SIMULATIONS OF SINGLE MOLECULAR DYNAMICS IN HYDRODYNAMIC AND ELECTROKINETIC FLOWS

DISSERTATION

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ABSTRACT

The dynamics of single DNA molecules in micro/nanofluidics has attracted a great deal of attention due to its importance in the biomedical applications such as DNA separation, gene mapping, and gene therapy.

The conformation change of these single long chain molecules in different hydrodynamic flows (pure extensional and simple shear flows) was first observed with the fluorescence microscopy in experiments. The Brownian dynamics simulation was then carried out and it successfully explained the interesting phenomena in experimental observation.

In this dissertation, two major flows (i.e., generated by either the hydrodynamic or electrokinetic forces) to control the DNA dynamics are thoroughly investigated. The main effort is concentrated on the electrokinetic micro-flows produced by different microfluidic patterns. The finite element method is used to simulate the electrokinetic flows and the solutions are used as inputs for the coarse-grained Brownian dynamics simulation, which can capture the dynamics of single DNA molecules.

In the electrokinetic flows, the electroosmotic and electrophoretic interactions affect the flow patterns of charged particles. When the electrophoretic mobility of a charged particle is higher than the surface electroosmotic mobility, the flows in the microfluidic
devices are essentially the electrophoresis-dominated extensional flows even with surface charge patterning. To avoid this limitation, a novel design of a five-cross microfluidic device is proposed based on simulations. This design can generate and maintain different particle flow patterns even when the electrophoretic mobility is much higher than the electroosmotic mobility.

Different responses of single DNA molecules under various hydrodynamic and electrokinetic flows are also studied. The complicated DNA molecule is simplified as either a bead-spring or a bead-rod chain in the Brownian dynamics simulations. Different forces in the governing equation of a bead-spring or bead-rod chain are discussed thoroughly. Different time-marching schemes are used and compared in the simulation of the dynamics of single DNA molecules. The simulations of DNA dynamics in the hydrodynamic and electrokinetic flows agree well with the experiments and the previous simulation results.
Dedicated to my family.
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CHAPTER 1

INTRODUCTION

The dynamics (i.e., conformation change and movement) of a single DNA molecule in micro/nano-scaled geometries has attracted a great deal of attention lately. This is mainly attributed to increasing biomedical applications such as DNA separation, DNA conjugation, gene mapping, and gene delivery. These applications require the capability of moving, stretching, and packing the individual DNA molecules in a faster and more efficient way.

There are many methods to manipulate DNA molecules at the micro/nanoscale, including using the mechanical forces (such as optical tweezers [Perkins94a], magnetic tweezers [SmithS92], and atomic force microscopy (AFM) [Hansma01], etc.), the hydrodynamic forces [Perkins95, Perkins97, SmithD98, SmithD99, Shrewsbury01, Wong03], and the electrokinetic (electroosmotic, electrophoretic, and dielectrophoretic) forces [Namasivayam02, Washizu03, Randall04, Juang04]. The mechanical forces are suitable for stretching or twisting a single DNA molecule into different shapes [Perkins94a], but they could hardly be used for large-scaled processes due to high costs and complicated operations. On the contrary, the hydrodynamic and the electrokinetic forces could use the micro- or nanofluidic devices to accomplish the DNA manipulation in a low-cost and efficient way.
1.1 Micro/Nanofluidics

Micro/Nanofluidics is a multidisciplinary field comprising of physics, chemistry, engineering, and biotechnology that studies the behavior of fluids at the micro/nanoscale [http://en.wikipedia.org/wiki/Microfluidics]. Although the common fluids such as gases and liquids are very important in this field, the concept of “fluids” can be extended to include the behaviors of particles (rigid or soft) and molecules (large or small) in the common fluids. The particle-fluid (or molecule-fluid) mixtures are often called the “complex fluids”.

Micro/nanofluidics has been widely used in many applications, such as particle separation, transportation, mixing, and even chemical reaction [Krishnan01]. Typically, there are two major types of micro/nanofluidics based on two different driving forces: hydrodynamic and electrokinetic forces.

The first type of driving forces works very well in many microscaled systems through the difference of a hydrodynamic pressure between the inlets and outlets of a microfluidic device. One of the advantages of hydrodynamic forces is that it can easily generate well-defined flow patterns. An example is given by the design shown in Figure 1.1(a) [Hudson04]. This microfluidic design mimics the well known “four-roll mill” device [Lagnado90], but without any moving part. By adjusting the flow fluxes in six different micro-channels, the flow pattern in the center of the device could be controlled easily. It can produce extensional, mixed shear, and rotational flow patterns shown in Figures 1.1(b), (c), and (d), respectively. Thus one can generate different flow patterns using just one design, instead of different devices in the conventional way.
However, one severe problem associated with the devices driven by the hydrodynamic forces is that the hydrodynamic pressure needs to increases dramatically in order to keep the flow flux the same as the channel size decreases. This is because the pressure drop in a straight rectangular channel is a reciprocal cubic function of the channel width when the flow flux is constant, e.g., \[ \frac{\delta p}{L} = \frac{12\eta Q}{WD^3} \], where \( \delta p \) is the pressure drop, \( \eta \) is the viscosity, \( Q \) is the flow flux; \( L \), \( W \), and \( D \) are the length, depth,
and width of the channel, respectively. When the size of the channel is small, it requires a high pressure to drive the fluid flow in a micro-channel, thus the bonding of the microfluidic device becomes a very important issue because the microfluidic devices usually cannot sustain such a high pressure and the leakage problem may occur.

In fluid mechanics, the driving forces of the fluid flow are classified into two types: one is the body force $f_b$, and the other is the surface force $F_s$. If these two types of forces have the same effect on the fluid flow, it means $|f_b \delta V| \approx |F_s \delta S|$, where $\delta V$ and $\delta S$ are the volume and surface of a fluid element. For the flow in a circular-shaped channel, the volume of the fluid element is $\delta V = \frac{\pi D^2}{4} \delta L$ and the surface area which could be exerted by the surface force along the channel axis (only this type of surface force can have the same driving effect as the body force) is $\delta S = 2\pi D \delta L$, where $\delta L$ is the length along the channel axis. Thus the ratio of volume to surface of a fluid element is inversely proportional to the channel size; thus $|f_b| / |F_s| \approx D^{-1}$. As the scale decreases to the micro- or nanoscale, it is difficult to use the hydrodynamic pressure, a body force, instead of a surface force, to drive the fluid flow because the magnitude of a body force becomes too high.

The electrokinetic force is an alternative to the hydrodynamic force when the channel size is small. According to [Shaw92], there are typically four types of electrokinetic effects:

(1) Electrophoresis, which is the motion of charged particles relative to the stationary liquid by an applied external electric field. Since the electrophoretic force is only effective to the charged particles, it won’t directly drive the fluid to flow.
(2) Electroosmosis, which is the motion of the ionized liquid relative to the stationary charged surface by an applied external electric field. Since electroosmotic force is essentially a surface force, it can replace the hydrodynamic pressure to drive the fluid to flow in micro/nanofluidics.

(3) Streaming potential, which is the electric field created by the motion of the ionized liquid along the stationary charged surfaces. The effect of the streaming potential is opposite to that of the electroosmosis.

(4) Sedimentation potential, which is the electric field created by the motion of the charged particles relative to the stationary liquid. The effect of the sedimentation potential is opposite to that of the electrophoresis.

But this classification neglects another important electrokinetic effect: dielectrophoresis, which is the motion of polarizable particles suspended in an electrolyte and subjected to a spatially non-uniform electric field [Pohl78]. Some people also combine dielectrophoresis with electrophoresis into the category (1) although dielectrophoresis itself does not require the particles to be charged.

To drive the fluid flow, we can use the electroosmotic force. Since the wall surface carries charges, the counterions and coions in the aqueous solution will form an electric double layer (EDL). Under the external electric field, the movement of counterions and coions in EDL will drag the fluid to flow. Since the concentration of counterions is higher than that of coions in the ionized solution, the overall driving force points to the movement of counterions, thus the fluid has the same flow direction as the movement of counterions. By controlling the surface charge density and types, we can generate different space distributions of ions and cations, thus form different flow patterns, such as
rotational and shear flows [Stroock00]. If one only wants to move the charged particles, the electrophoretic force can be used without driving the fluid. One can also use the dielectrophoretic force to manipulate the movements of uncharged or slightly charged particles by producing the electric dipoles in them. We will discuss these three forces in Chapter 3.

Thus, all kind of flow patterns can be generated in micro- or nano-fluidics by using the hydrodynamic and electrokinetic forces to control the movements of particles and the dynamics of macromolecules such as DNA molecules.

1.2 Dynamics of Single DNA Molecules

The helix structure widely exists in many objects such as the tendril of a climber plant, trumpet shell, bolt, and spring. There are two types of helices: right-handed and left-handed helices. If one moves along a helix in the direction of the right hand thumb, and the helix turns in the direction of right hand fingers, then it's a right-handed helix, otherwise it is a left-handed one. Note that handedness is a property of the helix, not of the perspective. One can turn a right-handed helix around, but it would still remain right-handed [http://en.wikipedia.org/wiki/Helix].

DNA is a right-handed double-stranded molecule. East of the strand consists of a backbone, to which four different nucleci acids (simplified as A, T, C, G) are connected. Thus one strand itself is a sequence of these acids and this sequence carries the genetic information. Two strands are linked by the opposing base pairs (A-T and C-G) to form the double-stranded DNA structure. In the complicated replication procedure, the double stranded DNA can be unwinded by some enzymes. Usually the DNA molecule is quite
large compared with other molecules. For example, λ-DNA molecule has 48,000 base pairs (or 48 kbps) and its molecular weight is around $31.5 \times 10^6$ daltons.

The behaviors of the long chain polymers in solvent are largely dependent on their concentrations and the external temperature. Typically, there are two kinds of solvent: good solvent and poor solvent. A good solvent dissolves polymers over a wide range of temperature, while a poor solvent precipitates polymers when the temperature is changed or the polymer concentration is increased. For a good solvent, the polymer chain would contact as many solvent molecules as possible and the mixture can be divided into three catalogs: dilute, semi-dilute, and concentrated solutions based on the concentration of polymers [Doi86]. There is another solvent, called the “theta solvent”, which is the solvent in the theta state (a state of polymer solution in the theta temperature at which the excluded volume effect in solvent is zero) [Doi86]. In this dissertation, only the dynamics of single polymer chain in dilute solutions are considered, i.e., each polymer chain can move freely in the solution and the effect of the chain entanglement is not considered.

According to the second law in thermodynamics [Moran04], the entropy of an isolated system undergoing a spontaneous process tends to increase, equivalent to the increasing disorder of the isolated system in statistical thermodynamics. The entropy is associated with the notion of disorder by the Boltzmann relation, $S = k_B \ln W$, where $S$ is the entropy, $k_B$ is Boltzmann’s constant, and $W$ stands for the probability of states in a system, or the number of disorder in a system. Since a DNA molecule in the fully stretched state has the highest order, or the lowest disorder, its entropy is the lowest; while a DNA molecule in a totally random state has the lowest order, or the highest disorder, its entropy is the highest. Thus DNA molecules in the equilibrium state are
coiled, reaching their highest entropy state, or their minimum Gibbs free energy state. The Gibbs free energy is given by \( G = H - TS \), where \( G \) is the Gibbs free energy, \( H \) is the enthalpy, and \( T \) is the absolute temperature. For example, the ensemble-averaged radius of the \( \lambda \)-DNA molecules in a dilute solution is around 0.67 \( \mu \)m in equilibrium state.

Without flow and the external forces, a fully stretched DNA molecule would relax to its equilibrium state. The relax process is dependent on the initial conformation and the full length of a DNA chain. This was first observed in experiments by Perkins et al. [Perkins94b] in the group of Professor S. Chu, the 1997 Nobel Prize Laureate in Physics. In Figure 1.2, they found that relations of the visual length vs. time are different for three different types of DNA molecules with different full lengths (or contour lengths, to be introduced in Chapter 2): long molecules have a full length of 39.1 \( \mu \)m, medium ones 21.1 \( \mu \)m, and short ones 7.7 \( \mu \)m. The relax process of a single labeled DNA molecule is shown in the small figure inserted in Figure 1.2. The DNA molecule became shorter and brighter with time. Also, the chain configuration tends to be random due to the fluctuation effect coming from the Brownian forces of solvent molecules.

From the experimental data of the mean square end-to-end distance vs. time in relaxation, the longest relaxation time can be calculated by fitting the experimental data with an exponential curve

\[
\langle x(t)x(t) \rangle = C_1 \exp(-t/\tau_{\text{long}}) + C_2
\]

(1.1)

where \( \langle \rangle \) stands for the ensemble average, \( x(t) \) is the end-to-end distance of a relaxing chain at time \( t \), \( \tau_{\text{long}} \) is the longest relaxation time, \( C_1 \) and \( C_2 \) are two undetermined constants.
Perkins et al. [Perkins94b] found that the longest relaxation time follows a scaling law with the full length of a chain $\tau_{\text{long}} = L^\alpha$, $\alpha = 1.66 \pm 0.10$ in their experiments. On the other hand, the Rouse theory gives $\alpha = 2$ for the freely draining chain; while $\alpha = 1.5$ for the theta-solvent by the Zimm theory (considering the hydrodynamic interactions, to be mentioned in Chapter 5), and $\alpha = 1.8$ for a good-solvent [Larson88, Larson99a]. Thus, none of the current theoretical models can well predict the scaling law in the relaxation process of DNA molecules.

Figure 1.2 shows the visual length vs. time of the tethered DNA molecules (one end of the molecule was attached to a polystyrene (PS) latex microsphere, which was trapped by the optical tweezers). Wong et al. [Wong03] also studied the relaxation process of
untethered DNA molecules in a microchannel. Both tethered and untethered DNA molecules in the dilute solution have the similar relaxation process. In experiments, the measured longest relaxation time for $\lambda$-DNA is around 0.9 sec.

When an ensemble average of the end-to-end distance of DNA molecules becomes nearly constant (or oscillates slightly around a constant value with time), DNA molecules could be thought in the equilibrium state. In such case, DNA molecules move randomly under the Brownian forces exerted by surrounding solvent molecules. The transition of DNA configuration from the equilibrium state to the non-equilibrium state is a rather interesting topic to study. There are many ways to drive DNA molecules to the non-equilibrium state. Typically, hydrodynamic and electrokinetic forces are two major forces of great interest, which will be investigated in this and the following chapters.

The dynamics of a single DNA molecule in well-defined hydrodynamic flows was also first investigated by S. Chu’s group. They studied the coil-stretch transition of single DNA molecules in different flow fields. For example, they studied the tethered DNA molecules in the steady uniform flow [Perkins95], the untethered DNA molecules in the steady extensional flow [Perkins97], in the start-up extensional flow [SmithD98] and in the steady simple shear flow [SmithD99].

Usually the untethered DNA molecules in the uniform flow will not be stretched at all. But when they are tethered on one end, they will be stretched in the uniform hydrodynamic flow [Perkins95]. Figure 1.3 shows the extension vs. flow velocity for the six types DNA molecules with different contour lengths (22.4, 34.8, 44.0, 53.1, 63.6 and 83.8 μm, respectively). It can be seen that DNA molecules can be stretched to different length at different flow velocity. The faster the flow is, the higher the extension a DNA
molecule is stretched to. While at the same flow velocity, the longer the DNA molecule is, the more stretching it will experience.

Figure 1.3: Extension vs. flow velocity for 6 different DNA molecules. (Inset) The stretching process of a tethered DNA molecule (reprinted with permission from [Perkins95]).

The dynamics of the free (untethered) DNA molecules in the extensional flow is very important in understanding the behavior of polymer chains in polymer processing. Chu’s group used the device shown in Figure 1.4(a) to study the dynamics of DNA in the extensional flow [Perkins97, SmithD98]. The flow generated by this device could be described as \((u, v) = (-\dot{\varepsilon}x, \dot{\varepsilon}y)\), where \(\dot{\varepsilon}\) is the extensional rate. The DNA molecule is stretched continually as long as the Deborah number \(De = \tau_{long}\dot{\varepsilon} > 0.5\), where \(\tau_{long}\) is the longest relaxation time of a DNA molecule (the reason why a critical Deborah number
exists for a free DNA molecule can be found in Chapter 2). Also, the initial conformation of a DNA molecule affects the process of stretching greatly. The initially “dumbbell-like” or “kinked” DNA will be much more easily stretched than the “half-dumbbell-like” and “folded” shaped DNA as shown in Figure 1.4(b).

![Figure 1.4](image)

Figure 1.4: (a) Device to generate the extensional flow; (b) Coil-stretch transitions for DNA molecules with different initial conformations (reprinted with permission from [Perkins97, SmithD99]).

Chu’s group also examined the conformation change of a single DNA molecule in the simple shear flow [SimthD99]. Their experiment setup is shown in Figure 1.5(a). The flow field is \((u, v) = (\dot{\gamma} y, 0)\), where \(\dot{\gamma}\) is the shear rate. They observed that there are three typical behaviors of DNA molecules in the shear flow. In the first row in Figure 1.5(b), we see the so-called “recoil” behavior. The initially coiled DNA is stretched to a certain length, and then recoils back and is re-stretched under the velocity gradient. In the second row, the DNA molecule is stretched gradually to a certain length. In the third row, the stretching of DNA molecule is weak, but its conformation changes greatly. They called the DNA molecule was “tumbling”.

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Figure 1.5: (a) Device to generate the shear flow; (b) Dynamics of three DNA molecules with different initial conformations (reprinted with permission from [SmithD99]).

The above examples are of the DNA conformation in the well-defined hydrodynamic flow patterns, which are useful for understanding the mechanism of DNA chains response in simple flows. The conclusion could be generalized to more complicated flows in microfluidics. Figure 1.6(a) shows a device named hydrodynamic focusing, which has been widely used in microfluidic based flow cytometry [Huh05]. There are three streams in this device. Since two outer streams have a much higher averaged velocity than the middle stream, the width of middle stream is greatly suppressed by two outer streams to form a thin layer. It was reported that the velocity is nearly constant in the spanwise direction around the interface between the streams, while the velocity gradient along streamwise direction (or extension rate) maintains constant in the middle stream for a fairly long streamwise distance [Wong03]. Thus in this unique flow, the mixing rate (without chemical reaction) and diffusion are low at the interface between the streams. Wong et al. used this device to study the stretching of DNA molecules, which were placed in the middle stream. They also found that the coil-stretch
transition of DNA molecules and the results are similar to the dynamics of DNA in the extensional flow [Perkins97, SmithD98].

![Image](image1.png)

(a) Device of hydrodynamic focusing; (b) Coil-streching transition (extension vs. time) of DNA molecules in hydrodynamic focusing (reprinted with permission from [Wong03]).

In microfluidics, the flow from a reservoir to a microchannel is also very important because the flow contains both regions of high elongation along the centerline as the fluid converges from the upstream reservoir to the channel (i.e., similar to the hydrodynamic focusing in [Wong03])) and high shear near the channel wall when the flow rate is high. It has been shown that DNA molecules can be stretched in the entrance region from the reservoir to the microchannel [Shrewsbury01]. Figure 1.7 clearly shows that the conformations of DNA molecules are different at different locations. In the reservoirs A and F, DNA molecules are in the coiled state. At the entrance B, DNA molecules are stretched nearly to its full length due to the high extensional rate. In the microchannel, DNA molecules is also affected by the shear flow when they are close to the wall because the velocity profile is parabolic. Thus one can see the recoil of DNA molecules at
locations C, D, and E.

![Diagram of microfluidic device](image)

Figure 1.7: Dynamics of DNA molecules in the microfluidic device (reprinted with permission from [Shrewsbury01]).

Dynamics of DNA molecules in electrophoresis has also been thoroughly studied due to the needs of DNA separation. The conventional capillary electrophoresis (CE) needs a sieving matrix (usually the randomly distributed cross-linking polymer gel) to create different barriers for DNA molecules with different lengths. The longer molecules will move more slowly than the shorter ones because more hooking of DNA molecules in the porous media of the gels [Kuhn93]. A problem for the conventional CE is its low efficiency and resolution for the long chain DNA molecules (> 20 kbps).

The artificial electrophoresis sieving structure for DNA separation is to optimize the efficiency and resolution of DNA capillary electrophoresis. The uniform and well-defined pattern of small obstacles (usually the pillars or circular posts) is fabricated on a surface
using the lithographic techniques. Kaji et al. [Kaji04] showed that they can achieve very
good separation, even for the long DNA molecules such as \( \lambda \)-DNA (48 kbps) and T4-
DNA (166 kbps) by fabricating uniform nanopillars in the microchannel as shown in
Figure 1.8a. It is very difficult (almost impossible) for the conventional CE to separate
such two long chain DNA molecules.

Figure 1.8: (a) Schematic of artificial electrophoresis structure in microchannel; (b)  
Dynamics of a single \( \lambda \)-DNA and T4-DNA in this device (from [Kaji04]).
Another important DNA separation method is entropy trapping. This method uses the nanochannel with two different depths as shown in Figure 1.9. The depth of the thick region is comparable to the gyration radius of DNA molecules, while the depth of the thin region is only 90 nm. Entropy trapping of DNA molecules in the small-scaled confined geometry sometimes shows very surprising results. Han et al. [Han99, Han00] showed that the larger T2-DNA molecules move faster in the entropic trapping array than the smaller T7-DNA ones. This is opposite to the results of DNA separation using the gel electrophoresis method. The DNA movement in the entropic trapping array evidently shows that the size effect is important and the “effective” mobility should be size-dependent. For the smaller size T7-DNAs, it is more difficult for them to obtain enough energy to move out of the trap than for the larger size T2-DNAs because their gyration radius is smaller than the size of the traps.

Figure 1.9: DNA molecules in entropy trapping device (reprinted with permission from [Han00]).
DNA separation using the micro/nanofluidics is an important area both in research and in business. More information on this topic can be found elsewhere [Slater00, Slater02, Ashton03].

The behaviors of DNA molecules in the small-scaled domains are still poorly understood. This is because it is difficult to observe the DNA dynamics in such a small scale in the experiments. The interactions between inter- and intra-molecules, between DNA molecules and the domain surfaces are also make the simulation difficult.

1.3 Aims and Outline of Dissertation

This dissertation focuses on the simulation methods in micro/nanofluidics and single molecular dynamics. It has two major purposes: one is to provide a better understanding of the dynamics of single long chain polymer in the dilute solution, and the other is to provide better design of micro/nanofluidic devices for the control of biomolecule movement.

The dissertation is organized as follows: Chapter 1 is the introduction of basic topics and important experimental observations. Chapter 2 concentrates on the modeling of DNA chains using the Brownian dynamics simulation (BDS) methods. Chapter 3 elaborates different electrokinetic flows solved by the finite element method. Chapter 4 combines the methods in Chapter 2 and Chapter 3 and focuses on how to use the Brownian dynamics simulations to simulate the single molecular dynamics in the electrokinetic flows. Chapter 5 presents suggested future work with a list of unsolved issues in this dissertation.
CHAPTER 2

BROWNIAN DYNAMICS SIMULATION OF SINGLE DNA MOLECULES IN HYDRODYNAMIC FLOWS

In this chapter, the basic knowledge on the modeling of single linear polymer chains (including DNA molecules) is introduced. To simulate the DNA dynamics in an affordable and efficient way, we use the Brownian dynamics simulation (BDS) method. Different coarse-grained models such as the bead-spring and bead-rod chain models are elaborated in this chapter. The mechanisms of the different responses of DNA chains to different hydrodynamic flows (extensional, shear and mixed flows) are explained through the examples. Simulation results of the dynamics of single DNA molecules in extensional and shear flows are given and compared with the published results.

2.1 Basic Knowledge on Modeling of Single Polymer Chains

A polymer chain could be modeled as a continuous curve in the 3D space as shown in Figure 2.1. The only independent variable is the curve length \( s \), which is measured from one end of the chain where \( s = 0 \) is set. The position vector and the unit tangent vector at curve length \( s \) are given as \( \mathbf{r}(s) \) and \( \mathbf{p}(s) = \frac{\partial \mathbf{r}(s)}{\partial s} \), respectively.
By using the Frenet-Serret formulas in the classical differential geometry [O’Neill66], we have the following relations:

\[
\frac{\partial \mathbf{p}}{\partial s} = c \mathbf{n}, \quad \frac{\partial \mathbf{n}}{\partial s} = -c \mathbf{p} + \tau \mathbf{b}, \quad \frac{\partial \mathbf{b}}{\partial s} = -\tau \mathbf{n}
\] (2.1)

where \( c \) and \( \tau \) are the curvature and torsion of this 3D curve, \( \mathbf{n} \) is the principal normal (unit vector towards the center of curvature), \( \mathbf{b} = \mathbf{p} \times \mathbf{n} \) is the binormal.

This orthonormal set of basis vectors \((\mathbf{p}, \mathbf{n}, \mathbf{b})\) is known as the intrinsic coordinate frame. It can continuously move along the 3D curve. An example of the intrinsic coordinate frame is shown in Figure 2.2 on a right-handed helix.

Under the exerted external force or moment, a DNA chain will be stretched or bended. First, let us consider the bending of a DNA chain. By taking the simple elastic model used to describe the bending of an elastic beam [Hibbeler03], we have

\[
\kappa \frac{\partial^2 r(s)}{\partial s^2} = \kappa c \mathbf{n}(s) = M(s)\mathbf{n}(s)
\] (2.2)
where $M(s)$ is the torque or the bending moment, and $\kappa$ is the bending modulus, which could be connected with the Young’s modulus $Y$ and the moment of inertia $I$ by $\kappa = YI$. Equation (2.2) indicates that the curvature of a chain is given by $c = M(s)/\kappa$.

