region and thus a sharp increase in strain rate.

We obtained the strain rate at the front stagnation point ($\dot{c}^{\text{f}}_0$) by numerically computing an eigenvalue with local electrophoretic velocity gradient at the front stagnation point. We remind the reader that $x=-10 \text{ μm}$ corresponds to the front stagnation point and $x=+10 \text{ μm}$ is the rear stagnation point. De is defined as $\dot{c}^{\text{f}}_0 \times \tau$ for the confined geometry. The numerically computed dimensionless strain rate at the stagnation point for confined geometry ($\dot{c}^{\text{f}}_0$) was 1.45 times larger than that of the unconfined case and thus for the same De number, the corresponding unperturbed electric field ($E_0$) of confined geometry is smaller than the unconfined case. The time step was also decreased to $\delta t=10^{-4}$ at De=9 for the confined geometry because of the large strain rate in the constricted region and for other values of De, this time step scales as $1/\text{De}$.

We obtained the ensemble-averaged stretch histories at various De numbers and compare the data in the constricted geometry with unconfined cases. As shown in Fig. 14, the extent of stretching in the constricted geometry is dramatically increased at low De compared with the unconfined case but this difference of the maximum stretch becomes smaller as De increases. At large De, the stretch approaches $\sim 2\pi R_{\text{obs}}/4L \sim 0.8$ as previously discussed. In Fig. 14 (inset coordinates), we also show the ensemble-averaged strain corresponding to each $x$ coordinate of the DNA center of mass. For each DNA we saved the accumulated strain according to its trajectory $x_{\text{c.m.}}, y_{\text{c.m.}}$, and then we computed the ensemble-averaged strain as a function of $x_{\text{c.m.}}$.

DNA in the confined geometry overall experience ~2 more strain units than the unconfined case when we look at strain values at the rear stagnation point. For example, when we examine Fig. 14(c) which corresponds to De=9, DNA in both constricted and unconfined geometries experience...
similar strains (−2) up to x = 10 μm since we match local strain rates of the two geometries at the front stagnation point. However, the existence of sidewalls results in the dramatic increase of strain rate when a DNA passes through the constricted region (x ≈ 0 μm). The overall strain increase for the confined geometry is due to the strain increase in the constricted region (cf. inset x axis in Fig. 14). This results in the increased DNA extension for a constricted geometry.

Furthermore, the constricted geometry more tightly compresses the DNA in the region x ≈ −10 μm (near the rear stagnation point) than the unbounded case. Again, this is due to the large strain rates generated in the constriction. There is less overall stretching as the DNA leaves the obstacle (x < −10 μm) for the constricted case since the DNA starts from a more compact state near x = −10 μm.

We here treated an instructive example to show that our numerical algorithms can be applied to a complicated geometry. Suffice it to say that there is no geometrical constraint due to the flexibility of our method. Thus, DNA electrophoresis problems in microchannels involving many obstacles, constriction, and expansion region could be analyzed without difficulty using the present schemes. For example, recently, DNA dynamics through postarrays is in focus for a separation process and many theoretical or experimental analyses have been attempted. We expect that our schemes will be a plausible tool to analyze this problem based on a more rigorous approach including the effect of finite size of obstacles.

IV. SUMMARY

We propose a flexible BD-FEM to simulate DNA electrophoresis. Our study was motivated by current engineering problems which often involve microchannels with variable widths and obstacles. Our method has three main components: a bead-spring BD, FEM, and the connection algorithm between BD and FEM. We devised a target-induced searching algorithm to quickly address the electric field obtained via FEM at specific coordinates and adapted the “potential-free” Heyes and Melrose’s algorithm to work with boundaries described by the FEM.

We applied our technique to λ-DNA deformation around a cylindrical obstacle in an unbounded domain to verify our method. The new numerical method was verified and benchmarked against purely analytical treatments of the electric field and boundary description. Our simulations are qualitatively and quantitatively comparable to previous experiments. The successive stretching-compression-stretching modes of DNA dynamics observed in experiments can be successfully reproduced in our simulations with a nonhomogeneous electric field. We also obtained results for a wide range of Deborah numbers in order to examine in more detail trends observed in experiments. To show the broad capability of our method, we applied our method to a more complicated geometry: a post with two closely spaced sidewalls. Our simulation predicts that the extent of DNA stretch is dramatically increased in the case of tightly confined geometry for low De whereas the difference is not large at high De numbers.

In the future we plan to use our new method to study DNA stretch in hyperbolic geometries used for genomic mapping. We hope to show that the ability to uniformly stretch DNA in hyperbolic geometries can be achieved by using new channel designs guided by simulation results.

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