![Figure 2.2: Intrinsic coordinate frame for a 3D curve.](image)

The total bending energy for a curve with a total length of $L$ could be written as

$$U_{Bend} = \frac{\kappa}{2} \int_0^L \left( \frac{\partial p}{\partial s} \right)^2 ds$$

Equation (2.3) could be integrated as follows:

$$U_{Bend} = \frac{\kappa}{2} \int_0^L \frac{\partial p}{\partial s} \cdot \frac{\partial p}{\partial s} ds = \frac{\kappa}{2} \int_0^L c \frac{\partial p}{\partial s} \cdot n ds = \frac{\kappa}{2} \left\{ (cp \cdot n) \right\}_0^L - \int_0^L cp \cdot \frac{\partial n}{\partial s} ds$$

Further simplification would be reached by using equation (2.1),

$$U_{Bend} = -\frac{\kappa}{2} \int_0^L c(s)p(s) \cdot \{-c(s)p(s) + \tau(s)b(s)\} ds = \frac{\kappa}{2} \int_0^L c^2(s) ds$$

Equation (2.5) could be simplified to a discretized form for the bead-rod chain model (will be given in Section 2.4 of this chapter).

Under an external point force $F$ applied to one end of the molecular chain, we should have a stretching energy and the total energy is [Bouchiat99]
\[ E^{\text{total}} = \int_0^L \left\{ \frac{\kappa}{2} \left( \frac{\partial \mathbf{p}}{\partial s} \right)^2 - F \cos \theta(s) \right\} ds \] (2.6)

where \( \theta(s) \) is the angle between \( \mathbf{p}(s) \) and the axis of the external force.

In the equilibrium state (in this case, only the bending energy counterbalances the thermal diffusion), \( E^{\text{total}} = U^{\text{Bend}} \), the probability function of the polymer conformation obeys the Boltzmann distribution [Doi86]:

\[
\Psi(\mathbf{p}) \propto \exp\left(-\frac{U^{\text{Bend}}}{k_B T}\right) = \exp\left(-\frac{\kappa}{2k_B T} \int_0^L ds \left( \frac{\partial \mathbf{p}}{\partial s} \right)^2 \right) \quad (2.7)
\]

Equation (2.7) is known as the Kratky-Porod model and from this equation, we can define a parameter \( \lambda_p = \kappa / k_B T \), the ratio of bending rigidity to the thermal force, which is called the persistence length, a very important parameter describing a chain’s resistance to the thermal fluctuation.

From equation (2.7), we can get the following law for the polymer chain conformation, based on the ensemble average of polymer chains [Doi86]:

\[
\left\langle (\mathbf{p}(s_1) - \mathbf{p}(s_2))^2 \right\rangle = 2 \left| s_1 - s_2 \right| / \lambda_p \quad (2.8)
\]

Equation (2.8) indicates that the distribution of polymer chains satisfies the Gaussian law at the equilibrium state. We can have the ensemble average for the inner product of two unit tangent vectors at different locations [Doi86]:

\[
\left\langle \mathbf{p}(s_1) \cdot \mathbf{p}(s_2) \right\rangle = \exp\left(-\left| s_1 - s_2 \right| / \lambda_p \right) \quad (2.9)
\]

In modeling single polymers in solution, we need to know another important parameter: the contour length \( L_c \), which is the maximum length that a polymer chain can reach. The ratio of the polymer contour length to the persistence length can also describes
the correlation between two ends of a chain. Taking $s_1 = 0$ and $s_2 = L_c$ in equation (2.8), we have $\langle \mathbf{p}(0) \cdot \mathbf{p}(L_c) \rangle = \exp(-L_c / \lambda_p)$. Thus the ratio of polymer contour length to the persistence length can be used to classify the types of polymers. Typically, we have three different types of polymer as follows:

(1) Stiff polymers if $L_c / \lambda_p << 1$. For example, microtubule is a stiff polymer with $L_c / \lambda_p \sim 0.01$; In this type of polymers, two ends are highly correlated because the value of $\langle \mathbf{p}(0) \cdot \mathbf{p}(L_c) \rangle$ is close to 1.

(2) Semi-flexible polymers if $L_c / \lambda_p \approx 1$. For example, actin is semi-flexible with $L_c / \lambda_p \sim 1$; In this type of polymers, two ends are mediately correlated.

(3) Flexible polymers if $L_c / \lambda_p >> 1$. For example, $\lambda$-DNA molecules belong to this type with $L_c / \lambda_p \sim 150$ and two ends are uncorrelated because the value of $\langle \mathbf{p}(0) \cdot \mathbf{p}(L_c) \rangle$ is close to 0. In fact, in the flexible polymers, even the segments on a larger scale $(|s_1 - s_2| >> \lambda_p)$ are uncorrelated although pieces shorter than $\lambda_p$ are rather stiff.

In the modeling, we often need to determine the average size of polymer chains. One way is to study the end-to-end distance vector $\mathbf{R} = \mathbf{r}(L_c) - \mathbf{r}(0)$ for one chain and collect the information for all the chains to calculate the mean square end-to-end distance

$$\langle R^2 \rangle = \langle \mathbf{R} \cdot \mathbf{R} \rangle$$

by ensemble average. With $\mathbf{p}(s) = \frac{\partial \mathbf{r}(s)}{\partial s}$ and equation (2.7), we have

$$\langle R^2 \rangle = \langle (\mathbf{r}(L_c) - \mathbf{r}(0))^2 \rangle = \int_0^{L_c} \int_0^{L_c} \langle \mathbf{p}(s) \cdot \mathbf{p}(s + s') \rangle ds ds'$$

$$= 2 \int_0^{L_c} \int_0^{L_c} \exp((s - s') / \lambda_p) ds ds' = 2L_c \lambda_p [1 - \frac{\lambda_p}{L_c} \exp(-\frac{L_c}{\lambda_p})]$$

(2.10)
For the stiff polymer chain $L_c / \lambda_p \ll 1$, equation (2.10) can be written as

$$\langle R^2 \rangle = 2L_c^2 \lim_{L_c / \lambda_p \to 0} \frac{1}{L_c / \lambda_p} [1 - \frac{1}{L_c / \lambda_p} (1 - \exp(-L_c / \lambda_p))] = L_c^2$$  \hspace{1cm} (2.11)$$

While for the flexible polymer chain $L_c / \lambda_p \gg 1$, equation (2.10) is simplified as

$$\langle R^2 \rangle = 2L_c \lambda_p \lim_{L_c / \lambda_p \to \infty} \frac{\lambda_p}{L_c} (1 - \exp(-\frac{1}{\lambda_p / L_c})) = 2L_c \lambda_p$$  \hspace{1cm} (2.12)$$

Figure 2.3: Freely jointed chain model (from [Bird77b]).

Currently, we are considering a linear polymer chain as a continuous 3D curve in space without adding any phenomenological condition, thus it can be thought as a fine-grained method compared with other coarse-grained methods, which will be thoroughly discussed in the late parts of this chapter. Here, we introduce several important parameters through a well-known coarse-grained model named freely jointed chain (FJC) model as shown in Figure 2.3. It treats a polymer chain as a system of $N$ joints and $N-1$ rigid links (or steps). The length of each link is $b_K$, which is called the length of a Kuhn step. Each link of this model can freely rotate (without consideration of the bending
energy) in any directions. The end-to-end distance vector is defined as \( \mathbf{R} = \sum_{k=1}^{N-1} \mathbf{R}_k \), where \( \mathbf{R}_k = \mathbf{r}_{k+1} - \mathbf{r}_k \) is the \( k \)-th link vector. Note that this definition is only for the linear chain polymer, whose two ends can be clearly determined. Thus the mean square end-to-end distance can be written as:

\[
\langle R^2 \rangle = \left( \sum_{i=1}^{N-1} \mathbf{R}_i \cdot \sum_{j=1}^{N-1} \mathbf{R}_j \right) = \sum_{i=1}^{N-1} \sum_{j=1}^{N-1} \langle \mathbf{R}_i \cdot \mathbf{R}_j \rangle
\] (2.13)

Since this model is one of the random walk model [Doi86, Doi96], we will have \( \langle \mathbf{R}_i \cdot \mathbf{R}_j \rangle = b_K^2 \delta_{ij} \) because there is no correlation between the directions of different link vectors. Thus for FJC model, the mean square end-to-end distance can be written as:

\[
\langle R^2 \rangle = (N-1)b_K^2 = L_C b_K
\] (2.14)

where the contour length \( L_C = (N-1)b_K \). Compared equation (2.14) with equation (2.12) for the flexible polymer chain, we will get \( b_K = 2\lambda_p \). Thus in the coarse-grained model, the length of a Kuhn step is twice of the persistence length for the flexible polymer.

Persistence length is a very important parameter in polymer chain modeling. It is temperature-dependent and the ratio of the persistence length to the molecular radius \( \gamma = \lambda_p / r \) decreases with increasing temperature roughly as the function of \( \gamma \propto \exp(-\alpha T) \), where \( \alpha \) is a material-dependent parameter [Krigbaum85, Larson99a]. Usually, the radius of the molecule is nearly constant, thus it means that as the temperature increases, the chain becomes more flexible and we need more links (or more numbers of degrees of freedom) to describe the molecular chain in the simulation. Typically, there are two methods to measure the persistence length in the experiments.
One is the light scattering method [Fishman96], which needs to sample a large population and produces an averaged result; the other is the AFM imaging method based on equation (2.9) or its modifications in the 2D case, which can be conducted at the level of individual molecules and is suited for heterogeneous samples [Round02]. For a naked λ-DNA chain in a dilute solution at room temperature, the persistence length is around 53 nm; after being dyed by YOYO-1, the persistence length will increase to 66 nm because the chain rigidity or bending modulus $\kappa$ and the contour length increase (YOYO-1 molecules have been inserted in the DNA helix structure to make it more rigid, and the DNA contour length increases from 16.3 μm to 21 μm).

Another important statistical parameter is the radius of gyration $R_g$, which is a more convenient way of expressing the size of a polymer than the average of the square of the end-to-end distance vector $\langle R^2 \rangle$ because the radius of gyration can be directly measured in experiments and has an unambiguous definition for both linear and branched polymers [Doi96]. The radius of gyration is defined as:

$$R_g = \sqrt{\frac{1}{N} \sum_{n=1}^{N} \langle (\mathbf{r}_n - \mathbf{r}_c)^2 \rangle}$$  \hspace{1cm} (2.15)

where $\mathbf{r}_c$ is the coordinates of the center of mass of a chain. Replacing $\mathbf{r}_c = \frac{1}{N} \sum_{m=1}^{N} \mathbf{r}_m$ in equation (2.15) above, we can rewrite it into

$$R_g^2 = \frac{1}{N^2} \sum_{n=1}^{N} \langle (N \mathbf{r}_n - \sum_{m=1}^{N} \mathbf{r}_m)^2 \rangle = \frac{1}{2N^2} \sum_{n=1}^{N} \sum_{m=1}^{N} \langle (\mathbf{r}_n - \mathbf{r}_m)^2 \rangle$$  \hspace{1cm} (2.16)
Following the book by M. Doi [Doi96], we have $\langle(r_n - r_m)^2\rangle = |n-m|b^2_K$ when $|n-m|$ is large for an ideal chain, thus the summation in equation (2.16) can be replaced by an integration for a large $N$: 

$$R_g^2 = \frac{b^2_K}{2N^2} \int_1^N dn \int_1^n dm |n-m| = \frac{b^2_K}{N^2} \int_1^N dn \int_1^n (n-m)dm = \frac{1}{6}(N-1)b^2_K \quad (2.17)$$

Compared with the mean square end-to-end distance in equation (2.14), we have the square of radius of gyration $R_g^2 = \langle R^2 \rangle / 6$. From equation (2.17), we know that the radius of gyration $R_g$ is proportional to the square root of its contour length $L_C$. For example, the contour length of a YOYO-1 stained $\lambda$-DNA (48 kbps) molecule in a dilute solution is around 21 µm and its radius of gyration is around 0.73 µm [Larson05].

### 2.2 Coarse-grained Modeling of DNA Chain

The contour length of a naked $\lambda$-DNA molecule is around 16.3 µm, while its diameter is only 2 nm, thus the aspect ratio is up to 8150. It is almost impossible to calculate both the slowest and fastest changes of such a complicated system. To simulate the conformation change of a single DNA molecule in an affordable way, we need a coarse-grained approach which neglects the details of DNA chain under certain length (say, one Kuhn step length), while still captures the DNA dynamics (conformation change and movement) in an acceptable way.

This approach is the Brownian dynamics simulation (BDS), which simplifies the DNA chain into beads and links. The beads mark the locations of the segments and feel different forces (inter- or intra-molecular forces and external forces), while the links
connect and exert intra-molecular forces to the neighboring beads. Typically, there are two types of links: rigid rod and flexible spring. Correspondingly, we have two chain models: bead-rod chain and bead-spring chain. In a bead-rod chain, each rod is a rigid link with a length of one Kuhn step, while in a bead-spring chain, each spring is a flexible link with the maximum extensibility of several Kuhn steps. Thus the bead-spring chain is a coarser model than the bead-rod chain. Of course, the bead-rod chain model requires more computational resources and is more time consuming than the bead-spring chain to simulate the same DNA molecule, although it is more accurate in nature.

Brownian dynamics simulation (BDS) of DNA molecules have been successfully used in the dynamics of single DNA molecules in hydrodynamic or electrokinetic driven flows [Larson97, Larson99b, Doyle98, Hur00, Panwar03, Randall04, Juang04]. We will show in this chapter and Chapter 4 how to use the BDS method to capture the dynamics of DNA molecules in dilute solutions.

2.3 Bead-Spring Chain Model

The bead-spring chain model is a simple but powerful model. Each spring is an elastic link with the maximum extensibility equivalent to several Kuhn steps (but some bead-spring models such as the Hookean spring model have no maximum extensibility).

A real DNA molecule could be simplified to a bead-spring chain with a very low number of degree of freedom. In Figure 2.4, we have a chain consisting of \( N \) beads (numbering from 1 to \( N \)) connected by \( N_s = N - 1 \) elastic springs. The total number of degree of freedom (the overall unknown coordinates for these \( N \) beads) is \( 3N \) [Bird77b].
According to the Newton’s second law, we have the following equation on the relationship of the forces and the acceleration for the bead $i$,

$$m_i \frac{d^2 \mathbf{r}_i}{dt^2} = \mathbf{F}_{i,\text{Drag}} + \mathbf{F}_{i,\text{Brownian}} + \mathbf{F}_{i,\text{Spring, total}} + \mathbf{F}_{i,\text{External}}$$

(2.18)

where four major forces on the right hand side are balanced with each other. They are the drag force $\mathbf{F}_{i,\text{Drag}}$, the Brownian force $\mathbf{F}_{i,\text{Brownian}}$, the total spring force $\mathbf{F}_{i,\text{Spring, total}}$, and the external force $\mathbf{F}_{i,\text{External}}$. For the massless bead ($m_i = 0$), the inertia term on the left hand side of equation (2.18) could be neglected [Larson05], thus we only need to consider the forces on the right hand side of equation (2.18).

2.3.1 Drag Force

Drag force could be expressed as: $\mathbf{F}_{i,\text{Drag}} = -\zeta(\frac{d\mathbf{r}_i}{dt} - \mathbf{u}_i - \mathbf{u}_i')$, where $\zeta$ is the drag coefficient, $\mathbf{r}_i$ is the coordinates for bead $i$, $\mathbf{u}_i$ is the neighboring fluid velocity, which
could be produced by either the hydrodynamic pressure or the electroosmotic flow (EOF), and \( u_i' \) is the so-called hydrodynamic interaction (HI) velocity, which is the disturbance in the flow field due to the existence of the polymer chain. HI is very important when the distance of two beads is short (for example, when a DNA chain is in a confined geometry where the size is comparable with the persistence length, the distance between any two beads will be short enough for us to consider the HI effect; also in this case, the wall induced HI effect is important). But in this dissertation, we neglect the hydrodynamic interaction term. There are three major reasons given as follows:

(1) First, the induced velocity by the hydrodynamic interaction has no analytical expression except for the flow in bulk (infinite domain), passing over a flat plane, or in the simple straight channel [Oseen27, Rotne69, Yamakawa70, Blake61]. However, we always encounter the problem of DNA solution flowing in micro/nanochannels with all kind of complex geometries. We need to calculate the HI by computational fluid dynamics (CFD) methods in each time step, which is very complicated and time-consuming and has never been put in practice. In fact, although HI has analytical solutions for the flow in the simple geometry, the procedure to include it to the Brownian dynamics simulation itself is complicated. For more information on the effect of HI to the dynamics of DNA molecules, please refer to [Jendrejack02, Hsieh03, Schroeder04].

(2) Second, in the bead-spring chain simulation, usually the distance between two beads is around several Kuhn steps (in Chapter 4, the width of our microchannels are around 250 \( \mu \)m, much larger than the DNA persistence length), making the contribution of the HI effect very small because the HI is inversely proportional to the square of the distance of two beads. This is more distinct for the bead-spring chain in the extensional
flow, which tends to stretch the chain and make two neighboring beads far apart.

(3) Third, according to [Hur01, Larson05], the effect of HI can, in some cases, be subsumed into the effective drag properties of the chain. Thus, we just need to use an effective drag coefficient in equation (2.18) to “screen out” the HI effect. Also Woo et al. [Woo04a, Woo04b] showed that by using a configuration dependent anisotropic or an effective isotropic drag coefficient, the DNA relaxation process in micro/nanochannel can still be captured by the simulation.

2.3.2 Brownian Force

Brownian force is produced by the collision of solvent molecules to the polymer chain due to the thermal fluctuation. This force is time dependent. Generally, we have the following fluctuation-dissipation equation for its components [Kubo85]:

\[
\langle F_{\alpha}^{\text{Brownian}}(t) \rangle = 0
\]

\[
\langle F_{\alpha}^{\text{Brownian}}(t)F_{\beta}^{\text{Brownian}}(t') \rangle = 2\xi k_B T \delta_{\alpha\beta} \delta(t-t')
\]

where \(\alpha\) and \(\beta\) are the indices for components of the Brownian force, \(t\) and \(t'\) are two time points. \(\langle \rangle\) is the ensemble average for all the probabilities, \(\delta_{\alpha\beta}\) is the Kronecker delta, and \(\delta(t-t')\) is the delta function.

In literature, most people take

\[
F_{i}^{\text{Brownian}} = \sqrt{\frac{6\xi k_B T}{\Delta t}} n_i,
\]

where \(n_i\) is a uniform random vector and each component is uniformly distributed in \([-1, 1]\) and \(\Delta t\) is the time step in simulation. We can also use the Gaussian random vector \(g_i\) with each component falling in \((\sim\infty, \infty)\) and satisfying the 1D Gaussian normal distribution with zero mean and unit
variance; then the Brownian force is given by \( \mathbf{F}_{i}^{\text{Brownian}} = \sqrt{\frac{2\varepsilon k_{B}T}{\Delta t}} \mathbf{g}_{i} \). These two expressions look different, but both have the same mean and variance. The proof is given as follows:

(1) For the first expression, any component of the Brownian force is \( x = an \), where \( a = \sqrt{\frac{6\varepsilon k_{B}T}{\Delta t}} \) and \( n \) is a random number uniformly distributed in \([-1, 1]\), thus \( x \) is uniformly distributed in \([-a, a]\). So the probability density function (PDF) for this component is \( p(x) = \frac{1}{2a} \). Thus the mean is \( \int_{-a}^{a} x p(x)dx = 0 \) and the variance is

\[
\int_{-a}^{a} x^2 p(x)dx = \frac{1}{3} a^2 = \frac{2\varepsilon k_{B}T}{\Delta t}.
\]

(2) For the second expression, any component of the Brownian force is \( x = bg \), where \( b = \sqrt{\frac{2\varepsilon k_{B}T}{\Delta t}} \) and \( g \) is a Gaussian random number in \((\infty, \infty)\) with zero mean and unit variance, thus its probability density function is \( p(x) = \frac{1}{\sqrt{2\pi b}} \exp(-\frac{x^2}{2b^2}) \). Still the mean is \( \int_{-\infty}^{\infty} x p(x)dx = 0 \) and the variance is \( \int_{-\infty}^{\infty} x^2 p(x)dx = b^2 = \frac{2\varepsilon k_{B}T}{\Delta t} \).

Thus these two expressions have the same mean and variance. We can also prove that these two expressions satisfy equations (2.19) and (2.20) if we calculate the ensemble average (or integration on probability density function) with different time. In fact, theoretically, any other Brownian force satisfying the equations (2.19) and (2.20) will have the same mean and variance as these two expressions.
In Brownian dynamics simulation, we actually cannot have the real random numbers as assumed in theory. The “random” numbers we generate with the computer (using some algorithms) are in fact the pseudo-random numbers and they will repeat after a certain length (long or short, depending on how good an algorithm is). Practically, it is much easier to generate a uniform random number in \([-1, 1]\] than to have a Gaussian random number. Currently, the Box-Muller method is widely used to generate a Gaussian random number with zero mean and unit variance [Knuth81, Press01]. This method generates a pair of Gaussian random numbers and we just take one of them each time.

Considering a 2D probability distribution \(p(x_1, x_2)dx_1dx_2\), each random deviate \(x_i = x_i(y_1, y_2)\) is the function of all the \(y_k\) \((i, k = 1, 2)\). Thus, the joint probability distribution for the random deviate \(y\) is:

\[
p(y_1, y_2)dy_1dy_2 = p(x_1, x_2) \left| \frac{\partial(x_1, x_2)}{\partial(y_1, y_2)} \right| dy_1dy_2 \tag{2.21}
\]

If the following relation between \(x\) and \(y\) is satisfied,

\[
y_1 = \sqrt{-2 \ln x_1 \cos 2\pi x_2}, \quad y_2 = \sqrt{-2 \ln x_1 \sin 2\pi x_2} \tag{2.22}
\]

we can make the Jacobian determinant in equation (2.21) to be a Gaussian function

\[
\left| \frac{\partial(x_1, x_2)}{\partial(y_1, y_2)} \right| = \frac{1}{2\pi} \exp(-\frac{y_1^2 + y_2^2}{2}) \tag{2.23}
\]

If \((x_1, x_2)\) is uniformly distributed in a unit square (thus \(p(x_1, x_2) = 1\)), then the random deviate of \(y\) satisfies the Gaussian normal distribution with zero mean and unit variance. Thus we need to first generate two uniform random numbers in \([-1, 1]\), then use the Box-Muller method (transformation in equation (2.22)) to get the Gaussian normal
distribution with zero mean and unit variance.

2.3.3 Total Spring Force

The total spring force exerted on bead \( i \) could be written as \( \mathbf{F}_{i, \text{total}} = \mathbf{F}_i - \mathbf{F}_{i+1} \) (\( 2 < i < N - 1 \)), where \( \mathbf{F}_i \) is the spring force in spring \( i \). Note that, for \( i = 1 \), \( \mathbf{F}_{1, \text{total}} = \mathbf{F}_1 \), and for \( i = N \), \( \mathbf{F}_{N, \text{total}} = -\mathbf{F}_{N-1} \). We can use different spring laws such as Hookean, FENE (or Warner force law) \cite{Bird77b}, Cohen Padé approximant inverse Langevin chain (ILC) \cite{Cohen91} and worm-like chain (WLC) \cite{Bustamante94, Marko95} models. Their expressions (the force laws \( F_i = |\mathbf{F}_i| \)) are shown in Table 2.1. For more details, see \cite{Somasi02, Larson05}.

<table>
<thead>
<tr>
<th>Models</th>
<th>Force Laws</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hookean</td>
<td>( F_i^s = H R_i = 3 k_b T R_i / b_x R_o )</td>
</tr>
<tr>
<td>FENE</td>
<td>( F_i^s = H / (1 - (R_i / R_o)^2) R_i = k_b T (3 / (1 - (R_i / R_o)^2) R_i / b_k) )</td>
</tr>
<tr>
<td>ILC</td>
<td>( F_i^s = H (3 - (R_i / R_o)^2) / 3 / 1 - (R_i / R_o)^2 R_i = k_b T (3 - (R_i / R_o)^2) R_i / b_k (1 - (R_i / R_o)^2) R_o )</td>
</tr>
<tr>
<td>WLC</td>
<td>( F_i^s = k_b T / \lambda_p \left[ \frac{1}{4 (1 - R_i / R_o)^2} - \frac{1}{4} + \frac{R_i}{R_o} \right] )</td>
</tr>
</tbody>
</table>

Table 2.1: Spring models and the corresponding force laws.

In Table 2.1, \( \mathbf{R}_i = \mathbf{r}_{i+1} - \mathbf{r}_i \) is the \( i \)-th spring vector, \( R_i = |\mathbf{R}_i| \), \( R_o \) is the maximum extensibility for one spring. Here the Hookean spring has no maximum extensibility and
the spring constant is defined as $H = \frac{3k_B T}{b_K R_0}$, where the value of $R_0$ is based on the maximum extensibility of the FENE spring. With $R_i / R_0 \rightarrow 0$, the Hookean, FENE and inverse Langevin chain become identical.

To well simulate the dynamics of single long chain polymers such as DNA molecules, we need to use a reasonable spring model; otherwise, the conformation and location of the polymer chain cannot be well predicted or captured. Currently, we use the worm-like chain model to simulate the dynamics of DNA molecules. The WLC model was derived by Bustamante et al and Marko et al. [Bustamante94, Marko95]. The original expression, dealing with the relationship between the extension $x$ and exerted force $F$, is a little bit different from that given in Table 2.1,

$$F = \frac{k_B T}{\lambda_p} \left( \frac{1}{4} \left( 1 - \frac{x}{L_C} \right)^2 - \frac{1}{4} + \frac{x}{L_C} \right)$$

(2.24)

This force law was compared with data taken from the experiment by Smith et al. for the single tethered T2 DNA (one end of the T2 DNA molecule was chemically bound on a glass slide, while the other end was attached to a magnetic bead) stretched by the magnetic and hydrodynamic forces [SmithS92]. Bustamante et al. used a nonlinear least-square fitting method to get values for the two unknown parameters: the persistence length $\lambda_p$ and the contour length $L_C$. They found that $\lambda_p = 53.4 \pm 2.3$ nm and $L_C = 32.8 \pm 0.1$ μm (90% confidence level errors for 303 data points), which are very close to those measured by other experiments. Thus the stretching of single tethered DNA could become another accurate (but indirect) method for determination of the persistence length and the contour length of DNA molecules in solution.
Equation (2.24) was obtained by stretching the whole DNA, but we can extend it to each spring because each spring was stretched by the same force $F$. We can replace the contour length $L_c$ with $R_0$, the maximum extensibility in one spring, and replace the total stretching length $x$ with $R_i$, the stretching length in one spring. Because of the relation $\frac{x}{L_c} = \frac{R_i}{R_0}$ for a straight chain, we can get $F = \frac{k_B T}{\lambda_p} \left( \frac{1}{4(1-R_i/R_0)^2} \right) - \frac{1}{4} \frac{R_i}{R_0}$, which has been shown in Table 2.1.

The worm-like chain model leads to a small overestimate in the value of persistence length and the error is typically about 5%. A further updating for the WLC model could be found in the work by Bouchiat et al. [Bouchiat99], where they added a seventh-order polynomial function to the original expression for better fitting.

\[
F = \frac{k_B T}{\lambda_p} \left\{ \frac{1}{4(1-x/L_c)^2} - \frac{1}{4} \frac{x}{L_c} + \sum_{i=2}^{7} \alpha_i \left( \frac{x}{L_c} \right)^i \right\}
\]  

(2.25)

with $\alpha_2 = -0.51642$, $\alpha_3 = -2.73742$, $\alpha_4 = 16.07497$, $\alpha_5 = -38.87602$, $\alpha_6 = 39.49944$, and $\alpha_7 = -14.17718$. Its accuracy could be as low as 0.01% in calculating the persistence length. But equation (2.25) is so complicated that almost no one used it in the Brownian dynamics simulation.

According to the literature [Larson99b], to simulate a $\lambda$-DNA, a 10-bead bead-spring chain is enough to show the evolution of the chain end-to-end distance with time in an extensional flow. To better describe the conformation change, we need to increase the bead number to 20. At the same time, we should use a higher value of the “effective” persistence length $\lambda_p^{\text{eff}}$ to take the effect of the bending energy into consideration.
(otherwise, it seems that the over-stretching of the worm-like chain in the pure extensional flow will happen). For the stained $\lambda$-DNA, its persistence length is $\lambda_p = 0.066 \ \mu m$; but in simulation, for $N = 5$, we have $\lambda_p^{\text{eff}} = 0.075 \ \mu m$; for $N = 10$, $\lambda_p^{\text{eff}} = 0.082 \ \mu m$; and for $N = 20$, $\lambda_p^{\text{eff}} = 0.096 \ \mu m$. Although nobody has reported it before, it seems that the “effective” persistence length and the number of beads have the following connection:

$$\lambda_p^{\text{eff}} = 0.0014 \times N + 0.068 \ (\mu m) \quad (2.26)$$

In the bead-spring chain simulation for a $\lambda$-DNA molecule, the bead number should be less than or equal to 20. This is because we are increasing the flexibility of the chain with more than 20 beads to simulate $\lambda$-DNA, and it will affect the accuracy of the simulation results, which can not be corrected by merely increasing the effective persistence length [Larson99b].

2.3.4 External Force

The external force in equation (2.18) could be the electrophoretic, dielectrophoretic or magnetic force (since buoyant force and gravity force usually balance with each other, we don’t consider them here). In this dissertation, we only discuss the electrophoretic effect to the DNA dynamics and the external force is written as $F_i^{\text{External}} = qE_i$, where $q$ is the charge density for each bead and $E_i$ is the electric field at the location of bead $i$. The electric field gradient plays an important role in the conformation and movement of DNA molecules and we will study the effect of electric field to the dynamics of single $\lambda$-DNA molecules in some microfluidic devices in Chapter 4.
2.3.5 Numerical Methods and Procedures

Before solving the governing equation (2.18), we need to transform it into a dimensionless form. Here, we follow the steps in [Panwar03]. The characteristic length is chosen to be the root-mean-square spring length \( b = \sqrt{N_{K,S} b_K} \), where \( N_{K,S} \) is the Kuhn steps in one spring. The total Kuhn steps in one chain are \( N_K = N_{K,S} N_S \), then the contour length is \( L_c = N_K b_K \). The characteristic time is \( \tau = \xi b^2 / k_B T \), the characteristic velocity is set to be \( U_{ref} \). The governing equation in the dimensionless form is written as:

\[
\frac{d\mathbf{b}_i}{dt} = S_0 \tilde{\mathbf{u}}_i + \tilde{\mathbf{f}}_{i,\text{random}} + \tilde{\mathbf{f}}_{i,\text{spring, total}} + \tilde{\mathbf{f}}_{i,\text{external}} \tag{2.27}
\]

where \( \mathbf{b}_i = r_i / b \), \( \tilde{t} = t / \tau \), \( S_0 = U_{ref} b / (k_B T / \xi) \) is a parameter defining the ratio of the bead diffusion time to the characteristic flow time and it has the similar physical meaning as the Peclet number.

The dimensionless velocity is \( \tilde{\mathbf{u}}_i = \mathbf{u}_i / U_{ref} \) and the dimensionless Brownian force is \( \tilde{\mathbf{f}}_{i,\text{random}} = \sqrt{6 / \Delta \tilde{t}} \mathbf{n}_i \). The dimensionless total spring force on bead \( i \) is given by

\[
\tilde{\mathbf{f}}_{i,\text{spring, total}} = \tilde{\mathbf{f}}_{i}^s - \tilde{\mathbf{f}}_{i-1}^s \quad \text{with} \quad \text{\textit{i-th spring force}} \quad \tilde{\mathbf{f}}_{i}^s = \mathbf{\vartheta} \left( \frac{1}{2 \lambda_i (1 - \lambda_i)^2} - \frac{1}{2 \lambda_i} + 2 \right) (\mathbf{b}_{i+1} - \mathbf{b}_i) ,
\]

where \( \lambda_i = |\mathbf{b}_{i+1} - \mathbf{b}_i| / \sqrt{N_{K,S}} \) and \( \mathbf{\vartheta} = b_K / (2 \lambda_p^{\text{eff}}) \). For a 20-bead chain, we use \( \lambda_p^{\text{eff}} = 0.096 \ \mu m \), \( b_K = 0.132 \ \mu m \), and \( \mathbf{\vartheta} = 0.6875 \). The external force is

\[
\tilde{\mathbf{f}}_{i,\text{external}} = E_0 \tilde{\mathbf{E}}_i \quad (\text{where} \quad \tilde{\mathbf{E}}_i = \mathbf{E}_i / E_{ext} \quad \text{is the dimensionless electric field, if possible}). \]

The parameter \( E_0 = q E_{ext} b / k_B T \), where \( E_{ext} \) is the characteristic external electric field, \( q \) is the
charge density for each bead. We can rewrite \( E_0 = E_{ext} \frac{e b^2}{k_B T} \frac{q_{bp}}{l_{bp}} (1 - \frac{1}{N}) \sqrt{N_{k,S}} \) to get the expression in [Panwar03], where \( e \) is the electronic charge, \( q_{bp} \) the charge density per base pair, and \( l_{bp} \) is the length of a base pair.

For simplification, we drop the tilde (‘\( \sim \)’) in equation (2.27) in the following sections, but be aware that the variables are dimensionless now.

There are many advantages of the non-dimensionalization in simulation and analysis. First, we only have two dimensionless controlling parameters: \( S_0 \) and \( E_0 \) in equation (2.27), thus we condense the controlling parameters and it also indicates the results should be the same as long as \( S_0 \) and \( E_0 \) are the same (of course with the same initial conditions) although the dimensional controlling parameters might be different in the experiments. Second, we only need to choose the appropriate dimensionless time step with respect to the magnitudes of \( S_0 \) and \( E_0 \), while in the original dimensional equation (2.18), we need to adjust the dimensional time step according to the values of many controlling parameters.

Equation (2.27) is a time evolution equation and we need to use a time integration (or time marching) method to solve it. For the generalized time evolution equation

\[
\frac{dy}{dt} = f(t, y), \quad \text{for } t \geq 0 \text{ with initial condition } y(0) = y_0
\]

(2.28)

the conventional time integration methods are the first order forward Euler method and the second order mid-point method [BakerG01].
Figure 2.5: Forward Euler’s method and mid-point method.

(1) Forward Euler method

\[ y(t_{k+1}) = y(t_k) + \Delta t_k f(t_k, y(t_k)) \]  

(2.29)

where \( t_k \) and \( t_{k+1} \) are two adjacent time, \( \Delta t_k = t_{k+1} - t_k \) is the step size at time step \( k \). In principle, we can use the different step size, but for simplicity, we take a constant step size, \( \Delta t_k \equiv \Delta t \) in the following part of this dissertation.

(2) Mid-point method

\[
\begin{cases}
\qquad \dot{y}(t_{k+\frac{1}{2}}) = y(t_k) + \frac{\Delta t_k}{2} f(t_k, y(t_k)) \\
y(t_{k+1}) = y(t_k) + \Delta t_k f(t_{k+\frac{1}{2}}, y^{p}(t_{k+\frac{1}{2}}))
\end{cases}
\]

(2.30)
where we define a mid-point or time step at time $t_{k+\frac{1}{2}} = t_k + \frac{\Delta t_k}{2}$. In this method, we first calculate the value at time step $k + \frac{1}{2}$, then evaluate its derivative $f(t_{k+\frac{1}{2}}, y^p(t_{k+\frac{1}{2}}))$, finally, the forward Euler method with the calculated derivative at the mid-point is used to calculate the value at time step $k + 1$.

The mid-point method is more accurate than the forward Euler’s method. Figure 2.5 shows the difference between these two methods and the real value. We can see the value calculated by the mid-point method is closer to the real value than that with the forward Euler’s method.

Since each spring has a maximum extensibility in the worm-like chain model, the conventional forward Euler’s method or mid-point method cannot assure that the length of a spring will never exceed its full length after many time steps even a small time step size is used. In fact, the same problem happens to the dumbbell model with FENE spring and Laso et al. and Hu et al. [Laso93, Hu05] used the mirror-reflecting method to solve this problem. That is, when the spring length $R_i$ exceed the maximum extensibility $R_o$, the spring length will be replaced with $2R_o - R_i$ (of course, we still assume that the relation $R_o < R_i < 2R_o$ is satisfied because of the small time step). The direction of the spring is also kept the same. To keep the accuracy for the trajectory of the center of mass of the chain, we will recover its location after the mirror-reflecting method is used. The problem of this method is that a very small time step needs to be used when the flow velocity gradient is large because the spring length will exceed $2R_o$ to make the mirror-reflecting method fail.
(3) Multi-step predictor-corrector method

[Öttinger96, Somasi02, Hsieh03] used the different algorithms to keep this physical impossibility from happening, but essentially, they all used the multi-step predictor-corrector methods and explicitly calculated the length of spring vector \( R_i = |R_i| \) through solving the high order polynomial function. By using these methods, the excess over the full spring length is avoided. Here, we modified the method by Somasi et al [Somasi02] to keep the length of each spring shorter than the maximum extensibility. The procedures are given as follows:

(i) Predictor step

Since the external force is the electrophoretic force, we have the following equations for bead \( i \) and bead \( i+1 \)

\[
\begin{align*}
\frac{db_i}{dt} &= (S_0 u_i + E_0 E_i) dt + (f_i^s - f_{i-1}^s) dt + f_{i}^{random} dt \\
\frac{db_{i+1}}{dt} &= (S_0 u_{i+1} + E_0 E_{i+1}) dt + (f_{i+1}^s - f_i^s) dt + f_{i+1}^{random} dt
\end{align*}
\] (2.31) (2.32)

then we subtract (2.31) from (2.32) to get the equation for the length of spring \( i \).

\[
\begin{align*}
\frac{dR_i}{dt} &= S_0 (u_{i+1} - u_i) dt + E_0 (E_{i+1} - E_i) dt + (f_{i+1}^s - 2f_i^s + f_{i-1}^s) dt + \\
&\quad (f_{i+1}^{random} - f_i^{random}) dt
\end{align*}
\] (2.33)

We use the forward Euler method to get the predicted \( i \)-th spring vector

\[
\begin{align*}
R_i^{(p)} &= R_i^{(n)} + S_0 (u(b_{i+1}^{(n)}) - u(b_i^{(n)})) dt + E_0 (E(b_{i+1}^{(n)}) - E(b_i^{(n)})) dt + \\
&\quad (f_{i+1}^{s(n)} - 2f_i^{s(n)} + f_{i-1}^{s(n)}) dt +(f_{i+1}^{random(n)} - f_i^{random(n)}) dt
\end{align*}
\] (2.34)

where \( R_i^{(p)} \) is the predicted \( i \)-th spring vector; \( R_i^{(n)} \) and \( f_i^{s(n)} \) are the \( i \)-th spring vector and spring force at time step \( n \), and \( f_i^{random(n)} \) is the Brownian force for the \( i \)-th bead at time step \( n \).
Generally speaking, \( u_i = u(b_i) \) and \( E_i = E(b_i) \) are location-dependent, but for some simple flows such as the pure extensional and simple shear flows, we can simplify \( u(b_i^{(n)}) - u(b_j^{(n)}) = \nabla u \cdot R_i^{(n)} \) because the dimensionless velocity field can be written as \( u_i = \nabla u \cdot b_i \) and the velocity gradient \( \nabla u \) is constant. Furthermore, if the similar condition holds true for the electric field, i.e., \( E(b_i^{(n)}) - E(b_j^{(n)}) = \nabla E \cdot R_i^{(n)} \), the equation (2.34) can be further simplified into

\[
R_i^{(p)} = R_i^{(n)} + S_0 \nabla u \cdot R_i^{(n)} dt + E_0 \nabla E \cdot R_i^{(n)} dt + 
(f_i^{(n)} - 2f_i^{x(n)} + f_{i-1}^{x(n)})dt + (f_i^{random(n)} - f_i^{random(n)})dt \tag{2.35}
\]

Somasi et al. and Hsieh et al. [Somasi02, Hsieh03] have used the equation (2.35) in the study of DNA dynamics in the pure extensional and simple shear flows. For other general flows, however, we need to calculate the location of each bead in the corrector steps. Generally, there are two methods to determine each bead’s location.

The first method is to solve the movement of one arbitrary bead, say, the bead 1. We can calculate its location \( r_1 \) at any time by solving the equation (2.31). Since the spring length vectors \( R_i \) have been calculated, we can get any bead’s location by using the relations \( b_2 = b_1 + R_1, \ldots, b_i = b_{i-1} + R_{i-1}, \ldots, b_N = b_{N-1} + R_{N-1} \). This method is straightforward, but the accuracy of calculation of any bead’s location is of the order of \( \Delta t^{1/2} \) because the accuracy of calculation of the single random force is \( O(\Delta t^{1/2}) \).

Here we propose a better method to achieve higher order accuracy. This method is to first calculate the location of the center of mass, which can be solved by doing the ensemble average of all the beads’ locations from equation (2.31). Since the rod tensions are the internal forces, the ensemble average of tensions is zero, thus we have
\[ \frac{d \mathbf{b}_c}{dt} = \left( S_0 \frac{1}{N} \sum_{i=1}^{N} \mathbf{u}(\mathbf{b}_i) + E_0 \frac{1}{N} \sum_{i=1}^{N} \mathbf{E}(\mathbf{b}_i) \right) dt + \frac{1}{N} \sum_{i=1}^{N} \mathbf{f}_{i \text{random}} dt \]  

(2.36)

where \( \mathbf{b}_c = \frac{1}{N} \sum_{i=1}^{N} \mathbf{b}_i \) is the location of the center of mass. The ensemble average of the random forces can achieve higher order accuracy because it smooths out the fluctuation of the different random forces.

We can use the forward Euler method to get the location of the center of mass at time \( n \), then by using the equation (2.35) to get the predicted spring vector \( \mathbf{R}_i = \mathbf{b}_{i+1} - \mathbf{b}_i \).

It can be shown that \( N \mathbf{b}_1 = N \mathbf{b}_c - \mathbf{R}_{N-1} - 2 \mathbf{R}_{N-2} - \cdots - (N-2) \mathbf{R}_2 - (N-1) \mathbf{R}_1 \). Thus we can get the location of each bead at the predictor step as follows:

\[
\begin{align*}
\mathbf{b}_1 &= \mathbf{b}_c - \frac{1}{N} \sum_{k=1}^{N-1} k \mathbf{R}_{N-k} \\
\mathbf{b}_2 &= \mathbf{b}_1 + \mathbf{R}_1 \\
\vdots & \quad \vdots \\
\mathbf{b}_N &= \mathbf{b}_{N-1} + \mathbf{R}_{N-1}
\end{align*}
\]

(2.37)

Since the calculation of the location of the center of mass is of higher accuracy compared with the direct simulation of a bead’s location by the previous method, our method can achieve a high order of accuracy.

(ii) First corrector step

If we remove the term associated with the spring force in spring \( i \) to the left hand side of the equation (2.31), we will get the corrected spring length

\[
\begin{align*}
\mathbf{R}_{i}^{(*1)} + 2 \mathbf{f}_{i}^{(*1)} dt &= \mathbf{R}_{i}^{(*)} + S_0 (\mathbf{u}\left(\frac{\mathbf{b}_{i+1}^{(p)} + \mathbf{b}_{i+1}^{(n)}}{2}\right) - \mathbf{u}\left(\frac{\mathbf{b}_i^{(p)} + \mathbf{b}_i^{(n)}}{2}\right)) dt + \\
E_0 \left( \mathbf{E}\left(\frac{\mathbf{b}_{i+1}^{(p)} + \mathbf{b}_{i+1}^{(n)}}{2}\right) - \mathbf{E}\left(\frac{\mathbf{b}_i^{(p)} + \mathbf{b}_i^{(n)}}{2}\right) \right) dt + (\mathbf{f}_{i+1}^{(*)} + \mathbf{f}_{i+1}^{(c1)}) dt + (\mathbf{f}_{i+1}^{(*)} + \mathbf{f}_{i+1}^{(c1)}) dt + (\mathbf{f}_{i+1}^{(*)} - \mathbf{f}_{i}^{(*)}) dt
\end{align*}
\]

(2.38)
where $\mathbf{R}_i^{(cl)}$ and $\mathbf{f}_i^{(cl)}$ are $i$-th spring vector and spring force in the first corrected step.

The term $\mathbf{f}_i^{(cl)}$ on the right hand side is known because we can sweep the subindex $i$ from 1 to $N - 1$ and for bead 1 and $N$, we only have one spring force on the right hand side.

By using the worm-like chain model, the left hand side of equation (2.38) is denoted as $\mathbf{R}_i^{(cl)} + 2\mathbf{f}_i^{(cl)} dt = \mathbf{R}_i^{(cl)} + 2 \partial dt (\frac{1}{2\lambda_i (1 - \lambda_i)^2} - \frac{1}{2\lambda_i} + 2) \mathbf{R}_i^{(cl)}$, where $\lambda_i = \mathbf{R}_i^{(cl)}/\sqrt{N_{K,S}}$.

If we take $\lambda_i = \mathbf{R}_i^{(cl)}/\sqrt{N_{K,S}}$ and assign the right hand side of equation (2.38) to be a vector $\mathbf{p}_i (\mathbf{b}_j^{(n)}, \mathbf{b}_j^{(p)})$ and take $\mathbf{q}_i = \mathbf{p}_i / \sqrt{N_{K,S}}$, then equation (2.38) can be rewritten as

$$\lambda_i \{1 + \partial dt (\frac{1}{\lambda_i (1 - \lambda_i)^2} - \frac{1}{\lambda_i} + 4)\} = \mathbf{q}_i \quad (2.39)$$

If we let $s = \partial dt$ and take the modulus of the above equation to get a cubic equation of $\lambda_i$ as follows:

$$(1 + 4s)\lambda_i^3 - (2 + 9s + q)\lambda_i^2 + (1 + 6s + 2q)\lambda_i - q = 0 \quad (2.40)$$

where $q$ is the modulus of the right hand side vector $\mathbf{q}_i$ of equation (2.39).

By taking $F(\lambda_i) = (1 + 4s)\lambda_i^3 - (2 + 9s + q)\lambda_i^2 + (1 + 6s + 2q)\lambda_i - q$, we can find that $F(0) = -q < 0$ and $F(1) = s > 0$, thus there is one root or three roots of the function $F(\lambda_i)$ falling in the domain of $(0, 1)$. By taking the derivative of this function, we have $F'(\lambda_i) = (3 + 12s)\lambda_i^2 - (4 + 18s + 2q)\lambda_i + (1 + 6s + 2q)$, and the two roots for $F'(\lambda_i)$ are 1 and $(1 + 6s + 2q)/(3 + 12s)$. Because $F'(1) = 0$ and $F(1) > 0$, we know that there couldn’t be three roots of $F(\lambda) = 0$ falling in between 0 and 1 (otherwise there will be two more
roots of the function of $F'(\lambda_i) = 0$ in $(0, 1)$; with $F'(1) = 0$, that means there are three roots of $F'(\lambda_i) = 0$. Since $F'(\lambda_i)$ is only a quadratic equation, we know that is impossible). Thus we prove that there is only one root in $(0, 1)$. We can use the semi-divide method to solve this root (the conventional Newton-Raphson iteration method is not good for this case because $F'(1) = 0$ and probably there is another $\lambda$ in $(0, 1)$ to satisfy $F'(\lambda) = 0$, making the Newton-Raphson iteration never converges).

After calculating the root $\lambda_i$ for equation (2.40), we can get the first corrected $i$-th spring length vector $\mathbf{R}_i^{(1)} = \lambda_i \sqrt{N_{K,x}} \mathbf{q}_i / q_i$. Using the similar method mentioned in the predictor step, we can figure out the first corrected location $\mathbf{b}_i^{(1)}$ for bead $i$.

(iii) Second corrector step

We have the second corrector step similar to the first corrector step except some terms on the right hand side of the equation change:

\[
\mathbf{R}_i^{(2)} + 2\mathbf{f}_i^{(c2)} dt = \mathbf{R}_i^{(n)} + S_0 (u(\frac{b_{i1}^{(c1)} + b_{i1}^{(n)}}{2} - u(\frac{b_{i1}^{(c1)} + b_{i1}^{(n)}}{2}))dt +
\]
\[
E_0 (E(\frac{b_{i1}^{(c1)} + b_{i1}^{(n)}}{2}) - E(\frac{b_{i1}^{(c1)} + b_{i1}^{(n)}}{2}))(f_{11}^{(c1)} + f_{11}^{(n)})dt + (f_{11}^{(c1)} + f_{11}^{(n)})dt + (f_{11}^{(c1)} + f_{11}^{(n)})dt)
\]

where $\mathbf{R}_i^{(c2)}$ and $\mathbf{f}_i^{(c2)}$ are $i$-th spring vector and spring force in the second corrected step.

Using the similar method mentioned in the first corrector step, we can figure out the second corrected spring vector $\mathbf{R}_i^{(2)}$ and location $\mathbf{b}_i^{(2)}$ for bead $i$.

(iv) Checking step

Check whether the condition $\delta = \sqrt{\sum_{i=1}^{N-1} |\mathbf{R}_i^{(c2)} - \mathbf{R}_i^{(c1)}|^2} < \delta_0$ is satisfied or not, where $\delta_0$ is the prescribed criteria for the error, here we assign it to be $10^{-6}$. If this condition is
satisfied, we let $R_i^{(n+1)} = R_i^{(c2)}$ and begin the next time step; if it is not satisfied, then we let $R_i^{(c1)} = R_i^{(c2)}$ and go back to step (iii) and repeat steps (iii) and (iv) again until the residual condition is satisfied.

The biggest advantage of the multi-predictor-corrector method is that it can predict a higher order of the spring length because we calculated the difference of two Brownian forces in equations (2.33) instead of simulating the Brownian forces individually. The difference of two Brownian forces is in the order of $\Delta t^{1/2}$ and $(f_{i+1}^{\text{random}} - f_i^{\text{random}}) \Delta t = O(\Delta t^{3/2})$, thus this method can predict the spring length vector very accurately compared with the Euler’s method and the mid-point method.

However, in the conventional predictor-corrector method, it cannot, in principle, reduce the order of the truncation error coming from the random force because the calculation of location of each bead is also around the order of $\Delta t^{1/2}$. The time step still needs to be small in order to get an accurate result of the beads’ location although the calculated spring lengths are much more accurate (around $\Delta t^{3/2}$) than the conventional Euler’s method or mid-point method. But our modified predictor-corrector method can reduce the order of truncation error in beads’ locations because we calculate the location of the center of mass instead of one individual bead’s location.

2.4 Bead-Rod Chain Model

The bead-rod chain model is another choice when one needs to consider more degree of freedoms especially when the DNA chains are in a confined geometry whose size is comparable with the length of a Kuhn step of the DNA chains.
As shown in Figure 2.6, we have a bead-rod chain consisting of \( N \) beads connected by \( N_s = N - 1 \) rigid rods [Bird77b]. The rigid links in bead-rod chain model are required to satisfy the constrained conditions \( |\mathbf{R}_i| = |\mathbf{r}_{i+1} - \mathbf{r}_i| = b_K \), \( i = 1, \ldots, N - 1 \).

![Schematic for a bead-rod chain.](image)

Considering the force balance for the massless bead \( i \), we have the following equation [Liu89, Doyle98, Pasquali02, KimS04, Montesi05, Panwar05],

\[
\mathbf{F}_i^{\text{Drag}} + \mathbf{F}_i^{\text{Tension, total}} + \mathbf{F}_i^{\text{External}} + \mathbf{F}_i^{\text{Pseudo}} + \mathbf{F}_i^{\text{Brownian}} + \mathbf{F}_i^{\text{Bend}} = 0 \tag{2.42}
\]

where \( \mathbf{F}_i^{\text{Drag}} = -\zeta (\frac{d\mathbf{r}_i}{dt} - \mathbf{u}_i - \mathbf{u}_i') \) is the drag force, which has the similar definition as the bead-spring chain in equation (2.18); \( \mathbf{F}_i^{\text{Tension, total}} = \tau_i \mathbf{d}_i - \tau_{i-1} \mathbf{d}_{i-1} \) is the total tension at bead \( i \), where \( \tau_i \) and \( \mathbf{d}_i = (\mathbf{r}_{i+1} - \mathbf{r}_i) / |\mathbf{r}_{i+1} - \mathbf{r}_i| \) are the tension and unit direction vector of the \( i \)-th rod, respectively; \( \mathbf{F}_i^{\text{External}} \) is the external force, which was described before; \( \mathbf{F}_i^{\text{Pseudo}} \), \( \mathbf{F}_i^{\text{Brownian}} \), and \( \mathbf{F}_i^{\text{Bend}} \) are the pseudo-potential force, Brownian force and bending force.
force, respectively.

Different from the bead-spring chain described in the previous section, the governing equation of the bead-rod chain model is, in fact, a constrained differential equation. At least the conditions of constraints for the bond length (the length of each rod)

\[ |R_i| = |r_{i+1} - r_i| = b_K \]

should always be satisfied. If there are other conditions such as the bond angles \( \theta = \arccos(d_i \cdot d_{i+1}) \) to be constant, we need to add more constraints into the final equations group.

### 2.4.1 Pseudo-potential Force

According to references [Hinch94, Grassia95, Grassia96, Pasquali02, KimS04, Morse04, Montesi05, Panwar05], a metric pseudo-potential force \( F_{i}^{\text{pseudo}} \) is required in simulations of chains with constraints to mimic the behavior of infinitely stiff bead-spring chains. Otherwise, simulations with equation (2.42) for a bead-rod chain will not yield the correct random walk distribution (Gaussian distribution) in equilibrium.

Before introducing the pseudo-potential force, we need to take a look at the pseudo-potential, which is dependent on the configuration of a bead-rod chain. It has been demonstrated [Bird77b, Hinch94] that the probability of the chain configurations in equilibrium is proportional to the square root of the determinant of the bead-rod chain’s metric matrix \( G \), which is a \((N-1) \times (N-1)\) tridiagonal matrix defined as
where \( a_i = -\mathbf{d}_i \cdot \mathbf{d}_{i-1} \), \( b_i = 2\mathbf{d}_i \cdot \mathbf{d}_i = 2 \), and \( c_i = -\mathbf{d}_i \cdot \mathbf{d}_{i+1} \) as the only three nonzero elements in the \( i \)-th column. Since \( c_i = a_{i+1} \) \((i = 1, \cdots, N-2)\) and \(|b_i| \geq |a_i| + |b_i|\), the metric matrix \( \mathbf{G} \) is a symmetric diagonal-dominated tridiagonal matrix. We can rewrite equation (2.43) into a simpler form \( \mathbf{G} = [a_i; b_i; c_i] \) by following the denotation of Baker and Overmann [BakerG01].

Recall the definition of entropy \( S = k_B \ln w \) and the Gibbs free energy \( G = H - TS \), where \( w \) is the probability of states in a system, \( H \) is the enthalpy, and \( T \) is the absolute temperature, we can see that \( TS \) has the same physical meaning as a energy or potential. Now we have the probability of states of polymer chain in equilibrium \( w = \sqrt{\det(\mathbf{G})} \), thus we can write pseudo-potential as \( P^{\text{Pseudo}} = k_B T \ln(\sqrt{\det(\mathbf{G})}) \) to make it the same form as \( TS \).

The configuration-dependent pseudo-potential force is then defined as

\[
\mathbf{F}_i^{\text{Pseudo}} = -\nabla_i P^{\text{Pseudo}} = -\frac{1}{2} k_B T \frac{\partial}{\partial \mathbf{r}_i} \ln(\det(\mathbf{G}))
\]  

(2.44)

To simulate the same polymer chain, the bead-rod chain model usually needs a much higher number of degrees of freedom than the bead-spring chain model. It is important to calculate the pseudo-potential force in a fast way in order to speed up the bead-rod chain
simulations.

With the denotation of Grassia and Hinch [Grassia96], we can define $\det_{<i}$ to be the determinant of the submatrix $A_{<i}$, which is formed by rows and columns 1 to $i-1$ of the $(N-1)\times(N-1)$ metric matrix $G$, then $\det(G) = \det_{<N}$. Similarly, we can define $\det_{>i}$ to be the determinant of the submatrix $B_{>i}$, which is formed by taking rows and columns $i+1$ to $(N-1)$ of the metric matrix $G$, then $\det(G) = \det_{>0}$. The structure of the metric matrix $G$ and its submatrices $A_{<i}$ and $B_{>i}$ are shown in Figure 2.7:

![Figure 2.7: Structure of the metric matrix.](image)

Using the Laplace expansion theorem on $i$-th column, we have the recurrence relation [Fixman74] as follows:

$$\det_{<i} = 2\det_{<i-1} - (\mathbf{d}_{i-2} \cdot \mathbf{d}_{i-1})^2 \det_{<i-2}$$  \hspace{1cm} (2.45)
Since $\det_{<2} = 2$ and $\det_{<3} = 4 - (d_1 \cdot d_2)^2$, we can conclude that $\det_{<1} = 1$ from equation (2.45) although it could not be determined from the definition in Figure 2.7. It can be proved that $\det_{<i} < \det_{<i+1}$ by using the mathematical induction method on the recurrence relation of equation (2.45). Thus the determinant of the metric matrix $\det(G)$ is always great than 0. Also since $\det_{<1} = 1$ and $\det_{<2} = 2$ are fixed for any configuration of a polymer chain, we can prove that the value of $\det(G)$ gets its minimum $\min(\det(G)) = N$ when all the $d_{i-2} \cdot d_{i-1} = 1$ and gets its maximum $\max(\det(G)) = 2^{N-1}$ when all the $d_{i-2} \cdot d_{i-1} = 0$. Both cases correspond to the zero value of the pseudo-potential force. For other cases, we have $N < \det(G) < 2^{N-1}$ and $F^{\text{Pseudo}}_i \neq 0$. This also indicates that when a bead-rod chain in a strong pure extensional flow, the pseudo-potential force is not so important because the chain has been stretched out to make $d_{i-2} \cdot d_{i-1} = 1$ satisfied.

Similarly, using the Laplace expansion theorem on $(i+1)$-th column, we have the other recurrence relation:

$$
\det_{>i} = 2\det_{>i+1} - (d_{i+1} \cdot d_{i+2})^2 \det_{<i+2}
$$

(2.46)

A more complicated recurrence relation connecting $\det_{<i}$ and $\det_{>i}$ is to expand the metric matrix $G$ along the $i$-th column [Grassia96] by using the Laplace expansion theorem

$$
\det(G) = b_i \det(S_1) - a_i \det(S_2) - c_i \det(S_3)
$$

(2.47)

where the structure of matrices $S_1$, $S_2$, and $S_3$ are given in Figure 2.8.
Figure 2.8: Structures of matrices $S_1$, $S_2$, and $S_3$. 

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Since \( S_1 = \begin{bmatrix} A_{<i} & 0 \\ 0 & B_{>i} \end{bmatrix} = \begin{bmatrix} A_{<i} & 0 \\ 0 & I_{>i} \end{bmatrix} \begin{bmatrix} I_{<i} & 0 \\ 0 & B_{>i} \end{bmatrix} \), where \( I_{>i} \) is a unit matrix with the same dimension as \( B_{>i} \), and \( I_{<i} \) is also a unit matrix with the same dimension as \( A_{<i} \), we can prove that \( \det(S_1) = \det(A_{<i}) \det(B_{>i}) = \det_{<i} \det_{>i} \).

Using the Laplace expansion theorem successively for \((N - 1)\) times, we can prove that \( \det(S_2) = c_{i-1} \det_{<i-1} \det_{>i} \) and \( \det(S_3) = a_{i+1} \det_{<i} \det_{>i+1} \) (here the deduction is omitted because it is just a tedious work).

For simplicity, we let \( \det(G) = \det \) and equation (2.47) can be further written as

\[
\det = 2 \det_{<i} \det_{>i} - (d_i \cdot d_{i+1})^2 \det_{<i} \det_{>i+1}(1 - \delta_{i,N-1}) - (d_{i-1} \cdot d_i)^2 \det_{<i-1} \det_{>i}(1 - \delta_{i,1})
\]

(2.48)

The reason why we need to add \((1 - \delta_{i,N-1})\) and \((1 - \delta_{i,1})\) to equation (2.48) is that this equation only works for \(1 < i < N - 1\).

Considering the recurrence relations of equations (2.45) and (2.46), we have

\[
\det = [4 - (d_{i-1} \cdot d_i)^2] \det_{<i-1} \det_{>i} - 2(d_i \cdot d_{i+1})^2 \det_{<i-1} \det_{>i+1}(1 - \delta_{i,N-1}) - 2(d_{i-2} \cdot d_{i+1})^2 \det_{<i-2} \det_{>i}(1 - \delta_{i,2}) + (d_{i-2} \cdot d_{i+1})^2 (d_i \cdot d_{i+1})^2 \det_{<i-2} \det_{>i+1}(1 - \delta_{i,2})(1 - \delta_{i,N-1})
\]

(2.49)

This equation is slightly different from what appeared in [Grassia96] because they marked their beads number from 0 to \(N\), while we number beads from 1 to \(N\).

Since \( F^{pseudo}_i = -\frac{1}{2} k_B T \nabla_i \ln(\det(G)) = -\frac{1}{2} k_B T \frac{\nabla_i \det}{\det} \), we need to calculate \( \nabla_i \det \).

It can be easily proved that

\[
\nabla_i d_j = \nabla_i \left( \begin{bmatrix} r_{i+1} - r_i \\ r_{i+1} - r_{<i} \end{bmatrix} \right) = d_j - I
\]

(2.50)
\[ \nabla_i d_{i-1} = \nabla_i \left[ \frac{r_i - r_{i-1}}{r_i - r_{i-1}} \right] = I - d_{i-1} d_{i-1} \]  
(2.51)

\[ \nabla_i d_{i+1} = \nabla_i d_{i+2} = 0 \]  
(2.52)

where \( I \) is a \( 3 \times 3 \) unit matrix. Also, since the determinants \( \det_{<i-2}, \det_{<i-1}, \det_i \), and \( \det_{>i+1} \) do not include any of \( d_i \) and \( d_{i+1} \) (thus do not have any term of \( r_i \)), their derivate with respect to \( r_i \) are all zero.

\[ \nabla_i \det_{<i-2} = \nabla_i \det_{<i-1} = \nabla_i \det_i = \nabla_i \det_{>i+1} = 0 \]  
(2.53)

Thus from equation (2.49), we get the following equation

\[
\begin{align*}
\nabla_i \det & = -2(d_{i-1} \cdot d_i)(d_i - (d_{i-1} \cdot d_i)d_{i-1}) + (d_i - d_{i-1} \cdot d_i)d_{i+1} \det_{<i-1} \det_i \\
& \quad - 4(d_i \cdot d_{i+1})(d_i \cdot d_{i+1})d_i - d_{i+1} \det_{<i-1} \det_{>i} (1 - \delta_{i,N-1}) \\
& \quad - 4(d_{i-2} \cdot d_i)(d_{i-2} \cdot d_i)d_{i-1} \det_{<i-2} \det_{>i} (1 - \delta_{i,2}) \\
& \quad + 2(d_{i-2} \cdot d_i)(d_i \cdot d_{i+1})^2[d_{i-2} - (d_{i-2} \cdot d_i)d_{i-1}] \det_{<i-2} \det_{>i} (1 - \delta_{i,2}) (1 - \delta_{i,N-1}) \\
& \quad + 2(d_{i-2} \cdot d_i)^2(d_i \cdot d_{i+1})(d_i \cdot d_{i+1})d_i - d_{i+1} \det_{<i-2} \det_{>i+1} (1 - \delta_{i,2}) (1 - \delta_{i,N-1})
\end{align*}
\]  
(2.54)

The pseudo-potential force \( F_i^{\text{Pseudo}} = -\frac{1}{2} k_B T \frac{\nabla_i \det}{\det} \) can be calculated by using equation (2.54) and the recurrence relations of equations (2.45) and (2.46).

### 2.4.2 Projected Random Force

In the bead-rod chain model, the Brownian force is slightly different from what we have in the bead-spring chain model. According to [Montesi05], it should be a so-called geometrically projected random force, which satisfies

\[ F_i^{\text{Brownian}} \cdot n_{i\mu} = 0 \]  
(2.55)

where the vector \( n_{i\mu} = r_\mu (\delta_{i,\mu+1} - \delta_{i,\mu}) \) (which is the gradient of the \( i \)-th constraint.
\[ C_i = \left| \mathbf{R}_i \right| = \left| \mathbf{r}_{i+1} - \mathbf{r}_i \right| \] with respect to the coordinate vector \( \mathbf{r}_\mu \), i.e., \( \mathbf{n}_{\mu} = \partial C_i / \partial \mathbf{r}_\mu \).

Suppose the number of the constraints is \( K \), then from the Lagrangian multiplier method, the number of the degree of freedom of a \( N \)-bead chain system decreases to \( 3N - K \).

Equation (2.55) means that the \( 3N \) dimensional random force \( \mathbf{F}_i^{\text{Brownian}} \) is only allowed to move on the \( 3N - K \) dimensional hypersurface to which the system is confined and any possible move normal to this hypersurface should be deducted.

Thus the geometrically projected random force has the following expression

\[ \mathbf{F}_i^{\text{Brownian}} = \mathbf{F}_i^{\text{UP,Brownian}} - \mathbf{n}_{\mu i} \hat{F}_\mu \] (2.56)

where \( \mathbf{F}_i^{\text{UP,Brownian}} \) is the so-called unprojected random forces, which could be determined by equations (2.19) and (2.20). We use the same expression as that in the bead-spring chain model. \( \hat{F}_\mu \) is the so-called “hard” component of the unprojected random force along the direction \( \mathbf{n}_{\mu i} \) [Montesi05]. Equation (2.56) has eliminated the components normal to the \( 3N - K \) hypersurface of the system (or along the direction of \( \mathbf{n}_{\mu i} \)). Since the constraint conditions \( C_i = b \) should be always satisfied, the random force in a bead-rod chain, in fact, is not so “random” as that in a bead-spring chain and it is prohibited in the direction of \( \mathbf{n}_{\mu i} \), which is the gradient (or the steepest direction) of the constraints.

The hard components of the unprojected random force \( \hat{F}_\mu \) can be obtained by solving the following \( N \) equations [Montesi05]:

\[ G_{\nu \mu} \hat{F}_\mu = n_{i\nu} \cdot n_{i\mu} \hat{F}_\mu = n_{j\nu} \cdot F_j^{\text{UP,Brownian}} \] (2.57)

where \( G_{\nu \mu} = n_{i\nu} \cdot n_{i\mu} \) is the component of the tri-diagonal metric tensor \( \mathbf{G} \) given in
equation (2.43). Once all the $\hat{F}_\mu$ are calculated, we can get the projected random force from equation (2.56).

### 2.4.3 Bending Force

The bending force $\mathbf{F}_i^{Bend}$ in a bead-rod chain can be obtained by solving the derivative of the bending energy with respect to coordinate vector $\mathbf{r}_i$. Recalling equation (2.5) for the total bending energy of a continuous curve, we can rewrite it in a discretized form, $U_i^{Bend} = \frac{\kappa}{2} \int_0^l c^2(s)ds = \frac{\kappa}{2} \sum_{i=1}^{N-1} c_i^2 b_K$, where $c_i$ is the curvature of $i$-th rod. Since the unit tangent vector for $i$-th rod is $\mathbf{p}_i = \mathbf{d}_i$, and $c_i \mathbf{n}_i = \left. \frac{\partial \mathbf{p}}{\partial s} \right|_i = \frac{\mathbf{p}_i - \mathbf{p}_{i-1}}{b_K}$ in a bead-rod chain, we have $c_i \mathbf{n}_i = \frac{\mathbf{d}_i - \mathbf{d}_{i-1}}{b_K}$. Thus the total bending energy for a bead-rod chain is

$$U_i^{Bend} = \frac{\kappa}{b_K} (N - 1 - \sum_{i=1}^{N-1} \mathbf{d}_i \cdot \mathbf{d}_{i-1}) = \frac{k_BT}{2} (N - 1 - \sum_{i=2}^{N-1} \mathbf{d}_i \cdot \mathbf{d}_{i-1})$$

which has already considered $\mathbf{d}_0 = 0$ and bending rigidity $\kappa = k_BT \lambda_p = \frac{b_K}{2} k_BT$. In [Pasquali02, Montesi05], the bending energy is written as $U_i^{Bend} = -\frac{\kappa}{b_K} \sum_{i=2}^{N-1} \mathbf{d}_i \cdot \mathbf{d}_{i-1}$ with the negative sign, which dissatisfies the physical law unless the referenced energy is prescribed as $\frac{\kappa}{b_K} (N - 1)$. The bending force at bead $i$ ($2 < i < N - 1$) could be written as

$$\mathbf{F}_i^{Bend} = -\frac{\partial U_i^{Bend}}{\partial \mathbf{r}_i} = \frac{k_BT}{2b_K} \frac{\partial}{\partial \mathbf{r}_i} \sum_{k=2}^{N-1} \mathbf{d}_k \cdot \mathbf{d}_{k-1}$$
which could be further transformed to

\[ F_i^{\text{Bend}} = \frac{k_B T}{2b_K} (d_{i-2} - d_{i-1} + d_i - d_{i+1}) \]  \hspace{1cm} (2.60)

by considering \( d_{i-1} = r_i - r_{i-1} \) and \( d_i = r_{i+1} - r_i \). But for \( i = 1, 2, N - 1, N \), equation (2.60) needs to be modified a little bit and we have the following expression

\[
\begin{cases}
F_1^{\text{Bend}} = -\frac{k_B T}{2b_K} d_2 \\
F_2^{\text{Bend}} = \frac{k_B T}{2b_K} (-d_1 + d_2 - d_3) \\
F_i^{\text{Bend}} = \frac{k_B T}{2b_K} (d_{i-2} - d_{i-1} + d_i - d_{i+1}) & 2 < i < N - 1 \\
F_{N-1}^{\text{Bend}} = \frac{k_B T}{2b_K} (d_{N-3} - d_{N-2} + d_{N-1}) \\
F_N^{\text{Bend}} = \frac{k_B T}{2b_K} d_{N-2}
\end{cases}
\]  \hspace{1cm} (2.61)

Since the bending force is the internal force for a polymer chain, the contribution of the total bending force to the movement of the center of mass should be zero, that means \( \sum_{i=1}^{N} F_i^{\text{Bend}} = 0 \). It is easy to find that this condition is satisfied by adding all the bending force is equation (2.61).

2.4.4 Further Discussions

Most polymer chains have the extra constraints requiring the bond angle \( \theta_i = \arccos(d_i \cdot d_{i+1}) \) to be constant. Of course, we can handle them just in the same way as we dealt with the constraints for the rod lengths. It was found that the pseudo-potential force, the projected Brownian force and the bending force are very important in
describing the correct distribution of the bond angles in a bead-rod chain in the equilibrium state [Pasquali02, Montesi05].

However, we found that in the pure extensional flow with even a medium extensional rate, the contributions of these three forces to the stretching amount of DNA chain are almost negligible compared with those coming from the tension force, the drag force and the external force. This should be true because the bead-rod chain is in a state far away from equilibrium and in this bead-rod chain, each rod can freely bend and rotate (without any constraint of the bond angle), making the effect of these three forces invisible since the other forces dominate.

In this dissertation, we still consider the pseudo-potential force because we need to calculate the relaxation process of a DNA molecule (the effects of the projected Brownian force and the bending force are small in the equilibrium state if we do not consider the constraints of the bond angle). But its effect to the dynamics of a bead-rod chain can be neglected in a state far away from equilibrium.

2.4.5 Numerical Method And Procedures

The dimensionless form of the governing equation (2.42) for the bead-rod chain is given as follows:

\[
\frac{d\mathbf{b}_i}{dt} = S_0 \mathbf{u}_i + \mathbf{f}_{i}^{\text{random}} + (\tau_i \mathbf{d}_i - \tau_{i-1} \mathbf{d}_{i-1}) + \mathbf{f}_i^{\text{pseudo}} + \mathbf{f}_{i}^{\text{external}}
\]  

(2.62)

where \( \mathbf{b}_i = \mathbf{r}_i / b_K \), the characteristic time is \( \xi b_K^2 / (k_B T) \), \( S_0 = U_{\text{ref}} b_K / (k_B T / \xi) \) and \( U_{\text{ref}} \) is the characteristic velocity. The dimensionless Brownian force is \( \mathbf{f}_i^{\text{random}} = \sqrt{6/Dt} \mathbf{n}_i \) (unprojected random force). \( \tau_i \) is the tension in \( i \)-th rod, \( \mathbf{d}_i = \mathbf{r}_{i+1} - \mathbf{r}_i \) is the \( i \)-th rod
vector. The dimensionless pseudo-potential force is \( f_i^{\text{pseudo}} = -\nabla_i \ln \sqrt{\text{det} G} \), where \( G \) is the metric tensor. The external force is \( f_i^{\text{external}} = E_0 E_i \) if electrophoretic force is considered with \( E_0 = qE_{\text{ext}} b_k / (k_B T) \); \( E_{\text{ext}} \) is the characteristic external electric field, \( q \) is the charge density for each bead.

The tensions on the right hand side of equation (2.62) are unknown, but they can be calculated from the constraints of the rod length \( |R_i| = |r_{i+1} - r_i| = b_k \), or \( |b_{i+1} - b_i|^2 = 1 \). By taking the time derivative of \((b_{i+1} - b_i) \cdot (b_{i+1} - b_i)\), we have

\[
(b_{i+1} - b_i) \cdot (b_{i+1} - b_i) = (b_{i+1} - b_i) \cdot d_i = 0 \tag{2.63}
\]

By inserting equation (2.62) for \((i+1)\)-th and \(i\)-th beads, we obtain

\[
-(d_{i-1} \cdot d_i) r_{i-1} + 2(d_i \cdot d_{i+1}) r_i - (d_i \cdot d_{i+1}) r_{i+1} = S_0 (u_{i+1} - u_i) \cdot d_i + (f_i^{\text{random}} - f_i^{\text{pseudo}}) \cdot d_i + (f_i^{\text{external}} - f_i^{\text{external}}) \cdot d_i \tag{2.64}
\]

The components on the left hand side of equation (2.64) are the element for the tridiagonal metric tensor \( G \). If the right hand side of equation (2.64) is denoted as \( f_i^{\text{rhs}} \), then the tensions can be obtained by solving equations \( G \{ \tau_i \} = \{ f_i^{\text{rhs}} \} \).

According to [Grassia96], a higher order numerical integration scheme must be used to solve equation (2.62) in order to get correct solution. Here, we use the mid-point method, which is a second-order time marching scheme.

The simulation procedures are given as follows:

1. Calculate the velocity field, the Brownian force, the pseudo-potential force and the external force for all beads at time step \( n \).

2. Solve the tensions by the equation (2.64) at time step \( n \).
(3) Get the mid-point (time step $n + \frac{1}{2}$) value $\mathbf{b}_i^{n+\frac{1}{2}} = \mathbf{b}_i^n + \frac{1}{2} \Delta t \mathbf{\dot{b}}_i^n$ using the equation (2.62).

(4) Figure out the new values for $\mathbf{u}_i^{n+\frac{1}{2}}$, $\mathbf{f}_i^{\text{external}, n+\frac{1}{2}}$, $\mathbf{f}_i^{\text{pseudo}, n+\frac{1}{2}}$ (based on the new configuration of the chain).

(5) Use the equation (2.64) to get the new value for the tensions $\tau_i^{n+\frac{1}{2}}$.

(6) Finally, the bead location at time step $n + 1$ can be obtained by $\mathbf{b}_i^{n+1} = \mathbf{b}_i^n + \Delta t \mathbf{\dot{b}}_i^{n+\frac{1}{2}}$ from equation (2.62).

Bead-rod chain simulation is time-consuming because the number of the degrees of freedom is large (to simulate the dynamics of a $\lambda$-DNA molecule, we need 150 beads) and the calculation of pseudo-potential force is complicated. But it is still worth to use this approach when the size of the geometry is comparable with the length of a Kuhn step. In the following sections, we will use the bead-rod chain and bead-spring chain models to simulation the dynamics of single DNA molecules in hydrodynamic flows.

2.5 Relaxation of the Fully or Nearly Fully Stretched DNA Molecules

The relaxation process of a single DNA chain in dilute solution has been demonstrated by the Chu group [Perkins94b] (mentioned in chapter 1). The experimental data were frequently used for comparison with the simulations.

In this section, we studied the relaxation process of the YOYO-1 dyed $\lambda$-DNA and a longer DNA molecule with contour length of 67.2 $\mu$m. To simulate the $\lambda$-DNA molecule, we used the 20-bead bead-spring chain (each spring containing 8 Kuhn steps) and 150-
bead-bead-rod chains. To simulate the longer DNA molecule, we only use the 40-bead bead-spring chain with each spring containing 16 Kuhn steps (here we follow the paper [Larson99b] and use the same parameters).

The selection of the “effective” persistence length is important in the bead-spring chain simulation with the worm-like spring. For the 21 μm λ-DNA, we take 96 nm as the “effective” persistence length, while for the longer DNA with contour length of 67.2 μm, the “effective” persistence length is 61 nm.

To simulate the same λ-DNA molecules with the bead-spring and bead-rod chain models, we need to let these two models satisfy the following requirements:

1) First of all, these two chain models have the same contour length. If the Kuhn step lengths for the bead-spring and bead-rod chains are denoted as $b_{K,1}$ and $b_{K,2}$, respectively, then from the condition for the same contour length, we have $L_C = (N_1 -1)N_{K,s} b_{K,1} = (N_2 -1)b_{K,2}$, where $N_1$ and $N_2$ are the number of beads for bead-spring and bead-rod chains, and $N_{K,s}$ is the Kuhn steps in one spring. In this section, we let $N_1 = 20$, $N_{K,s} = 8$, and $N_2 =150$. Since $b_{K,1}/b_{K,2} = 0.9803$, we can simply assume these two chain models have the same Kuhn step length.

2) Second, the total drag coefficient for these two chain models should be the same, thus we have $N_1 \xi_1 = N_2 \xi_2$, where $\xi_1$ and $\xi_2$ are the single bead drag coefficients for bead-spring and bead-rod chain models, respectively. So $\xi_1/\xi_2 = N_2/N_1 = 7.5$. We use the value of $\xi_1/(k_B T) = 1 \ (s/\mu m)^2$ for the bead-spring worm-like chain [Larson99b]; correspondingly, for the bead-rod chain $\xi_1/(k_B T) = 0.1333 \ (s/\mu m)^2$. 

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Table 2.2 shows the parameters used in the simulation for these two chain models. For the bead-spring worm-like chain, there are two sets of parameters because we use this chain model to simulate two types of DNA molecules: λ-DNA and the longer DNA with contour length 67.2 μm.

<table>
<thead>
<tr>
<th></th>
<th>Bead-Spring (worm-like chain)</th>
<th>Bead-Rod</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bead number</td>
<td>20 or 40</td>
<td>150</td>
</tr>
<tr>
<td># of Kuhn step per link</td>
<td>8 or 16</td>
<td>1</td>
</tr>
<tr>
<td>Effective persistence length</td>
<td>96 or 61 nm</td>
<td>70 nm</td>
</tr>
<tr>
<td>$\xi/(k_\text{B}T)$</td>
<td>1 (s/μm)$^2$</td>
<td>0.1333 (s/μm)$^2$</td>
</tr>
<tr>
<td>Characteristic length $b$</td>
<td>0.3907 or 0.4308 μm</td>
<td>0.1409 μm</td>
</tr>
<tr>
<td>Characteristic time $\xi b^2/(k_\text{B}T)$</td>
<td>0.1526 or 0.1856 s</td>
<td>0.0199 s</td>
</tr>
</tbody>
</table>

Table 2.2: Parameters used in the bead-spring and bead-rod chain models.

Figure 2.9 shows the mean square end-to-end distance vs. time for the relaxation of ten 150-bead bead-rod chains (under different Brownian forces) with the initial conformation as a straight chain. The data are shown in different marks with different colors. Also the average mean square end-to-end distance is drawn in a solid red line. This figure indicates that by using the ensemble average, the fluctuation associated with the Brownian motion of DNA molecules in equilibrium state is smaller.
We also study the longest relaxation time of two types of bead-spring chains with different contour lengths (i.e., 21 and 67.2 μm) using the bead-spring chain model. It has been shown in Chapter 1 that the mean square end-to-end distance \( \langle x(t)x(t) \rangle \) can be fitted by an exponential function \( C_1 \exp(-t/\tau_{\text{long}}) + C_2 \), which can be used to calculate the longest relaxation time \( \tau_{\text{long}} \) for the DNA molecules.

When \( t \to \infty \), \( \langle x(t)x(t) \rangle \to C_2 \) (of course, we see the fluctuation near the value of \( C_2 \)). We can average \( x(t)x(t) \) with wide time period to get \( C_2 \) when the chain reach the equilibrium state. Then from \( \log(\langle x(t)x(t) \rangle - C_2) = \log C_1 - t + \tau_{\text{long}} \), we just need to use
the least-square method to fit the known numerical data \( \log \left( \langle x(t)x(t) \rangle - C_2 \right) \) by the linear function \( \log C_1 - t + \tau_{\text{long}} \) on time \( t \) to get the values for \( C_1 \) and \( \tau_{\text{long}} \).

Figures 2.10(a) and (b) (in log-log plot) show the best fitting functions for these two bead-spring chains. For the 20-bead chain (to simulate \( \lambda \)-DNA molecule), the dimensionless relaxation time is 6.1003, since the characteristic time is 0.1526 s (see Table 2.2), the dimensional relaxation time is \( 6.1003 \times 0.1526 = 0.9309 \text{ s} \), which is very close to the measured value 0.9 s in [Perkins94b]. For the DNA with contour length 67.2 \( \mu \text{m} \), the longest relaxation time is \( 23.9133 \times 0.1856 = 4.4383 \text{ s} \).
Figure 2.10: Simulation of the mean square end-to-end distance vs. time for (a) λ-DNA and (b) the longer DNA with contour length 67.2 μm.
2.6 DNA Molecules in the 2D Pure Extensional Flow

The dimensional 2D pure extensional flow is given by

\[ u = \dot{\epsilon} x, \quad v = -\dot{\epsilon} y, \quad w = 0 \]  \hspace{1cm} (2.65)

where \( u = (u, v, w) \) is the velocity vector, \( r = (x, y, z) \) is the coordinate vector, and \( \dot{\epsilon} \) is the extensional rate. In this dissertation, the expression of the extensional flow follows [Larson99b], which is slightly different from those in other papers, but the results are similar.

To observe the coil-stretch transition of a DNA molecule in the pure extensional flow, we need to make the extensional rate or Deborah number (\( De = \dot{\epsilon} \tau_{\text{long}} \), where \( \tau_{\text{long}} \) is the longest relaxation time) high enough. Both the experiments and simulation results [Perkins97, Larson99b] found that the critical Deborah number is \( De_c = 0.5 \).

We can set the characteristic velocity \( U_{\text{ref}} = b \dot{\epsilon} \), where the characteristic length \( b = b_k \sqrt{N_{K,S}} \) for the bead-spring chain and \( b = b_k \) for the bead-rod chain; thus the dimensionless velocity profile is \( \tilde{u} = (\tilde{x}, -\tilde{y}, 0) \).

In this section, we consider four different extensional rates \( \dot{\epsilon} = 0.125, 0.25, 1, \) and 10 (same extensional rates as [Larson99b]). We use same parameters given in Table 2.2 for the bead-spring and bead-rod chains in order to compare the results.

Now in the dimensionless equation (2.27), we have \( S_0 = \dot{\epsilon} \tilde{\xi} b^2 / (k_B T) \); from the Stokes-Einstein equation, the diffusion coefficient is \( D_{\text{diff}} = k_B T / \tilde{\xi} \), and the characteristic velocity is \( U_{\text{ref}} = b \dot{\epsilon} \), thus \( S_0 = U_{\text{ref}} b / D_{\text{diff}} \) has the same meaning as the Peclet number; we will temporary call it the Peclet number. But be aware that in the bead-spring and
bead-rod chain models, the Peclet number is different for the same extensional rate because the characteristic length and the single bead drag coefficient are different.

Let us first look at the results for the coil-stretching of the DNA molecules with contour length 67.2 μm. There are two sets of descriptions for DNA stretching. One is to examine the change of the fractional end-to-end distance (the end-to-end distance divided by the contour length) vs. time (or strain), and the other is to examine the relation of the fractional visual length (maximum distance between the beads divided by the contour length) vs. strain, because it is impossible to measure the end-to-end distance (only the visual length can be measured) in the experiment. The end-to-end distance might not be a monotonic function with respect to strain, while the visual strength is monotonic with strain. The difference between these two descriptions for a same chain (in the folded shape initially) at an extensional rate 10 is shown in Figure 2.11. The fractional end-to-end distance (in dash line) increases at the beginning, and then decreases with time until the chain is unfolded from one end, following by an increase again to the maximum amount of stretching at this extensional rate; while the fractional visual length (in solid line) increases monotonically with strain. Both descriptions reach the same amount of stretching when time is large enough.
Figure 2.11: Comparison between the relations of the fractional visual length vs. strain and the fractional end-to-end distance vs. strain.

The relation of the fractional visual length vs. strain has been studied in [Larson99b] with the forward Euler method and we use the multi-predictor-corrector to simulate the coil-stretching of the DNA molecule with contour length of 67.2 μm once again and the results of the fractional visual length vs. strain are given in Figure 2.12(a)–(d) (extensional rates $\dot{\varepsilon} = 0.125, 0.25, 1$, and 10), which are almost the same (initial configurations might not be the same) compared with those given in [Larson99b].

From Figures 2.12(a)–(d), we can see that the maximum fractional visual length increases with the extensional rate. When $\dot{\varepsilon} = 0.125$, at strain = 10, the amount of
fractional stretching is only 0.3, while when $\dot{\varepsilon} = 10$, it can go to 0.95, very close to the state for a fully stretched chain.

![Graphs showing fractional stretching vs. strain](image)

Figure 2.12: The fractional visual length vs. strain at extensional rate (a) 0.125, (b) 0.25, (c) 1, and (d) 10.

Now we discuss the coil-stretching of the $\lambda$-DNA molecules. As mentioned in the previous pages, we use both the bead-rod and bead-spring chain models to carry out the Brownian dynamics simulations.

Figures 2.13(a)–(d) shows the comparison of the fractional end-to-end distance for 100 bead-spring chains and 40 bead-rod chains at the extensional rate $\dot{\varepsilon} = 1$ and 10. We
can see that the calculated final amount of stretching using the bead-rod chain model is higher than that using the bead-spring chain model at the same extensional rate (by comparing Figures 2.13(a) with (c), and (b) with (d)). This indicates that the bead-rod chain model can be more easily stretched out than the bead-spring chain model (probably due to the flexible bead-spring worm-like chain is stiffer than the rigid bead-rod chain).

Figure 2.13: The fractional end-to-end distance vs. strain for bead-spring chain at extensional rate (a) 1, (b) 10; for bead-rod chain at extensional rate (c) 1, and (d) 10.

It would be interesting to study the extension process of single DNA molecules. Figures 2.14(a) and (b) show the conformations of two different bead-rod chains at five
time points under the extensional rate 10. With different initial shapes, the extension processes of these two chains are different. Figure 2.14(a) shows the DNA chain with the dumbbell shape at the initial time. It can be more easily stretched out than the DNA chain with the folded shape at the initial time. This can be confirmed by the Figure 2.13(d). The fastest one only takes 2 strains to be fully stretched, while the slowest one needs to take 7 strains to be fully stretched.

Figure 2.14: Conformations of (a) a dumbbell-shaped and (b) a folded bead-rod chains at five time points under the extensional rate 10.

2.7 DNA Molecules in the Simple Shear Flow

In this section, we use the bead-spring chain model to simulate the dynamics of DNA molecules in the simple shear flow, which is given as follows:

\[ u = \dot{\gamma} y, \quad v = 0, \quad w = 0 \]  

(2.66)

where \( u = (u, v, w) \) is the velocity vector, \( r = (x, y, z) \) is the coordinate vector, and \( \dot{\gamma} \) is the shear rate. In this section, we take the shear rate \( \dot{\gamma} = 3.3 \) and 6.6.
We use the bead-rod chain model to study the dynamics of the DNA chains in the shear flow. Figures 2.15(a) and (b) show the fractional end-to-end distance vs. strain for 40 bead-rod chains at these two shear rates. We can see that the end-to-end distance fluctuates with strain. In the extensional flow, usually the DNA molecules will be stretched to its maximum amount around strain = 4, while even at strain = 70, we cannot see any steady state of DNA molecules in the shear flow. This indicates that the DNA molecules are stretched first, and then coil back; the “coil-stretch-recoil” process takes for ever and never reaches the steady state.

![Figure 2.15: Fractional end-to-end distance vs. strain for bead-rod chains at the shear rate (a) 0.33 and (b) 0.66.](image)

Also we show the conformation change of two single DNA molecules at the shear rate $\dot{\gamma} = 6.6$ in Figure 2.16. We can clearly see the “coil-stretch-recoil” phenomenon, which has been shown in experiments [SmithD99] mentioned in Chapter 1. Also the orientation (the major direction of the chain, which can be quantitatively given by the radius of gyration tensor [Teixeira05]) of a DNA chain changes with time and it seems that the relation of orientation vs. time is a random function and affected by the Brownian
random force. Another interesting phenomenon is that the DNA chain conducts the tumbling motion around its center of mass. The simulation can also capture this phenomenon and we show it in Figure 2.17 at a shear rate $\dot{\gamma} = 6.6$.

Figure 2.16: Conformation change of two single DNA molecules.

Figure 2.17: Tumbling movement of a DNA chain at different time (time period is 800,000 $\Delta t$, where $\Delta t$ is the time step).
The tumbling and the “coil-stretch-recoil” phenomena of the DNA chain can be explained by Figure 2.18. We suppose that the location of the left part of the DNA chain is lower than the right part at the beginning (and the higher the location in the $y$ direction, the larger the velocity component in the $x$ direction). Since the velocity gradient exists only in the $y$ direction, the DNA chain (in different velocity planes) is stretched in the $x$ direction; at the same time, the chain is squeezed in the $y$ direction. When the chain is nearly aligned in the $x$ direction (or the chain is nearly at one velocity plane), the velocity gradient is nearly zero, thus the chain stops being stretching further. Due to the effect of the Brownian motion, the left part of the DNA chain might be lifted and the right part of the DNA chain might move down, thus making the left part of the chain move faster than the right part, and the chain starts to shrink back; at the same time, the chain rotates (or tumbles) with respects to its center of mass. This means that we can observe the “coil-stretch-recoil” and the tumbling phenomena at the same time.

![Figure 2.18: Schematic of DNA dynamics in the shear flow.](image)

2.8 Explanations of DNA Dynamics in the General 2D Mixed Flow

Different flow patterns have been generated in the micro-scaled geometry to study the dynamics of a single DNA molecule. By applying the similar criteria described by Babcock et al. [Bobcock03], the flow type can be characterized by a factor $\Lambda$ defined as
where \( \Pi = \frac{1}{2} (\nabla u + \nabla u^T) \) is the symmetric or extensional part of the velocity gradient \( \nabla u \), \( \Omega = \frac{1}{2} (\nabla u - \nabla u^T) \) is the anti-symmetric or rotational part, and \( \| \cdot \| \) is the Frobenius norm of a tensor (for an arbitrary tensor \( A \), \( \| A \| = \sqrt{\sum \sum A_{i,j}^2} \)). The value of \( \Lambda \) falls between –1 and 1. When \( \Lambda = -1, 0, \) or \( 1 \), the flow is pure rotational, simple shear or pure extensional, respectively. When \( -1 < \Lambda < 0 \), it is a rotation-dominated mixed flow and when \( 0 < \Lambda < 1 \), an extension-dominated mixed flow.

Let us study a generalized 2D mixed flow given as follows:

\[
\begin{align*}
    u &= ax + by \\
    v &= cx - ay
\end{align*}
\]  

(2.68)

where \( a, b, \) and \( c \) are three controlling parameters and the continuity equation \( \nabla \cdot u = \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} = 0 \) has already been considered. Equation (2.68) can be rewritten as

\[
\begin{pmatrix}
    u \\
    v
\end{pmatrix} = \begin{pmatrix}
    dx/\ dt \\
    dy/\ dt
\end{pmatrix} = \begin{pmatrix}
    a & b \\
    c & -a
\end{pmatrix} \begin{pmatrix}
    x \\
    y
\end{pmatrix}
\]  

(2.69)

Then the velocity gradient tensor is \( A = \nabla u = \begin{pmatrix}
    a & b \\
    c & -a
\end{pmatrix} \).

We can rewrite this tensor into three parts:

\[
\nabla u = \begin{pmatrix}
    a & b \\
    c & -a
\end{pmatrix} = a \begin{pmatrix}
    1 & 0 \\
    0 & -1
\end{pmatrix} + \frac{b+c}{2} \begin{pmatrix}
    0 & 1 \\
    1 & 0
\end{pmatrix} + \frac{b-c}{2} \begin{pmatrix}
    0 & 1 \\
    -1 & 0
\end{pmatrix}
\]  

(2.70)

By applying the criteria in equation (2.67), the first two terms on the right hand side of equation (2.70) are the extensional modes, and the last term is the rotational mode.
To study the flow type for this general mixed flow, we need to find the two eigenvalues for tensor $\nabla \mathbf{u}$. There are three different cases:

(1) two eigenvalues are $\lambda_1 = -\lambda_2 = \sqrt{a^2 + bc}$ if $a^2 + bc > 0$; which means that we have two real eigenvalues: one is positive, the other is negative. Thus we can have a coordinate transformation

$$\begin{pmatrix} x \\ y \end{pmatrix} = M^T \begin{pmatrix} \bar{x} \\ \bar{y} \end{pmatrix},$$

where $M$ is a positive-definite transformation matrix satisfies $MA M^T = I$, where $I$ is the unit matrix. In a new coordinate system $(\bar{x}, \bar{y})^T$ (it might not be an orthogonal coordinates), we can change equation (2.69) to

$$\begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = \begin{pmatrix} \lambda_1 & 0 \\ 0 & \lambda_2 \end{pmatrix} \begin{pmatrix} \bar{x} \\ \bar{y} \end{pmatrix}$$

which means we have an extensional flow in this new coordinate. But considering the new coordinate might not be the orthogonal coordinates, the flow might not be pure extension in the original coordinates, but it is definitely an extension-dominated mixed flow.

(2) two real eigenvalues are equal, $\lambda_1 = \lambda_2 = 0$ if $a^2 + bc = 0$; By doing the same process as (1), we will have

$$\begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = \begin{pmatrix} p & 0 \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \bar{x} \\ \bar{y} \end{pmatrix}$$

which means that in this coordinates, the flow is a simple shear flow.

(3) two eigenvalues are complex numbers, $\lambda_1 = -\lambda_2 = \sqrt{- (a^2 + bc)} I$ if $a^2 + bc < 0$, where $I = \sqrt{-1}$ is the imaginary unit. Also we will have
\[
\begin{pmatrix}
\frac{d\tilde{x}}{dt} \\
\frac{d\tilde{y}}{dt}
\end{pmatrix} = \begin{pmatrix}
0 & \sqrt{-a^2 + bc} \\
-\sqrt{-a^2 + bc} & 0
\end{pmatrix} \begin{pmatrix}
\tilde{x} \\
\tilde{y}
\end{pmatrix}
\]

(2.73)

which means that we have a pure rotational flow in the new coordinates (orthogonal or not), thus a pure rotation or rotation-dominated mixed flow in the original coordinate system. Thus by analyzing the value of \(a^2 + bc\), we can determine the flow types. Also from equation (2.67), we can get the flow type parameter

\[
\Lambda = \frac{a^2 + bc}{(\sqrt{a^2 + (b + c)^2} / 4 + \sqrt{(b - c)^2} / 4)^2}
\]

(2.74)

which also means that the value of \(a^2 + bc\) determines the flow types.

Figure 2.19: Responses of an initially square-shaped object under different velocity gradient tensor.
Suppose we have a lot of tiny tracer particles (different from the surrounding fluid only by their color) and initially they form a square-shaped object. We can show how this object responds under different velocity gradients. Since each tracer particle moves at the same velocity (which is only location dependent) as the surrounding fluid, its location at time $t$ could be obtained by solving the equations as follows:

$$\frac{dx}{dt} = ax + by \quad \text{and} \quad \frac{dy}{dt} = cx - ay \quad (2.75)$$

with the initial location at $x(0) = x_0$ and $y(0) = y_0$. According to the Lagrangian theorem, the tracer particles will still form an object, not two separated objects (topologically, it should be homeomorphic as the initial square-shaped object), but its shape might not be the square-shaped any more. In Figure 2.19, one can see different response of an initially square-shaped object to different velocity gradient tensor $A = \nabla u$.

For $A = \begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}$, $A = \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$, and $A = \begin{pmatrix} -1 & 0 \\ 0 & 1 \end{pmatrix}$, the square-shaped object will be stretched along its diagonal, the $x$-axis and the $y$-axis, respectively. The stretching of DNA molecule along the $y$-axis in experiments of Perkins et al. [Perkins97] is exactly what we see in the third row of Figure 2.18 under the velocity gradient $A = \begin{pmatrix} -1 & 0 \\ 0 & 1 \end{pmatrix}$.

While for $A = \begin{pmatrix} 0 & 1 \\ -1 & 0 \end{pmatrix}$, it will rotate with respect to its center. For the shear mode, $A = \begin{pmatrix} 0 & 1 \\ 0 & 0 \end{pmatrix}$, the square-shaped object becomes deformed along $x$-axis. That is also the reason why the DNA molecule will be stretched along the $x$-axis at first. When the DNA becomes aligned, the hydrodynamic drag (due to the velocity gradient) decreases and the
chain may begin to relax. If we further consider the Brownian motion, which can change the orientation of a stretched chain, the DNA chain either continues to stretch or becomes unstable and tumbles end-over-end, which is exactly what happens in [SmithD99].

Figure 2.20: Response of an initially square-shaped object to a mixed flow with velocity gradient (a) \(A = \begin{pmatrix} 1 & 2 \\ -1 & -1 \end{pmatrix}\) and (b) \(A = \begin{pmatrix} 1 & 2 \\ 1 & -1 \end{pmatrix}\).
In a general 2D mixed flow $A = \begin{pmatrix} a & b \\ c & -a \end{pmatrix}$, we are supposed to see the combination of the above responses.

For example, if $A = \begin{pmatrix} 1 & 2 \\ -1 & -1 \end{pmatrix} = \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} + \begin{pmatrix} 0 & 1 \\ -1 & 0 \end{pmatrix} + \begin{pmatrix} 0 & 1 \\ 0 & 0 \end{pmatrix}$, the combination of one pure extension, one pure rotation, and one simple shear, the response of an initially square-shaped object is shown in Figure 2.20(a). We can see that this object is stretched along one direction (this direction will change with time) and compressed along another direction, and at the same time it rotates with respect to its center point (0, 0). While if $A = \begin{pmatrix} 1 & 2 \\ 1 & -1 \end{pmatrix} = \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} + \begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix} + \begin{pmatrix} 0 & 1 \\ 0 & 0 \end{pmatrix}$, the combination of two pure extensions and one simple shear, the response of an initially square-shaped object is shown in Figure 2.20(b). We can see that now the object will be stretched along one direction and compressed along another direction, and at the same time it is sheared along the x-axis on the whole.

For the general 3D mixed flow, we can still use the same method to study the behavior of an initially square-shaped object under different velocity gradient. But this analysis can only partially explain the behavior of a flexible long chain polymer in the flow. One example is that it can’t explain the “coil-stretch-recoil” behavior of DNA molecules in the pure shear flow because we do not consider the Brownian force. Thus we still need to use the Brownian dynamics simulation method to fully explore the dynamics of the single long chain polymer in the arbitrary flow field.

The quantitative comparisons between the simulation and experiment such as the stretching length vs. the flow Deborah number (or strain) are only workable for the
simple flows such as the pure extensional and the simple shear flows because in these flows, the velocity gradient is constant in the whole flow domain. For an arbitrary flow, there is no such area where the velocity gradient is constant and the velocity gradient is not constant at all even along one single streamline.
CHAPTER 3

SIMULATION OF ELECTROKINETIC FLOWS

Electrokinetic phenomena have been well-known for nearly 200 years since the first paper by F. F. Reuss in 1809, who described the observations in his experiments on the electroosmosis and electrophoresis [Reuss09] in the porous media. Electrokinetic flows have been used for many applications, especially in micro/nanofluidics as mentioned in Chapter 1 because electrokinetic forces have more flexibility and are more powerful than the hydrodynamic forces. In this chapter, we will discuss different types of electrokinetic forces (i.e., electroosmotic, electrophoretic, and dielectrophoretic forces) and focus on how to simulate the electrokinetic flows in micro/nanofluidics. Also the effect of electrokinetic interactions to the movement of charged particles and how to “avoid” these interactions in the micro/nanofluidics will be elaborated in this chapter.

3.1 Electroosmosis

Electroosmotic flow (EOF) is the fluid movement relative to the stationary solid wall [Shaw92]. When a neutral object (such as silicon, glass, PMMA solid plate, and etc.) immerses into the aqueous solution at a certain pH value and ion strength, the surface molecules will take the H⁺ or OH⁻ ions from the solution, making its surface to be positively or negatively charged. Of course, now the aqueous solution is not neutral at all
due to the lose of $\text{H}^+$ or $\text{OH}^-$ ions. The concentration of the counterions in solution is higher than that of the coins. As shown in Figure 3.1, the charged surface wall will attract the counterions from the solution to form an immobilized ion layer called the “stern” layer. At the same time, an outer layer of distributed ions is created, just like the boundary layer in hydrodynamic flows; this layer is called the “diffusion” layer. The combination of the stern layer and diffusion layer is called electrical double layer (EDL) [Probstein94, Karniadakis02]. In experiment, the potential measured on the wall using the streaming potential measurement method or particle electrophoresis method, in fact, is the potential on a so-called “shear” layer (or shear plane) where ions start to move freely. The measured potential is called the zeta potential and denoted as $\zeta$.

Figure 3.1: Schematic of electrical double layer.
Figure 3.2 shows that how an electroosmotic flow is created in a microchannel with the wall surface negatively charged. Under the external electric field, the movement of counterions (now is the positive ions) and coions (the negative ions) in EDL will drag the water molecules (the neutral particle) to move. Since the concentration of counterions is higher than that of coions in the ionized solution, the overall driving force points to the movement of counterions, thus the fluid has the same flow direction as the movement of counterions [Probstein94, Karniadakis02].

![Diagram showing electroosmotic flow](image)

**Figure 3.2: Mechanism of the electroosmotic flow.**

### 3.1.1 Governing Equations

The distribution of ions in solution is very important and it determines the flow profile in micro/nanofluidics. There are two types of governing equations to describe the ion distribution in solution.
The first type of the governing equations is called the Poisson-Nernst-Planck (P-N-P) equations [Probstein94, Yang01b, Li04] given as follows:

\[ \nabla^2 \Psi = -\frac{1}{\varepsilon} \rho_e - \frac{1}{\varepsilon} \sum z_i e n_i \]  \hspace{1cm} (3.1)

\[ \frac{\partial n_i}{\partial t} = -\nabla \cdot \mathbf{J}_i \] \hspace{1cm} (3.2)

where \( \Psi \) is the total electric potential in the aquatic solution, \( \varepsilon \) is the permittivity of the media, \( \rho_e \) is the net charge density, which is the summation of all different ion species; \( z_i \) is the valence for species \( i \), and \( e \) is the electronic charge. For ion species \( i \), its concentration \( n_i \) obeys the convection-diffusion equation (3.2), where the ion flux for species \( i \) is [Cummings03]:

\[ \mathbf{J}_i = -D_i \nabla n_i + n_i (\mathbf{u} - \mathbf{\mu}_{EP} \mathbf{E} + \mathbf{\mu}_{DEP} \nabla (\mathbf{E} \cdot \mathbf{E})) \] \hspace{1cm} (3.3)

which includes two effects — diffusion and convection. The diffusion effect comes from the term \(-D_i \nabla n_i\), while the convection effect is \( n_i \mathbf{u}_{total} \), where \( \mathbf{u}_{total} \) is the total velocity. From equation (3.3), the total velocity has three contributions from (1) the flow velocity (including EOF velocity) \( \mathbf{u} \), (2) the electrophoretic (EP) velocity (more details on EP velocity will be given in the next section) \( \mathbf{\mu}_{EP} \mathbf{E} \), where \( \mathbf{\mu}_{EP} = q_i / \xi_i \) is the EP mobility and \( \mathbf{E} = -\nabla \Psi \) is the electric field, and (3) the dielectrophoretic (DEP) velocity \( \mathbf{\mu}_{DEP} \nabla (\mathbf{E} \cdot \mathbf{E}) \) (see [Cummings03]), where \( \mathbf{\mu}_{DEP} \) is the DEP mobility and we will give its expression later in this chapter. From the Stokes-Einstein equation \( \xi_i = \frac{k_B T}{D_i} \), we have \( \mathbf{\mu}_{EP} = q_i / \xi_i = D_i z_i e / (k_B T) \). Thus, the ion flux for species \( i \) could be rewritten as
When the flow is weak \((\mathbf{u} \approx 0)\), in the steady state \((\frac{\partial}{\partial t} = 0)\), and the dielectrophoretic effect is neglected, we know from equations (3.2) and (3.4) that

\[
\nabla \cdot \mathbf{J}_i = \nabla \cdot \left(D_i \nabla n_i + \frac{z_i e}{k_B T} D_i n_i \nabla \Psi\right) = 0,
\]

or \(\mathbf{J}_i \equiv \) constant in the whole domain. Since we have the impermeable condition \(\mathbf{n} \cdot \mathbf{J}_i = 0\) on the wall (where \(\mathbf{n}\) is the outer normal of the wall surface), we have \(\mathbf{J}_i \equiv 0\) on the wall and in the whole domain considering an arbitrary domain with its outer normal direction is changeable. So we have the second type of the governing equation

\[
\nabla n_i + \frac{z_i e}{k_B T} n_i \nabla \Psi = 0,
\]

or equivalently, the ion distribution satisfies the Boltzmann distribution:

\[
n_i = n_{i,0} \exp\left(-\frac{z_i e}{k_B T} \Psi\right)
\]  

(3.5)

where \(n_{i,0}\) is the bulk concentration for species \(i\). [Li04] has the similar conclusion, but without deduction.

The combination of equations (3.1) and (3.5) is called the Poisson-Boltzmann (P-B) equations [Probstein94, Yang01a, KimM02, Karniadakis02, Li04]. They are the second type of the governing equations in the electroosmotic flow simulation. Usually for different ion species, their valence and bulk concentration are different. But in this dissertation, for simplicity, we only consider two ions with equal but opposite charge in the solution and assume that their bulk concentrations are the same \(n_0\), so
\[ \nabla^2 \psi = \frac{2n_i ze}{\varepsilon} \sinh\left(\frac{ze}{k_B T}\psi\right) \quad (3.6) \]

Of course, to get the fluid velocity profile, we need to solve the modified Navier-Stokes equation, which considers the contribution from the ion movement:

\[ \rho \left( \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = -\nabla p + \eta \nabla^2 \mathbf{u} - \rho_e \nabla \psi \quad (3.7) \]

where \( \mathbf{u} \) is the EOF velocity, \( p \) is the pressure, \( \rho \) and \( \eta \) are the density and viscosity of the fluid.

Currently, we just study the Poisson-Boltzmann equations in this chapter. In equation (3.6), we decompose the total electric potential \( \Psi \) into two parts: \( \Psi = \psi + \phi \), where \( \psi \) is the electric potential associated with the surface zeta potential (we might call it the internal potential), while \( \phi \) is the external potential associated with the external electric field \( \mathbf{E} = -\nabla \phi \). Thus we have the following equations:

\[ \nabla^2 \psi = -\frac{1}{\varepsilon} \rho_e = \frac{2n_i ze}{\varepsilon} \sinh\left(\frac{ze}{k_B T}\psi\right) \quad (3.8) \]

\[ \nabla^2 \phi = 0 \quad (3.9) \]

In the following pages, we will use finite element method (FEM) to discretize the governing equations. To better capture the properties of EOF, we introduce the non-dimensionalized equations as follows:

\[ \text{Re}\left( \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = -\nabla p + \nabla^2 \mathbf{u} + \beta \sinh(\alpha \psi) \nabla \phi \quad (3.10) \]

\[ \nabla^2 \psi = \beta \sinh(\alpha \psi) \quad (3.11) \]

\[ \nabla^2 \phi = 0 \quad (3.12) \]
where \( \text{Re} = \rho Ud / \eta \) is the Reynolds number, \( U = \mu_{\text{EO}} E_c \) is the characteristic electroosmotic velocity, \( \mu_{\text{EO}} = \varepsilon \zeta / \eta \) is the electroosmotic mobility. \( D \) is the characteristic length, \( \alpha = z e \zeta / k_B T \) and \( \beta = 2n_0 z e D^2 / \varepsilon \zeta \) are two parameters associated with the surface zeta potential \( \zeta \) and the bulk ion concentration \( n_0 \) in the solution, respectively. The square root of the product of \( \alpha \) and \( \beta \) is given as

\[
K = \sqrt{\alpha \beta} = \sqrt{\frac{2n_0 z^2 e^2 \varepsilon}{k_B T \varepsilon}} D = D / \lambda_D, \text{ which may be thought as the ratio of characteristic length (usually it is the half of the channel width) to the Debye length } \lambda_D = \sqrt{\frac{\varepsilon k_B T \varepsilon}{2n_0 z^2 e^2}} ,
\]

the characteristic thickness of EDL [Probstein94].

When \( \alpha \psi \) is small enough, we will have \( \sinh(\alpha \psi) \approx \alpha \psi \), thus equation (3.11) could be approximated as [Yang01a]

\[
\nabla^2 \psi = \alpha \beta \psi = K^2 \psi
\]

but be aware that we won’t have such simple equation for all the EOF.

### 3.1.2 EOF in a Straight 2D Channel

In this subsection, we will study the EOF in a straight 2D channel analytically, which will be used for comparison with the numerical simulation. For this type of electroosmotic flow with small Reynolds number (\( \text{Re} \approx 0 \)) and a little pressure drop (\( p \approx 0 \)), we have the analytical solution for equations (3.10), (3.12), and (3.13). Since different channel surface can carry different charges (either density or polarity) in microfluidics, we consider a general situation as shown in Figure 3.3.
The boundary condition (in dimensionless form) is given as follows:

\[
\begin{align*}
\psi &= -1, \quad y = 1 \\
\psi &= m, \quad y = -1 \\
u &= 0, \quad y = 1 \\
u &= 0, \quad y = -1
\end{align*}
\] (3.14)

Figure 3.3: Schematic for the EOF in a 2D channel with an arbitrary value of the surface zeta potential m on the lower plate.

The exact solution for equation (3.13) can be written as \(\psi = ae^{ky} + be^{-ky}\). Using the boundary conditions in equation (3.14), we get

\[
a = \frac{-e^{k} - me^{-k}}{e^{2k} - e^{-2k}} \quad \quad b = \frac{me^{k} + e^{-k}}{e^{2k} - e^{-2k}}
\] (3.15)

It is clear to see the velocity profile satisfies \(u = u(y), \quad v = 0\), where \(u\) and \(v\) are the x-component and y-component of the velocity vector \(\mathbf{u}\). Thus the momentum equation (3.10) is reduced to

\[
\frac{\partial^2 u}{\partial y^2} + K^2 \psi \nabla \phi = \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 \psi}{\partial y^2} \nabla \phi = 0
\] (3.16)
Since $\nabla \phi$ is constant, we have $u = cy + d - \psi \nabla \phi$. Considering boundary conditions in equation (3.14), we have $c = -\frac{m+1}{2} \nabla \phi$, and $d = \frac{m-1}{2} \nabla \phi$. Thus $x$-direction velocity is $u = (-\frac{m+1}{2}y + \frac{m-1}{2} - \psi) \nabla \phi$.

For simplicity, we can let $\nabla \phi = -1$, thus $u = cy + d + \psi$. If $K = 10$, we have the Figure 3.4 showing the velocity profile for different value of $m$.

![Figure 3.4: EOF velocity profile for different value of $m$.](image)

Since the upper plate is negatively charged ($\psi = -1$), from Figure 3.4, we know that when the lower plate is also negatively charged (i.e., $m < 0$), the velocity profile is
always positive (i.e., the flow is in the same direction of $x$ axis). While if the lower plate is positively charged (i.e., $m > 0$), part of the velocity profile (close to the lower plate) is negative (the flow near the lower plate is just opposite to the $x$ axis) and the flow near the upper plate is still in the same direction of $x$ axis. Thus in such case, we have a bidirectional flow in one straight channel, forming a shear layer in the center domain of the channel. In fact, from the velocity profile, $u = cy + d - \psi \nabla \phi$, since $\psi$ is small in the bulk area, there is always a shear layer when the $y$-location is always from the upper and lower plates. Through the shear rate $c = \frac{m+1}{2}$, we can get $m = 2c - 1$, which indicates that we can obtain the zeta potential $m$ of one plate if we know the zeta potential for the other plate (here we non-dimensionalize it to $-1$ for negatively charged surface) and the shear rate $c$ of the shear layer (can be measured from the velocity profile by PIV, etc.).

Currently, the working solution in the electroosmotic flow is assumed to be a Newtonian fluid. We might find another important application: that is, using EOF to drive the Non-Newtonian fluid. Here, we use the Oldroyd-B fluid as an example to study the effect of EOF to the polymer stresses, which is given by the constitutive equation as follows [Hulsen97]:

$$T_p + Wi T_p^{(1)} = (1 - \beta_v) [\nabla u + (\nabla u)^T]$$

(3.17)

where $T_p^{(1)} = \frac{\partial T_p}{\partial t} + u \cdot \nabla T_p - (\nabla u)^T \cdot T_p - T_p \cdot \nabla u$ is the upper Maxwell operator, $Wi = \lambda_\eta U / D$ is the Weissenberg number, $\lambda_\eta$ is the relaxation time for the spring,
\( \beta_v = \frac{\eta_s}{\eta_0} \) is the viscosity ratio, here \( \eta_s \) is the solvent viscosity and \( \eta_0 \) is zero-shear-rate total viscosity of the fluid. Of course, we need to consider the momentum equation:

\[
\text{Re}(\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u}) = -\nabla p + \nabla \cdot \mathbf{T}_p + \nabla \cdot \beta_v (\nabla \mathbf{u} + (\nabla \mathbf{u})^T) + \alpha \beta \psi \nabla \phi \quad (3.18)
\]

Usually, we don’t have the analytical solution for such complicated constitution equation (3.17) and momentum equation (3.18) in arbitrary geometry. But for a steady state \(( \frac{\partial }{\partial t} = 0)\) and well-developed \(( \frac{\partial }{\partial x} = 0)\) flow in a straight 2D channel with a low Reynolds number \(( \text{Re} \approx 0)\) and low pressure drop \(( \text{p} \approx 0)\), we can still have the exact solution.

Since we still have \( u = u(y) \) and \( v = 0 \), thus the components of the stress tensor in equation (3.17) can be simplified as follows:

\[
T_{p11} - 2Wi \frac{du}{dy} T_{p12} = 0 \quad (3.19)
\]

\[
T_{p12} - Wi \frac{du}{dy} T_{p22} = (1 - \beta_v) \frac{du}{dy} \quad (3.20)
\]

\[
T_{p22} = 0 \quad (3.21)
\]

Here, we will have \( T_{p11} = 2Wi(1 - \beta_v) \left( \frac{du}{dy} \right)^2 \), \( T_{p12} = (1 - \beta_v) \frac{du}{dy} \), and \( T_{p22} = 0 \). The result has nothing to do with the surface charge polarity and density.

If we reconsider the problem in Figure 3.3 with the same boundary conditions, we will have the same velocity profile as before because equation (3.18) is the same as equation (3.16) if we place equations (3.19–21) into equation (3.18) \(( \nabla \cdot \mathbf{T}_p = 0)\). Also
the electric potential $\psi$ has the same expression. So we still have

$$u = (-\frac{m+1}{2} y + \frac{m-1}{2} - \psi) \nabla \phi, \text{ and } \psi = a e^{k_y} + b e^{-k_y}.$$

From the velocity profile, we can calculate the polymer stress tensor. Suppose $\beta_e = 0.9, \, Wi = 9, \, K = 10, \, \text{ and } \nabla \phi = -1$, then we will have the profiles of the components of stress tensor along the width of the channel in Figure 3.5(a) and (b).

The results indicate that the magnitude of the polymer stresses is very high near the wall surface with a viscoelastic fluid due to the high velocity gradient of the velocity profile. But be aware that the variables are in the dimensionless form. To drive the viscoelastic fluid, we still need a very high external potential drop because the zero-shear-rate total viscosity might be very high.
Figure 3.5: Distribution of the polymer stress component (a) $T_{p11}$ and (b) $T_{p12}$ of the EOF driven Oldroyd-B fluid flow in a 2D straight channel.
3.2 Electrophoresis

Electrophoresis (EP) is the movement of charged particles relative to the stationary solution [Shaw92]. Since a charged particle forms an electric double layer around its surface, the drag force coming from the moving ions in the EDL will affect the movement of charged particles. Thus the relative size and shape of the EDL is important to determine the particle EP velocity. Usually, the symmetry of the EDL will be distorted and its shape is more like an ellipsoid under the external electric field. But for simplicity, we assume that the distortion is small and the shape of the EDL is still a sphere.

We consider the following two cases regarding the relative ratio of the characteristic EDL thickness $\lambda_D$ and size of the particle $r$ [Probstein94]:

![Diagram](image)

Figure 3.6: (a) Particle size is much less than the EDL thickness $r/\lambda_D << 1$; (b) Particle size is much larger than the EDL thickness $r/\lambda_D >> 1$. 
(1) The first case is that the electrical double layer is much thicker than the particle size $r/\lambda_p \ll 1$ as shown in Figure 3.6(a), which means the particle can move freely as if it is not attached with the surrounding ions (except the ions in the stern layer, which is not drawn in the figure). Considering the equation for the movement of this particle-ion group, which is similar to equation (2.18) in Chapter 2, but now we only have the drag force, electrophoretic force and the Brownian force on the right hand side of the equation, we have

$$m \frac{d^2 \mathbf{r}}{dt^2} = -\xi \left( \frac{d\mathbf{r}}{dt} - \mathbf{u} + \mathbf{u}' \right) + q \mathbf{E} + \mathbf{F}^{Brownian} \tag{3.22}$$

Since the particle’s mass is usually negligible in equation (3.22), if the drag coefficient $\xi$ is divided on both sides of equation (3.22), we have

$$\frac{d\mathbf{r}}{dt} = \mathbf{u} + \mathbf{u}' + \frac{q}{\xi} \mathbf{E} + \frac{1}{\xi} \mathbf{F}^{Brownian} \tag{3.23}$$

which implies that the third term on the right hand side of equation (3.23) has the same dimension as the velocity. Since this velocity is driven by the electrophoretic force (electric field), we can write it as $\mathbf{u}_{\text{ep}} = \frac{q}{\xi} \mathbf{E}$.

(2) The second case is that the electrical double layer is much thinner than the particle size $r/\lambda_p \gg 1$ shown in Figure 3.6(b), which means the particle moves together with the most surrounding ions. In this case, the charged particle and the surrounding ions form a whole group, which can be seen as a larger charged particle. The reason why we cannot directly use equation (3.23) is that now the measured charge density $q$ is the overall charge density of this particle-ion group. To calculate the electrophoretic velocity
of the charged particle $\mathbf{u}_{EP}$, we can set a coordinate system (reference frame) on the charged particle. Thus the velocity of the fluid outside the particle-ion group is $-\mathbf{u}_{EP}$.

According to [Probststein94], since in this case the thickness of the EDL is small compared with the radius of the particle, we don’t need to consider the geometry of the EDL. Also the particle outer surface is as large as an infinite plate for the ions in the EDL. Thus, based on the reference frame of the charged particle, the fluid flow is just like that driven by the electroosmosis. Thus we have $-\mathbf{u}_{EP} = U_{EO} = \mu_{EO}^{p} E = \frac{\varepsilon \zeta_{p}}{\eta} E$, or $\mathbf{u}_{EP} = -\frac{\varepsilon \zeta_{p}}{\eta} E$, where $\zeta_{p}$ is the zeta potential of the charged particle.

In both cases, we have the EP velocity proportional to the external electric field. Of course, we haven’t considered the intermediate case $r/\lambda_{D} \sim 1$ yet, but we can make the same conclusion (probably by using the asymptotic method or just by the extrapolation), that is, $\mathbf{u}_{EP} = \mu_{EP} E$, where $\mu_{EP}$ is called the electrophoretic mobility.

### 3.3 Dielectrophoresis

There are two types of external electric field – the direct current (DC) field and the alternating current (AC) field. In a DC electric field, if a particle in the aqueous solution carries the net surface charge, it moves to the electrode under the electrophoretic force. At the same time, it attracts ions to form an electrical double layer and usually the symmetry of this EDL will be distorted by the external electric field. Also due to the discrepancy in the electrical properties between the particle and the surrounding aqueous solution, the external electric field induces electrical charges to appear at the boundary of the outer surface of the particle [Maxwell91, Wagner14], making the induced dipole
moment to be the maximum, which is shown in Figure 3.7. This phenomenon is called
the Maxwell-Wagner interfacial polarization [Maxwell91, Wagner14]. Be aware that this
polarization doesn’t require the particle to be charged, and it happens for particles
without net charges.

![Figure 3.7: Maxwell-Wagner interfacial polarization.](image)

When the external DC field is replaced by an AC field with a very high frequency
(>50 kHz), the electrophoretic effect and the distortion of the EDL become negligible
because of the inertia effect of the particle and counter-ion atmosphere [Chou02].
Nevertheless, the dipole moments associated with the Maxwell-Wagner interfacial
polarization still exist. That is the reason why the dielectrophoresis can be used to control
the movement of particles in the AC field and it does not require the particle to carry any
net electrical charge (although the purely neutral object in the aqueous solution does not
exist at all).
Because of the limited space in the dissertation, we only consider the DC dielectrophoresis although the AC dielectrophoresis is very important. The readers can find more information on the AC dielectrophoresis from the literature [Goater98, HughesM00, HughesM02].

Let us get the expression of the dielectrophoretic force. For an infinitesimal particle, the induced dipole can be simplified as two equal but opposite point charges (with charge density $q$) as shown in Figure 3.8 [Jones95].

For a non-uniform electric field, the electric force by an induced dipole on the particle can be written as:

$$F^{\text{Dipole}} = qE(r + d) - qE(r) = qd \cdot \nabla E + O(d^2)$$  \hspace{1cm} (3.24)
As the distance vector approaches zero, \( d \to 0 \), we can neglect the higher order terms associated with the quadrupole, octopole and higher multipolar moments. If the dipolar moment \( \mathbf{p} = q \mathbf{d} \) keeps its magnitude, equation (3.24) can be simplified as

\[
\mathbf{F}^{\text{Dipole}} = \mathbf{F}^{\text{DEP}} = \mathbf{p} \cdot \nabla \mathbf{E}
\]  

(3.25)

Using the same approach, we have the torque on this dipole as follows:

\[
\mathbf{M}^{\text{Dipole}} = \mathbf{M}^{\text{DEP}} = \frac{d}{2} \times q \mathbf{E}(\mathbf{r} + \mathbf{d}) - \frac{d}{2} \times (-q \mathbf{E}(\mathbf{r})) = q \mathbf{d} \times \mathbf{E} + O(d^2) \approx \mathbf{p} \times \mathbf{E}
\]  

(3.26)

According to [Griffiths99], the induced dipolar moment is a linear function of the electric field: \( \mathbf{p} = \alpha_D \mathbf{E} \), where \( \alpha_D \) is the electric susceptibility of the medium. Thus,

\[
\mathbf{F}^{\text{DEP}} = \frac{\alpha_D}{2} \nabla(\mathbf{E} \cdot \mathbf{E}) \quad \text{and} \quad \mathbf{M}^{\text{DEP}} = 0
\]  

(3.27)

for an infinitesimal particle (we will discuss the real particle with a finite size later).

For a particle in a DC field, it can be proved that the induce dipole \( \mathbf{p} \) is [Jones95]

\[
\mathbf{p} = 3V \varepsilon_m K(\varepsilon_m, \varepsilon_p) \mathbf{E} = 3V \varepsilon_m \frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m} \mathbf{E}
\]  

(3.28)

where \( \varepsilon_m, \varepsilon_p \) are the permittivity of the media and the particle, respectively. \( V \) is the volume of the particle, \( K(\varepsilon_m, \varepsilon_p) = \frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m} \) is the so-called the Clausius-Mossotti factor [Pohl78, Jones95]. Thus the dielectrophoretic force in equation (3.25) can be written as

\[
\mathbf{F}^{\text{DEP}} = \frac{1}{2} V \varepsilon_m \frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m} \nabla(\mathbf{E} \cdot \mathbf{E})
\]  

(3.29)

If the particle is in an AC field, the permittivity is a complex number, and the Clausius-Mossotti factor takes its real part \( K(\varepsilon_m, \varepsilon_p) = \Re \left\{ \frac{\varepsilon_p - \varepsilon_m}{\varepsilon_p + 2\varepsilon_m} \right\} \).
From the sign of Clausius-Mossotti factor $K(\varepsilon_m, \varepsilon_p)$, we can classify two kinds of dielectrophoresis: negative (if $\varepsilon_p < \varepsilon_m$) and positive (if $\varepsilon_p > \varepsilon_m$) dielectrophoresis.

We can get the DEP mobility of particle by using the equation of the particle movement (similar one has been given in equation (3.23))

$$m \frac{d^2 \mathbf{r}}{dt^2} = -\xi \left( \frac{d\mathbf{r}}{dt} - \mathbf{u} - \mathbf{u}' \right) + \mathbf{F}^{EP} + \mathbf{F}^{Brown} + \frac{1}{2} \alpha D \nabla (\mathbf{E} \cdot \mathbf{E}) \tag{3.30}$$

then the DEP mobility is $\mu_{DEP} = \alpha_D / 2 \xi$ and now we complete the expression in equation (3.3).

The conventional dielectrophoretic devices can obtain the high electric field gradient by moving two electrodes close. The so-called “electrodeless DEP” has been studied only recently. The electrodeless DEP uses “a constriction or channel in an insulating material instead of a metallic wire to squeeze the electric field in a conducting solution” [Chou02]. Cummings et al. [Cummings03] used the lithography technique to fabricate all kinds of microfluidic devices to generate this kind of DEP and use it to trap particles.

Generally speaking, equation (3.27) only considers the second-order approximation (usually, this is called the point dipole (PD) model), thus it neglects the size of the particle, which is a very important parameter in the real applications. To include the size effect to the dielectrophoresis, we need to integrate the so-called Maxwell’s stress tensor [Griffiths99] on the particle surface to get the dielectrophoretic force and torque. Here we only give the expression for the Maxwell’s stress tensor $\mathbf{\sigma}_M$

$$\mathbf{\sigma}_M = \varepsilon (\mathbf{EE} - \frac{1}{2} (\mathbf{E} \cdot \mathbf{E}) \mathbf{I}) + \frac{1}{\mu_B} (\mathbf{BB} - \frac{1}{2} (\mathbf{B} \cdot \mathbf{B}) \mathbf{I}) \tag{3.31}$$
We don’t consider the magnetic field \((\mathbf{B} \equiv 0)\) in this dissertation, thus equation (3.31) is reduced to \(\sigma_M = \varepsilon(EE - \frac{1}{2}(E \cdot E)I)\) and DEP force is

\[
\mathbf{F}^{DEP} = \oint_S \mathbf{n} \cdot \mathbf{\sigma}_M \, ds = \oint_S \mathbf{n} \cdot \varepsilon(EE - \frac{1}{2}(E \cdot E)I) \, ds
\]  

(3.32)

Singh and Aubry [Singh05] have demonstrated in studying the DEP force on a finite-sized particle in a DEP cage that when the ratio of the particle size to the characteristic length of the geometry \(\chi\) is less than 0.1, the dielectrophoretic forces obtained by using equations (3.29) and (3.32) don’t have much difference, but when \(\chi > 0.25\), the relative error is larger than 30%. Thus the DEP force could not be correctly predicted by the PD model when the size of the particle is comparable with the size of the geometry.

3.4 Simulation Process Using the Finite Element Method

Finite element method (FEM) is a very powerful and robust tool for the calculation of the electric and flow fields in electrokinetics.

The essential idea of FEM is to use the weighted residual method to get an approximate solution (high accuracy can be achieved by selecting a better trial function). Different from the finite difference method (FDM), which is the pointwise method to discretize the governing equations on the nodal point level, the finite element method is, in fact, a piecewise method. First it discretizes the whole domain into small elements, such as 2D triangular, 2D quadrilateral, 3D brick elements. Then on each element, it uses the variational method (or weak form in the integral from) in functional analysis to get the discretized equation groups.
FEM has been widely used in different areas such as the solid mechanics, fluid dynamics, heat transfer and mass transportation, etc. To find more details on the FEM and its applications in different problems, please refer to [HughesT87, Bathe96, Heinrich99, Reddy01, Chandrupatla02].

We now use the FEM to solve the Navier-Stokes (N-S) and the Poisson-Boltzmann (P-B) equations (3.10)–(3.12).

These governing equations should be satisfied for any variation of the unknowns in the integral form based on the element level. If \((\delta u, \delta p, \delta \psi, \delta \phi)\) are the variations for velocity, pressure, the internal potential, and the external potential, respectively, then we will have

\[
\int_{\Omega_e} \delta u \cdot \text{Re}(\frac{\partial u}{\partial t} + u \cdot \nabla u) d\Omega = \int_{\Omega_e} \delta u \cdot \{-\nabla p + \nabla^2 u + \beta \sinh(\alpha \psi) \nabla \phi\} d\Omega \\
\int_{\Omega_e} \delta p \nabla \cdot \mathbf{u} d\Omega = 0 \\
\int_{\Omega_e} \delta \psi \nabla^2 \psi d\Omega = \int_{\Omega_e} \delta \psi \beta \sinh(\alpha \psi) d\Omega \\
\int_{\Omega_e} \delta \phi \nabla^2 \phi d\Omega = 0
\]

where \(\Omega_e\) is the element volume (or surface in 2D case).

In this dissertation, we only consider the simulation in 2D case. The whole field domain was first discretized by different elements (usually each element has the same number of nodal points). On each element, we can set up a local coordinates \((\xi_1, \xi_2)\). And we use the interpolation method to get the function value at any point inside the element if we know the values of a function (or variable) at the nodal points. For example,
the velocity field can be written as \( \mathbf{u} = \sum_{i} N_i(\xi_1, \xi_2) \mathbf{u}_i \), where \( N_i(\xi_1, \xi_2) \) is called the shape function. In the conventional Galerkin FEM, the shape function for the variation of a variable is the same as that of the variable itself. But sometimes we need to use a different shape function for the variation of the variable. This approach is called the Petrov-Galerkin interpolation and we will discuss it later.

Since the P-B equation is decoupled from the N-S equation, we can solve the P-B equation first to get the values for \( \psi \) and \( \phi \), then put these known values into N-S equation to solve the electroosmotic velocity \( \mathbf{u} \). Let \( \delta \psi = \sum_i N_i \delta \psi_i \), we can rewritten equation (3.35) into

\[
\delta \psi_i \left( \int_{\Omega} N_i \nabla^2 \psi \, d\Omega - \int_{\Omega} N_i \beta \sinh(\alpha \psi) \, d\Omega \right) = 0
\]  

where the Einstein notation for summation is used.

Since equation (3.37) should be satisfied for any possible value of \( \delta \psi_i \), then the weak form for the P-B equation is given as follows:

\[
\int_{\Omega} N_i \nabla^2 \psi \, d\Omega = \int_{\Omega} N_i \beta \sinh(\alpha \psi) \, d\Omega
\]  

which can be further written as

\[
\int_{\Omega} \nabla N_i \cdot \nabla \psi \, d\Omega + \int_{\Omega} N_i \beta \sinh(\alpha \psi) \, d\Omega = \int_{\Gamma_e} N_i \mathbf{n} \cdot \nabla \psi \, d\Gamma = 0
\]  

where \( \Gamma_e \) is the boundary of the domain and the Neumann condition \( \mathbf{n} \cdot \nabla \psi = 0 \) has been considered on the boundary where the Dirichlet condition has not specified.
Equation (3.39) is in the nonlinear form, we use the Newton-Raphson iteration method to solve it. By following the procedure in [Borges02], the residue for equation (3.39) at the element level is:

\[ \mathcal{R}_i = \int_{\Omega_e} \sum_j \nabla N_i \cdot \nabla N_j \psi_j \, d\Omega + \int_{\Omega_e} \alpha \beta \sinh(\alpha \sum_j N_j \psi_j) \, d\Omega \]  

(3.40)

and the \(ij\)-component of the Jacobean matrix \(J\) is given by

\[ J_{ij} = \frac{\partial \mathcal{R}_i}{\partial \psi_j} = \int_{\Omega_e} \nabla N_i \cdot \nabla N_j \, d\Omega + \int_{\Omega_e} N_i N_j \alpha \beta \cosh(\alpha \sum_k N_k \psi_k) \, d\Omega \]  

(3.41)

We can get the converged value for \(\psi_i\) by using the Newton-Raphson iteration

\[ J_{ij} (\psi_{i}^{(m)}) (\psi_j^{(m+1)} - \psi_j^{(m)}) = -\mathcal{R}_i (\psi_{i}^{(m)}) \]  

(3.42)

here the Einstein’s notation for summation is used.

Equation (3.36) is much easier to solve and its weak form is

\[ \int_{\Omega_e} \nabla N_i \cdot \nabla \phi \, d\Omega = 0 \]  

(3.43)

Typically, there are two approaches to solve the N-S equation: the mixed FEM and the penalty FEM. The mixed FEM solves the coupled velocity and pressure field together, while the penalty FEM use the penalty function \(p = -\gamma \nabla \cdot \mathbf{u}\) (where penalty parameter \(\gamma\) is a very large constant number, usually \(10^7 \sim 10^9\)) to replace the continuity equation and remove the pressure from the momentum equation [Reddy01].

There are two available penalty function methods, namely the consistent penalty method and the reduced integration penalty method. In this dissertation, we choose the selective reduced integration (SRI) method. The selection of the penalty parameter for Newtonian fluid flow can be found elsewhere [Heinrich99].
In equation (3.33), when Reynolds number is large or the convective term dominates, the calculated velocity field is not stable and there are large oscillations in the velocity solution. This phenomenon is identical to that using the second order central difference scheme to solve the convection dominated difference equation in FDM. To solve this problem in the FEM, the SUPG method is used [Heinrich99]. The Petrov-Galerkin interpolation function \( W_i = N_i + \frac{\nu \bar{h}}{2|\mathbf{u}|} \mathbf{u} \cdot \nabla N_i \) is used, where \( \nu = \cosh \frac{\chi}{2} - \frac{2}{\chi} \) with \( \chi = \text{Re} |\mathbf{u}| \bar{h} \), the element length. So now the weak form for the momentum equation becomes:

\[
\int_{\Omega} N_i \operatorname{Re} \frac{\partial \mathbf{u}}{\partial t} \, d\Omega + \int_{\Omega} \nabla N_i \cdot (\nabla \mathbf{u} + (\nabla \mathbf{u})^T) \, d\Omega + \int_{\Omega} \gamma \nabla N_i \cdot \mathbf{u} \, d\Omega = \int_{\Omega} N_i \beta \sinh(\alpha \psi) \nabla \phi \, d\Omega - \int_{\Omega} W_i \operatorname{Re} \mathbf{u} \cdot \nabla \mathbf{u} \, d\Omega + \int_{\Gamma} N_i \mathbf{n} \cdot d\Gamma
\]

(3.44)

In this dissertation, we use the four-node bilinear quadrilateral element shown in Figure 3.9. The bilinear interpolation is used for the velocity, the internal and the external potentials at the nodal point, while the pressure is constant in the element level.

The transformation between the local coordinates \((\xi_1, \xi_2)\) and the Cartesian coordinates \((x, y)\) are given by

\[
x = \sum_i N_i(\xi_1, \xi_2) x_i, \quad y = \sum_i N_i(\xi_1, \xi_2) y_i
\]

(3.45)

where \((x_i, y_i)\) are the coordinates for the nodal points, and \(N_i(\xi_1, \xi_2)\) are given as:

\[
N_1(\xi_1, \xi_2) = \frac{1}{4} (1 - \xi_1)(1 - \xi_2), \quad N_2(\xi_1, \xi_2) = \frac{1}{4} (1 + \xi_1)(1 - \xi_2)
\]

\[
N_3(\xi_1, \xi_2) = \frac{1}{4} (1 + \xi_1)(1 + \xi_2), \quad N_4(\xi_1, \xi_2) = \frac{1}{4} (1 - \xi_1)(1 + \xi_2)
\]

(3.46)
With four-node element, the element length in the SUPG method is given by

\[ h = \frac{1}{|u|} (|h_1| + |h_2|) \]

with \( h_1 = \mathbf{r}_1 \cdot \mathbf{u} \) and \( h_2 = \mathbf{r}_2 \cdot \mathbf{u} \), where \( \mathbf{r}_1 \) and \( \mathbf{r}_2 \) are the vectors that connect the midpoints of opposite sides in a quadrilateral element.

The unsteady equation (3.44) for velocity can be solved by the time-marching method. We use the first-order Euler method. We use the penalty function to get the element pressure once the velocity field at each time step has been solved, and then we apply the extrapolation method to get the pressure on the nodal points [Heinrich99].

### 3.5 Simulations of the Electroosmotic Flow in a Straight Channel

To verify our numerical approach using FEM, we compare the numerical results with the theoretical solution from equation (3.16), which is the EOF in a 2D straight channel.
For simplicity, we only consider three cases $m = -1, 0, \text{and} 1$. Figure 3.10 shows the finite element meshes and boundary conditions in this 2D straight channel. Denser meshes are used near the wall in order to catch the flow in the double layer. The length of the channel is 12, and its width is 2. Thus the external electric field is $\nabla \phi = -1/12$. In this problem, we set $\alpha = 1, \beta = 100$, thus $K = \sqrt{\alpha \beta} = 10$, the same value used in the section 3.1.2. Be aware that the value for $K$ is not large, otherwise, we shall either make the mesh denser near the wall, or use the higher order element to avoid the oscillations near the wall (we have used the six-node triangular element with the same mesh density as that using the four-node element. For the value of $K = 10,000$, the result using the six-node element agrees very well with the analytical result and has no oscillations, while the result using four-node element has some large oscillations near the wall).

![Finite element meshes and boundary conditions](image)

Figure 3.10: Finite element meshes and boundary conditions of the electroosmotic flow in a 2D straight channel.
Figure 3.11: Comparison of calculated distribution of (a) the internal potential and (b) the velocity in $x$ direction across the width of the channel with the analytical solution (in solid lines).
Figures 3.11(a) and (b) show the calculated internal potential distribution and the electroosmotic flow velocity across the channel compared with the theoretical solutions (shown in solid lines) from equation (3.16). The data points (shown in ‘∗’, ‘o’, and ‘Δ’) were extracted across the channel from the simulation results. From the figures, the simulation results agree very well with the theoretical solutions. It indicates the validity of our numerical method.

3.6 Electroosmotic “Four-Roll Mill” Flows

Different surface charge patterning methods (such as the multi-phase laminar flow patterning and surface charge coating method) have been used to generate the rotational and shear electroosmotic flows [Stroock00, Juang05]. By making different surface walls different charge density and polarity, different electroosmotic flow patterns can be generated.

Figure 3.12(a)−(c) show that three different electroosmotic flow patterns (i.e., extensional, shear and rotational flows) could be generated in a simple cross-slot by charge-patterning the four wall surfaces with different charge polarity [Juang05]. If all the surfaces are negatively charged, then an extensional EOF can be produced and the flow direction is similar to that in the extensional flow produced by the four-roll mill. If two opposite walls are negatively charged and the other two uncharged, we will have a shear EOF, just like that created in the four-roll mill device (two rollers are rotating in the opposite direction). If two opposite walls are negatively charged and the other two positively charged, we can generate a rotational EOF.
The flow patterns can be confirmed by the FEM simulation shown in Figure 3.13(a), (b) and (c).

But in the real experiments, we can only find the extensional flow or the extension-dominated shear flow. It is almost impossible to observe the proposed rotational flow in this electrokinetic “four-roll mill” device. The reason we found is that the particles used in experiments carry the non-negligible charge. The electrophoretic effect needs to be considered for this “four-roll mill” flows. This EO/EP interactions affect the charged particle flow patterns. We will discuss it in the next section.
Figure 3.12: Schematic for the electrokinetic “four-roll mill” (a) extensional flow (b) shear flow, and (c) rotational flow.
Figure 3.13: Simulation of electroosmotic “four-roll mill” (a) extensional, (b) shear and (c) rotational flows.
3.7 Electrokinetic Interactions

The interactions between electroosmosis and electrophoresis has been known for years. For example, lowering the pH value, increasing the ion strength in the buffer solution, or modifying the capillary wall with covalent coatings have all been used to increase the peak resolution in capillary electrophoresis by suppressing the effect of electroosmosis [BakerD95, Kuhn93]. In particle image velocimetry (PIV), the particle electrophoretic effect has to be minimized by modifying the particle surface or choosing weakly charged particles [Taylor93, Meinhart03]. The interactions of EO and EP in complicated flow fields, however, have not been thoroughly studied before.

Since most particles carry charges in aquatic solution, the overall velocity of the particles is the combination of the electroosmotic velocity and the electrophoretic velocity (if other effects such as the dielectrophoretic force are neglected here), thus the dimensionless form of particle velocity could be written as

$$\frac{\mathbf{u}_p}{\lambda} = \mathbf{u} + \lambda \mathbf{E}$$

where $\lambda = \frac{\mu_{EP}}{\mu_{EO}}$ is the ratio of the particle EP mobility to the surface EO mobility.

The particle velocity is non-dimensionalized by the characteristic EOF velocity $U_{ref} = E_0 \mu_{EO}$.

Because of the incompressible conditions for $\mathbf{u}$ and $\mathbf{E}$, we will have that the particle velocity satisfies the continuity equation

$$\nabla \cdot \mathbf{u}_p = \nabla \cdot \mathbf{u} + \lambda \nabla \cdot \mathbf{E} = 0$$

Also when the Reynolds number is very small ($Re \approx 0$), the particle velocity satisfies the Stokes equation because both EOF and EP flows obey the Stokes equation.
As we know, the superposition law works for the Stokes equation. Thus the movement of charged particle could be thought as the particle flow at this case.

Recall the flow type parameter $\Lambda$ defined in Chapter 2, for particle flow, we have the similar definition $\Lambda = \frac{|| \Pi || - || \Omega ||}{|| \Pi || + || \Omega ||}$. Now $\Pi = \frac{1}{2}(\nabla u_p + \nabla u_p^T)$ is the symmetric or extensional part of the particle velocity gradient $\nabla u_p$, and $\Omega = \frac{1}{2}(\nabla u_p - \nabla u_p^T)$ is the anti-symmetric or rotational part. The electrophoretic flow is purely extensional ($\Lambda_{EP} = 1$) because $\nabla E$ is symmetric from $\nabla \cdot E = 0$ and $\nabla \times E = 0$ (or equivalently, $E = -\nabla \phi$, and $\nabla^2 \phi = 0$). While electroosmotic flow have both the extensional part and rotational part.

Here we study the proposed electroosmotic “four-roll mill” rotational flow under the effect of electrokinetic interactions. Figure 3.14(a) shows the schematic of the cross-slot device. We let walls A and C be negatively charged with the same surface charge density $\mu_-$, and walls B and D be positively charged with the same surface charge density $\mu_+$. It is assumed that the two surface EO mobilities satisfy $\mu_- = -\mu_+ < 0$. Different voltages can be imposed at the four reservoirs $R_1$, $R_2$, $R_3$, and $R_4$. By using particles with different charge, various flow patterns can be generated.

When the particle EP mobility $\mu_{EP}$ is negligible compared with the characteristic surface EO mobility $\mu_{EO} = -\mu_-$, there is a pure rotational flow in the center of the cross-slot (Figure 3.14(a)). When $\mu_{EP}$ becomes non-negligible, the EO-dominated rotational flow is skewed (Figure 3.14(b)). Figures 3.14(c) and 3.14(d) show the simulated flow patterns when the ratio of EP mobility to the characteristic surface EO mobility
$\lambda = \frac{\mu_{eo}}{\mu_{eo}}$ is less than or equal to $-1$ (i.e., negatively-charged particles are used). In these cases, the flow becomes mixed-shear where the extensional component dominates.

Figure 3.14: Flow patterns at $\mu_+ / \mu_- = -1$ for different particle charge density: $\lambda = (a) 0; (b) -0.2; (c) -1; (d) -5$.

Flow patterns can also be varied if the surface EO mobilities on the four walls are different. Figures 3.15(a) and (b) show that the flow patterns change from a rotation in
the center to a mixed-shear in the center with a rotation near the two diagonal corners. Here, the ratio $\lambda = \frac{\mu_{EP}}{\mu_{EO}} = -0.05$ is fixed, while $\mu_- / \mu_+$ changes from $-2$ to $-5$.

Figure 3.15: Flow patterns at $\lambda = -0.05$ for different surface charge patterns: wall zeta potentials $\mu_- / \mu_+ = (a) -2; (b) -5$.

Experimentally, fluorescence-dyed polystyrene (PS) microspheres (diameter = 750 nm from Polysciences, PA) and liposome nanoparticles intercalated with fluorescent dye were used as tracers in DI water (pH = 5.6). The PS microspheres are used as tracers in microfluidics, while liposome nanoparticles have applications ranging from tracers in microfluidics to drug delivery vehicles. Since they bear PEG functional groups, adsorption of particles onto the channel wall can be minimized. The particle EP mobilities and surface EO mobilities were measured using the zeta potential analyzers (ZetaPALS and BI-EKA from Brookhaven Instrument). The measured EP mobilities are $-4.78$ and $-2.75$ (\(\mu m/s\))/(V/cm) for PS microspheres and liposome nanoparticles, respectively. The EO mobilities of glass, APTES modified glass, and polymethyl
methacrylate (PMMA) are $-3$, $+4$, and $-0.2$ $(\mu m/s)/(V/cm)$, respectively. A packaging tape (Clearview, Staples) was also used to seal the device. Because ions may bind onto the tape surface, its EO mobility cannot be determined this way.

![Streamlines of PS microspheres](image)

**Figure 3.16**: Streamlines of PS microspheres in (a) EO elongational flow; liposome nanoparticles in (b) a mixed-shear; and (c) a rotational flow; (d) simulated rotational flow. Scale bars represent 200 $\mu m$.

To generate an extensional flow, four glass plates with dimensions $25 \times 25 \times 1$ mm were assembled to form a cross-slot with a channel width of approximately 500 $\mu m$, followed by placing either two PMMA films or two pieces of packaging tape on the top and bottom of the glass plates as the lids of microchannels, with reservoirs located 18 mm away from the center point. Microchannels were first filled with DI water, followed by
adding the nanoparticle solution. An electric power of 225 volts was applied to reservoirs R₂ and R₄ with 0 volts in reservoirs R₁ and R₃. Since the EP mobility of PS microspheres is larger than the EO mobility of glass plates and PMMA films, the movement of the particles is from reservoirs R₁ and R₃ to R₂ and R₄; i.e., an EP extensional flow pattern was observed (similar to Figure 3.14(d)). But when replacing the PMMA films with the packaging tape, the flow direction of the PS particles was reversed to an EO extensional flow (see Figure 3.16(a)). Apparently, the packaging tape has a high surface charge density that enhanced the EO mobility of the surfaces and it is probably due to the packing tape is highly negatively charged or attracts a lot of negative ions on it. By binding the packing tape on the top of the glass, it might also makes the glass surface more negatively charged. This influence can be treated as an added EO mobility to the channel wall in 2D simulation. The particle velocity profile in the arm region was measured as shown in Figure 3.17 and an apparent EO mobility of the channel wall was estimated. Since the term $\alpha \psi$ is small in most parts of the channel, we can use equation (3.13) to linearize the Poisson-Boltzmann equation. By adding the EP velocity, the particle velocity is:

$$v(x) = \mu_{EO}E_0[-1 + \frac{\mu_{EP} E_0}{\mu_{EO}} + \frac{\sinh(\sqrt{\alpha \beta} \frac{x}{D}) - \sinh(\sqrt{\alpha \beta} \frac{x}{D} - 1)}{\sinh(\sqrt{\alpha \beta})}] \quad (3.49)$$

where $D$ is the channel width, $x$ is distance measured from one wall. By fitting the experimental data shown in Figure 3.17 using the least-square method, the values of $\mu_{EO} = -\mu_-$ and $\sqrt{\alpha \beta}$ (although this value will be different in the later) can be determined. The enhanced surface mobility by sealing with the packaging tape is
\[ \mu_\gamma = -10.46 \text{ (\(\mu\)m/s)/(V/cm)} \]. This increase of the EO mobility is the reason why the PS microspheres reversed their flow direction.

Figure 3.17: Velocity profiles vs. distance from one wall of the straight channel.

To create a mixed-shear flow, the cross-slot flow device was constructed by placing two pieces of glass plate in the diagonal direction and two pieces of APTES-modified glass plate in the other diagonal direction with PMMA films serving as top and bottom lids. The experimental procedures and conditions were the same as in the previous case. A mixed-shear flow was created as shown in Figure 3.16(b). This experimental result \((\mu_\gamma / \mu_\gamma \sim -1.33 \text{ and } \lambda \sim -0.92)\) is similar to the simulation flow pattern \((\mu_\gamma / \mu_\gamma = -1 \text{ and } \lambda = -1)\) shown in Figure 3.16(c).
When replacing the PMMA films with the packaging tape, a shear flow was generated inside the arm region, and a rotational flow pattern at two corners was observed as shown in Figure 3.16(c). In any arm of the cross-slot, the electric field is nearly constant \( E_0 \). The exact solution of the particle velocity profile in this case, when \( \alpha \psi \) is small, is given as:

\[
v(x) = \mu_{EO} E_0 \left[ (\frac{\mu_+}{\mu_-} - 1) \frac{x}{D} - \frac{\mu_+}{\mu_-} \sinh(\sqrt{\alpha \beta} \frac{x}{D}) \right] \sinh(\sqrt{\alpha \beta} \frac{x}{D}) - \frac{\mu_{EP}}{\mu_{EO}} \right] (3.50)
\]

where \( x \) is distance measure from the APTES-modified glass wall to the non-modified glass wall. The parameters were determined by fitting the velocity data of liposome nanoparticles in Figure 3.17 and the simulated flow pattern is shown in Figure 3.16(d), which agrees fairly well with the experimental result shown in Figure 3.16(c). Geometric “offset” resulting from misalignment of 4 glass pieces in this experiment is considered, but the curved corners of glass plates are not considered in the simulation. The “offset” changes the vortex size but not the flow pattern.

Due to the electrokinetic interactions, the properties of the aqueous solution, the electrostatic charges of particles and the channel surface all need to be well regulated and controlled in order to generate and maintain a desired flow pattern. This presents a major challenge in actual biological applications because biomolecules have characteristic electric properties in physiological conditions.

### 3.8 Electrokinetic Five-Cross Flow

As shown in the previous section, the electrokinetic interactions affect the particle flows in the microfluidic devices and the conventional surface charge patterning method
can not avoid this effect. Thus how to design the microfluidic devices to avoid or minimize this effect becomes a challenging work for us.

Since the charge patterning method is very complicated and still can not control the particle flows when the particle EP mobility is larger than the surface EOF mobility, we don’t make the surfaces of the microfluidic device with different charge density or polarity. Also without patterning the surface with different charge polarity, the adsorption of charged particle on the oppositely charged surface can be avoided.

Recalling the electroosmotic "four-roll mill" rotational flow in the section 3.6, we find that there are four circumfluences in (shown in Figure 3.18). From the knowledge of the 2D nonlinear dynamics, we know that there must be four saddle points between these...
four circumfluences and the rotational streamlines in the center. Also there must be rotational flow zone if there are four circumfluences arranged this way.

Figure 3.19: (a) EOF pattern in a cross-slot with two circumfluences; (b) way to design the five-cross rotational flow.
Figure 3.19(a) shows the electroosmotic flow pattern in a cross-slot (without different charge patterning) with the given external potential setup. We find that there are two circumfluences in this cross-slot although no rational flow is generated. If we arrange four of this cross-slot setup in clockwise direction shown in Figure 3.19(b) (each one rotates 90 degrees anticlockwise) and because the inner arm (close to the center of mass of this system consisted by these four cross-slots) of each cross-slot has the same potential (here the potential is 0), we can connect them together to form a five-cross structure shown in Figure 3.19(b) (Due to the symmetry of potential and geometry, the potential in the center is zero). This device should also have four circumfluences in the center, thus it should produce a rotational flow.

The particle velocity is given by \( u_p = E_0 \mu_{EO} (\lambda E + u_{EO}) \), where \( \lambda = \mu_{EP} / \mu_{EO} \) is the ratio of the EP mobility to the EO mobility. The electrophoretic flow is purely extensional because \( \nabla \times E = 0 \) and \( \nabla \cdot E = 0 \). The rotation of particles can only come from the electroosmotic flow. In the conventional devices [Stroock00, Juang05], the dimensionless EOF velocity \( u_{EO} \) is the same magnitude of the dimensionless electric field \( E \) in the whole domain. Thus when \( |\lambda| > 1 \), the EP effects dominate the particle velocity, i.e., \( u_p = E_0 \mu_{EO} (\lambda E + u_{EO}) \), making the particle flow extensional. To generate a rotational flow independent of the relative magnitude of EP and EO mobility, the electric field \( E \) must be suppressed and the rotational part in the EOF velocity \( u_{EO} \) needs to be enhanced. Our five-cross microfluidic network can fulfill this purpose. Because both the geometry and the imposed external electric potentials are symmetric with respect to the center of the device, the four circumfluence flows from
four outer cross-slots impinge on one another at the center of the middle cross-slot. Thus, the electrokinetic flow near the center of the middle cross-slot has to be a rotation type as it is the only way to satisfy the continuity condition $\nabla \cdot \mathbf{u}_f = E_o \mu_{EO} (\lambda \nabla \cdot \mathbf{E} + \nabla \cdot \mathbf{u}_{EO}) = 0$.

By using this design and voltage setup, there is always a finite domain around the center of the device where $|u_{EO}| >> |E|$.

Figure 3.20: Electrokinetic rotational flow (contours are the electric potential). (Inserts) the rotational patterns for PS particle and $\lambda$-DNA molecules.

This predicted rotational flow is also successfully demonstrated experimentally using the same platform. The only difference is in the arrangement of voltage inputs, as shown in Figure 3.20. Here, the actual voltage (in Volts) needs to be multiplied by a factor of 50. The rotational flow was observed at the center of the device for both
polystyrene microspheres and λ-DNA molecules, as shown in Figure 3.20. The rotational direction is in accordance with the direction of the simulated streamlines.

The rotational direction is independent of the charge type and charge density of the particles. However, the size of the vortex varies. Two types of polystyrene microspheres were used: the 3 μm plain polystyrene microspheres used in previous figures, and 2 μm polystyrene microspheres with multiple carboxyl groups on the surface (Polysciences). The measured $\mu_{EP}$ for these two microspheres in DI water are –0.78 and –7.02 ($\mu$m/s)/(V/cm), respectively. Different sizes of vortex were observed when using these two PS microspheres. The computed vortex size (in diameter and non-dimensionalized based on the channel width $D$) is plotted as a function of $\lambda$ shown in Figure 3.21. The

![Figure 3.21: Dimensionless vortex size vs. EP/EO mobility ratio $\lambda$.](image)

The rotational direction is independent of the charge type and charge density of the particles. However, the size of the vortex varies. Two types of polystyrene microspheres were used: the 3 μm plain polystyrene microspheres used in previous figures, and 2 μm polystyrene microspheres with multiple carboxyl groups on the surface (Polysciences). The measured $\mu_{EP}$ for these two microspheres in DI water are –0.78 and –7.02 ($\mu$m/s)/(V/cm), respectively. Different sizes of vortex were observed when using these two PS microspheres. The computed vortex size (in diameter and non-dimensionalized based on the channel width $D$) is plotted as a function of $\lambda$ shown in Figure 3.21. The
actual experimental points were also added for comparison. The observed vortex sizes agree quite well with the simulation prediction.

There are several ways to generate the pure extensional and mixed-shear flow in this microfluidic network. The simplest method is to use only 4 electrodes and ground the other 8 electrodes. For example, by using the electrodes on the top, the bottom, the left and the right ends, the network is essentially a symmetric single cross-slot flow device that can generate either the EO dominated (if $|\lambda| < 1$) or EP dominated (if $|\lambda| > 1$) extensional flow [Juang05]. These two flows have similar streamlines, but opposite flow directions. A more sophisticated design is shown in Figure 3.22, where the extensional flow is generated in the middle cross-slot, and the mixed-shear flow in the four corner cross-slots simultaneously. The five-cross device was micro-machined on a poly(methyl methacrylate) (PMMA) plate sealed by a packaging tape (Clearview, Staples) to form the microfluidic network. The microchannels were first filled with DI water, followed by adding fluorescence-dyed polystyrene microspheres with a diameter of 3 μm (Polysciences) as the tracer at 0.00265% concentration for flow visualization. The arrangement of the voltages is shown in Figure 3.22, where the actual voltage (in Volts) needs to be multiplied by a factor of 25. The streamlines of the flow pattern are shown in Figure 3.22 by compounding the video graphs. A mixed-shear flow pattern was observed at all four side crosses, agreeing well with the simulation result. The movement of particles at the center of the five-cross device shows an EO dominated extensional flow pattern as predicted by the simulation.
This five-cross-slot flow network can be expanded to generate multiple rotational, extensional and shear flow patterns as shown in Figures 3.23(a) and (b). In Figure 3.23(a), there are five EO dominated rotational domains (shown as O shapes) and in Figure 2.23(b), there are five extensional flow domains (shown as □ shapes) and 16 mixed-shear flow domains (shown as Δ shapes). Further scale-up can be achieved in the manner of the fractal [Mandelbrot82]. If we define $n$ as the degree of fractalization, then $n = 1$ represents the single five-cross-slot network, and $n = 2$ is the five five-cross-slot network shown in Figures 3.23(a) and (b). This expansion leads to high-degree fractals as shown in Figure 3.23(c). The scale-up of this five-cross-slot network to a higher degree of fractalization may need proper integration of heat sinks to minimize the Joule heating.
problem.

Figure 3.23 Fractalization of five-cross network at n=2 to form (a) 5 rotational flow patterns; and (b) 5 extensional and 16 mixed-shear flow patterns; and (c) n=4.

This versatile microfluidic network can serve as a micro-reactor array in various chemical and biomedical applications. For examples, transportation and hybridization of a large number of single DNAs with proteins, lipids, cationic polymers and other biomolecules may be achieved to form well-defined nanoparticles for gene therapy. In the packaging of DNAs, the solution properties and charge density or types of DNA complexes will be dramatically changed with the adding of condensing agents. By using our five-cross design, the flow patterns for producing DNA conjugates can work unaffectedly.
3.9 Electrokinetic Flow in the Converging/Diverging Channel

Here we compare the electrokinetic flows in three different converging/diverging channels shown in Figure 3.24. The center part of the devices 1 and 2 are a straight channel with widths of $d_1$ and $d_2$ ($d_1 < d_2$), respectively; while the center part of the device 3 is tapering and the widths of the small end and the large end are $d_1$ and $d_2$, respectively.

![Figure 3.24: Three types of converging/diverging channel. Streamlines and the contours for the electric potential are also drawn.](image)

Figure 3.24: Three types of converging/diverging channel. Streamlines and the contours for the electric potential are also drawn.
Here, we take $d_2/d_1 = 6.5$, the length for the center part of the channel is $L = 15d_1$, and the width of the diverging channel (left or right end) is $D = 15d_1$ (in experiments, we let $d_1 = 20\mu m$).

The 2D electric fields in these three converging/diverging channels are non-uniform. Here, we extract the $x$ component (in dimensionless form) of the electric field along the center lines of the channels and multiple it by an assumed particle EP mobility $\mu_{EP} = -300$. Thus it should be the $x$ direction EP velocity distribution along the center line. The results are shown in Figure 3.25 (the $x$ axis is nondimensionlized by $d_1$).

![Figure 3.25: EP velocity distributions along the center lines.](image-url)
From Figure 3.25, we know that the device 3 can achieve the highest electric field distribution along the center line near the small end. Since the device 1 has the smallest width and device 2 has the largest width, the electric resistance $\mathcal{R}_1 > \mathcal{R}_3 > \mathcal{R}_2$. For each device, the electric field reaches its minimum value $E^{\text{min}}$ outside the center part and maximum value $E^{\text{max}}$ in the center part. Since the electric field is almost uniform outside the center part, we can see the electric field for device 2 is the largest there because its total electric resistance is the lowest, thus we have $E_2^{\text{min}} > E_3^{\text{min}} > E_1^{\text{min}}$. The condition $\nabla \cdot \mathbf{E} = 0$ is satisfied in these 2D devices and we can get the equivalent condition:

$$\int_{y_2(x)}^{y_2(x)} E_x(x) dy = \text{constant}$$

(3.51)

where $E_x(x)$ is the $x$ component of the electric field, $y_1(x)$ and $y_2(x)$ are the minimum and maximum values of the geometry on the vertical line $x$.

Equation (3.51) can be further simplified to $\bar{E}_x(x) d(x) = \text{constant}$, where $\bar{E}_x(x)$ is the averaged value and $d(x)$ is the channel width on line $x$. Thus we have

$$\bar{E}_1^{\text{min}} D = E_1^{\text{max}} d_1, \quad \bar{E}_2^{\text{min}} D = E_2^{\text{max}} d_2, \quad \bar{E}_3^{\text{min}} D = E_3^{\text{max}} d_1$$

(3.52)

From simulation, we find that along the center line, $E_1^{\text{max}} / E_1^{\text{min}} = 14.7$, $E_2^{\text{max}} / E_2^{\text{min}} = 2.275$, $E_3^{\text{max}} / E_3^{\text{min}} = 12.464$, and the relation between the minimum electric fields along the center line is $E_2^{\text{min}} : E_3^{\text{min}} : E_1^{\text{min}} = 2.586 : 1.863 : 1$. Thus the relation between the maximum electric fields is $E_3^{\text{max}} : E_1^{\text{max}} : E_2^{\text{max}} = 3.948 : 2.498 : 1$. So the device 3 can achieve the highest electric field near its small end of the converging channel.

Also from Figure 3.25, the electric field distribution for device 1 and 2 are nearly a flat line (except at two ends of the center part). We can see that in device 3, the electric
field gradual increases in the converging channel until it reaches its maximum value near the small end, and then suddenly drops to the minimum value. Thus the electric field gradient at the small end of the converging channel in the device 3 is very large.

The dielectrophoretic force is proportional to the gradient of the square of the electric field. \( \mathbf{F}^{\text{DEP}} = \frac{\alpha_D}{2} \nabla(\mathbf{E} \cdot \mathbf{E}) \), where \( \alpha_D \) is the electric susceptibility of the medium.

In the device 3 (from now on, we only study this device and call it the converging/diverging channel), the large electric field gradient will produce a large dielectrophoretic force, which will affect the movement of particles. This converging/diverging channel is essentially an electrodeless dielectrophoretic device mentioned in Chapter 3 and it can be used to trap particles.

Figure 3.26: Lip vortices of charged particles outside the small end of the converging/diverging channel.

Figure 3.26 shows two lip vortices formed by the charged PS particles (diameter 40 nm) under the electric field. Most of the charged PS particles (in the main flow) leave the converging channel very quickly, but there are still some charged particles trapped (move
in the counterclockwise direction for the vortex on top and in the clockwise direction for the other one at bottom) outside the small end (width 20 μm).

The formation of the lip vortices of the charged particles in this channel is still unknown. In simulation, we solved the Poisson-Boltzmann equation to calculate the electroosmotic flow, electric field and the gradient of electric field. We can determine the particle velocity by using the following equation

\[ u_p = \mu_{EO} E_0 u - \mu_{EP} E_0 E + \frac{\mu_{DEP} E_0^2}{D} \nabla (E \cdot E) \]  

(3.53)

where \( E_0 \) is the characteristic electric field, \( D \) is the characteristic length, \( \mu_{EO} \), \( \mu_{EP} \), and \( \mu_{DEP} \) are the electroosmotic, electrophoretic and dielectrophoretic mobility.

By considering many different values of \( \mu_{EO} \), \( \mu_{EP} \), and \( \mu_{DEP} \), we still couldn’t get the lip vortices of the charged particles observed in the experiments. There are several possible reasons and we list them as follows:

(1) Governing equations are not appropriate

In Chapter 3, we use the Poisson-Boltzmann (P-B) equation to solve the electroosmotic flow. One assumption is that the ion distribution follows the Boltzmann’s distribution. We know that this assumption has its required conditions, that is, the ion distribution is in the steady state, the flow velocity is low, and the dielectrophoresis does not exist.

Now in the diverging/converging channel, the zeta potential on the wall might not be constant as we assumed in the P-B equation. Also the dielectrophoretic effect might be very strong due to the large electric gradient near the small end. It is suggested that we should use the Poisson-Nernst-Planck (P-N-P) equation given as follows:
\[
\frac{\partial n_i}{\partial t} = \nabla \cdot (D_i \nabla n_i + \frac{z_i e}{k_B T} D_i n_i \nabla \Psi) - \nabla \cdot (n_i u_i + n_i \mu_{\text{DEP}} \nabla (E \cdot E))
\] (3.54)

\[
\nabla^2 \Psi = -\frac{1}{\varepsilon} \rho_e = -\frac{1}{\varepsilon} \sum z_i e n_i
\] (3.55)

In Equation (3.54), the dielectrophoresis can affect the ion distribution in the converging/diverging channel and the electroosmotic flow to be solved by

\[
\rho \left( \frac{\partial u}{\partial t} + u \cdot \nabla u \right) = -\nabla p + \mu \nabla^2 u - \rho_e \nabla \Psi
\] (3.56)

Then the combination of EO, EP, and DEP using equation (3.53) might produce the lip vortices for the charged PS particles used in experiments.

(2) Hydrodynamic interactions are not considered

Near the small end of the converging/diverging channel, the particle velocity is very large and the surrounding fluid is almost stagnant. The movement of the particle can drive the fluid to flow, just like the two trailing vortices generated behind a fighter plane in air, or the two attached vortices created by a moving sphere in fluid. The induced flow velocity is also called the hydrodynamic interaction (HI).

Since our converging/diverging channel is a confined geometry, the effect of HI will be stronger than that in the bulk. The HI induced velocity by the PS particles in the main flow will create two lip vortices outside the small end, which in turn will trap the PS particles outside the main flow.

The simulation of HI velocity in the confined geometry by using the FDM or FEM is very complicated [Ye04] and beyond the scope of this dissertation. We will briefly mention it in Chapter 5 for future work.
CHAPTER 4

BROWNIAN DYNAMICS SIMULATION OF SINGLE DNA MOLECULES IN THE ELECTROKINETIC FLOWS

Recently, some experiments of DNA dynamics in the electrokinetic driven flows in the micro- or nano-scaled geometries show many interesting results. As we know, the electrokinetic flows, especially the electrophoretic flows have many advantages over the conventional hydrodynamic pressure driven flows in the small-scaled geometry. The experiments on the electrokinetic driven micro- or nano-scaled flows, however, sometimes are very complicated and hard to handle (not to mention the hard work on how to fabricate the complicated devices). The simulation can provide a cheap and efficient way to direct the experiment to control the behavior of DNA molecules for the real application such as the gene delivery or gene mapping. In this chapter, we will study the configuration dynamics of single DNA molecules in the electrokinetic driven micro-devices such as the cross-slot device, the five-cross device and the converging channels.

4.1 DNA Stretching in a Cross-slot with Electrophoresis

Here, we utilized electrokinetic forces to generate a fairly homogeneous, 2D (planar) elongational flow pattern inside a microscale cross-slot channel.
Figure 4.1(a) shows the schematic of an electrokinetics-induced stagnation flow cell. The substrate used is a polymethyl methacrylate (PMMA) plate micromachined with cross-channels of 250 μm in width and 125 μm in depth. The diameter of the wells is 1.5 mm and the length of each arm is 7.5 mm. A 45 μm thick PMMA film was laminated onto the surface of the substrate to form closed channels. The PMMA surface possesses a low negative charge density when in contact with aqueous solution. To generate the elongational flow pattern, the microscale cross-channel was first filled with 1x Tris-Borate-EDTA (TBE) buffer solution (pH = 8.3). An electric power of 147 volts was applied to wells 2 and 4 with no voltage in wells 1 and 3. Negatively charged fluorescent polystyrene microspheres (Polysciences, Inc.) with 700 nm diameter were used as the tracer at 0.00265% concentration and the streamlines of the flow pattern are shown in Figure 4.1(b) by compounding video graphs. A clear elongational flow pattern with a stagnation point at the center was observed.

Figure 4.1: (a) Schematic of the flow cell design. (b) Streamlines of the electrokinetics-induced stagnation flow.
Under the applied electric field, the overall velocity of particles is the combination of electrophoretic movement of the particles and electroosmotic flow of the fluid, which can be expressed by \( \mathbf{u}_p = \mathbf{u}_{EOF} + \mathbf{u}_{EP} \), where the positive direction of the velocity is defined from cathode to anode. Note that the direction of particle movement was from wells 1 and 3 to wells 2 and 4. Hence, this indicates that the electrophoretic movement of polystyrene microspheres overcomes the electroosmotic flow generated by the PMMA surface at the experimental conditions.

To visualize the coil-stretch transition of single DNA molecules in the electrokinetics-induced stagnation flow, \( \lambda \)-DNA (New England Biolabs, 48K base-pairs) was used and labeled with fluorescent dye (YOYO-1) at a dye-base pair ratio of 1:5, followed by diluting in a pH = 8 buffer solution consisting of 10mM tris-HCl, 2mM EDTA and 10mM NaCl at a final concentration of about \( 10^{-4} \) C* (C* is the concentration at which the macromolecules completely fill the space without overlapping), i.e., \( \sim 0.03 \) μg/ml. An oxygen scavenger, beta-mercaptoethanol, was added in the solution at 4% (w/w) to prevent DNA from photobleaching. Incubation was conducted in the dark at room temperature for a minimum of 2 hours. 18% (w/w) glucose and 40% (w/w) sucrose were then added in the solution to increase the bulk viscosity to 30 cp. The DNA solution was delivered into the cross-channels and the flow cell was mounted onto an epi-fluorescence microscope equipped with a 100x/1.3 NA oil immersion objective lens.

Figure 4.2 shows the measured velocity distribution of DNA molecules in the spanwise (x) and vertical (z) directions. At \( y = 67 \) μm (inside the intersection zone), the velocity of DNA molecules was nearly the same in the spanwise direction up to \( x = 40 \) μm and then gradually increased afterwards. At \( y = 225 \) μm (outside the intersection), a
nearly constant velocity of DNA molecules was observed in the spanwise direction up to $x = 100 \, \mu m$ but then gradually decreased afterwards. Since DNA molecules have left the elongational flow field in the intersection area and are inside the straight channel, a more plug-like velocity profile is expected. However, the observed velocity of the DNA molecules near the channel wall decreased, which might result from the increase of viscous drag due to the hydrodynamic interactions between the DNA molecules and the solid wall []. Also we observed a depletion layer from $x = 115 \, \mu m$ to $x = 125 \, \mu m$ where almost no DNA molecule exists, the reason can be explained by the hydrodynamic interaction between the DNA molecules and the wall [Fang05].

![Figure 4.2: Velocity distribution of DNA molecules at various locations in the spanwise ($x$) and vertical ($z$) directions. $z = 0 \, \mu m$ is at the bottom of the channel.](image)

Figure 4.2: Velocity distribution of DNA molecules at various locations in the spanwise ($x$) and vertical ($z$) directions. $z = 0 \, \mu m$ is at the bottom of the channel.
In a pure elongational flow field, the velocity profile should satisfy 

\[(u, v) = (\dot{x}, -\dot{y}),\]

and the velocity magnitude \(V\) is given as:

\[V = \dot{\varepsilon} \times \sqrt{x^2 + y^2}\]  \hspace{1cm} (4.2)

where \(x\) and \(y\) are the distance away from the stagnation point and \(\dot{\varepsilon}\) is the elongational rate. Velocities of DNA molecules at \(y\) positions near the centerline other than 67 and 225 \(\mu\text{m}\) were also measured (not shown here). A straight line was obtained when plotting the \(y\) component of DNA velocity vs. \(y\) position. From the slope, the elongational rate was found to be 1.26 sec\(^{-1}\). Then the velocity distribution at \(y = 225\ \mu\text{m}\) can then be calculated using equation (4.2), which is represented by the solid line in Figure 4.2. It shows a very well agreement with experimental measurements up to around \(x = 90\ \mu\text{m}\), indicating that a nearly pure elongational flow field can be generated by electrokinetic forces. In the vertical direction, the velocities of DNA molecules at selected \(x\) and \(y\) positions with \(z\) locations ranging from 20 to 80 \(\mu\text{m}\) from the bottom of the channel are fairly uniform. These results show that a fairly homogeneous, two-dimensional (planar) flow field can be generated by the electrokinetics-induced flows in a microscale cross-channel.

To prove that the electric field is close to the pure extensional flow in this cross-slot, we use the finite element method to calculate the electric field. Since no electric source is inside the microchannel, the Laplace equation is satisfied for the electric potential \(\phi\) and the electric field vector \(E = -\nabla \phi\) can then be calculated by the finite element method. Figure 4.3 compares the calculated electric lines of the electric field (the thin solid lines) and the streamlines of the pressure driven flow (the dashed lines) with streamlines of the pure elongational flow (the thick solid lines) for the first quarter of the intersection area.
in the cross-channels. The streamlines of the pressure driven flow are calculated using the steady state Stokes equation (Re = 0). Because of the existence of sharp channel corners, both the electric lines and the streamlines of the pressure driven flow are different from the streamlines of the pure elongational flow near the channel wall. However, we can still see that the electric lines are closer to the streamlines of the pure elongational flow than the streamlines generated by the hydrodynamic pressure. Also near the stagnation point (0, 0), we found that all these three lines fall together; that means near the stagnation point, either flow generated by the hydrodynamic pressure or by the electric potential is nearly the pure extensional flow. That explains why the hydrodynamic flow near the stagnation point can be thought as the pure extensional flow [Perkins97, SmithD98].

Figure 4.3: Comparison of the electric lines, the streamlines of pressure driven flow, and the streamlines of pure elongational flow.
Also from Figure 4.3, we can see that at \( y = 67 \ \mu m \), the electric lines agree closely with the streamlines of the pure elongational flow up to around \( x = 90 \ \mu m \), which supports our results in Figure 4.2.

We have used the Brownian dynamics method with the worm-like chain model to simulate the coil-stretch transition of DNA molecules. Here a 20-bead chain with persistence length of 0.066 \( \mu m \) is used to simulate the movement of the \( \lambda \)-DNA molecule. The governing equation is given as follows:

\[
\frac{d\mathbf{b}_i}{dt} = S_0 \mathbf{u}_i + f_{i, \text{random}} + f_{i, \text{spring, total}} + E_0 \mathbf{E}_i \quad (4.3)
\]

where \( \mathbf{u}_i \) comes only from the electroosmotic flow since no hydrodynamic flow is produced by this device (the possible pressure built-up by the difference of the liquid surface level in the reservoirs has been neglected here). And because the counterions move in a direction opposite to the DNA molecules and screen the hydrodynamic interactions over a distance larger than the Debye length (only several nanometers) [Viovy00], we have neglected the hydrodynamic interactions in equation (4.3). The flow cell is fabricated using PMMA, which has a surface with a very low charge density in the buffer solution. Thus the electroosmotic effect is much weaker than the electrophoretic effect. Since the flow generated by electroosmosis is similar to the electric field [Cummings00], we can neglect the electroosmosis in equation (4.3) by simply combining this effect into the “effective” charge density \( q \) of the DNA molecule. In the simulation, \( \mathbf{r}_c \approx q \mathbf{E}_c / \zeta \), where \( \mathbf{r}_c \) is the velocity for the center of mass of DNA and \( \mathbf{E}_c \) is the electric field at \( \mathbf{r}_c \) (the location for the center of mass of DNA). By fitting the center of mass velocity of DNA with the electric field, we found that the DNA electrophoretic
mobility $q/\xi = -1.16 \ (\mu m/s)/(V/cm)$, which has been used in the Brownian dynamics simulation.

The electric field in this cross-slot device was calculated with the finite element. We can use the interpolation method to calculate the electric field at any bead’s location $(x, y)$ since the bead might not be just on the nodal point. Generally speaking, we need to figure out which element this bead is located, and then calculate the generalized coordinates $(\xi_1, \xi_2)$ for a bead’s location, finally use the interpolation method to get the electric field (similarly, we can get the velocity field or any other field at a bead’s location). For an isoparametric four-noded element, we can solve the equation (3.33) to get the generalized coordinates $(\xi_1, \xi_2)$

Since equation (3.33) is a 2D second-order polynomial of $(\xi_1, \xi_2)$, we can use the Newton-Ralphson iteration to find its roots. The equation (3.33) can be rewritten as:

\[
\frac{1}{4}(x_2 + x_3 - x_1 - x_4)\xi_1 + \frac{1}{4}(x_3 + x_4 - x_1 - x_2)\xi_2 + \frac{1}{4}(x_1 + x_3 - x_2 - x_4)\xi_1\xi_2
+ \frac{1}{4}(x_1 + x_2 + x_3 + x_4) - x = 0
\]  

\[
\frac{1}{4}(y_2 + y_3 - y_1 - y_4)\xi_1 + \frac{1}{4}(y_3 + y_4 - y_1 - y_2)\xi_2 + \frac{1}{4}(y_1 + y_3 - y_2 - y_4)\xi_1\xi_2
+ \frac{1}{4}(y_1 + y_2 + y_3 + y_4) - y = 0
\]

We can simplify the equations above to the form

\[
\begin{cases}
 f_1(\xi_1, \xi_2) = 0 \\
 f_2(\xi_1, \xi_2) = 0
\end{cases}
\]

The procedure for the Newton-Raphson’s iteration is given as follows:

\[
\left(\frac{\xi_1^{(v+1)}}{\xi_2^{(v+1)}}\right) = \left(\frac{\xi_1^{(v)}}{\xi_2^{(v)}}\right) - \left[ \frac{\partial f_1}{\partial \xi_1} \quad \frac{\partial f_1}{\partial \xi_2} \right]^{-1} \left[ f_1(\xi_1^{(v)}, \xi_2^{(v)}) \quad f_2(\xi_1^{(v)}, \xi_2^{(v)}) \right]
\]  

(4.6)
Usually, for equations (4.4) and (4.5), it takes two iteration steps to get the converging results because these equations are the bilinear form on \( (\xi_1, \xi_2) \).

After the electric and electroosmotic velocity fields are known, we can use the predictor-corrector or the Euler’s method (see the details in the previous chapters) to calculate the bead-spring chain conformation and locations with time.

It has been found that both the initial conformation and the residence time of DNA molecules inside the pressure-driven elongational flow field play important roles in DNA stretching \([\text{1}]\). This is also true in the electrokinetics-induced stagnation flow. In our DNA stretching experiments, the “electrokinetics-induced” Deborah number (De) was calculated to be 2.1 \(\sim\) 2.2, which is larger than the critical value of 0.5 for molecule stretching (the “electrokinetics-induced” Deborah number is defined as the product of the elongational rate, approximately 0.77 sec\(^{-1}\), and the longest relaxation time of DNA molecules, around 2.89 seconds in solution with 30 cp). With a similar initial conformation (a semi-dumbbell shape in this case), the DNA molecule having a longer residence time can be stretched longer than that having a shorter residence time as shown in Figure 4.4(a). On the other hand, two DNA molecules with different initial conformations (a curled and a partially stretched shape in this case) may end with a similar extent of stretching as shown in Figure 4.4(b), even though the residence times are substantially different. Our coarse-grain molecular simulation by using corresponding initial DNA shapes agrees qualitatively with the experimental observations.

Thus in this electrokinetic driven cross-slot, the initial conformation and the residence time of the DNA molecules still play important roles in the extent of DNA stretching. And the use of coarse-grain molecular modeling is able to qualitatively
simulate the conformational changes of DNA molecules observed in the experiments.

Figure 4.4: Experiment and simulation of the movements of two DNAs in the intersection region (a) with similar initial conformation but different residence time, (b) with different initial conformation and residence time.
4.2 DNA Dynamics in Five-Cross Electrokinetic Flow

It has been shown that the electrokinetic five-cross device can generate and maintain different flow patterns even for the charged particle. In this section, we study the DNA dynamics in the five-cross extensional/shear flow and compare the simulations with the experimental results.

In the five-cross extensional/shear flow, the electrokinetic flow is EO dominated extensional flow in the center cross. The “electrokinetically-induced” Deborah number (De) [Juang04] was calculated to be ~1.4, which is larger than the critical value of 0.5 for molecule to be stretched. DNA chains are gradually stretched when they approach the center of the cross, the stagnation point. As shown in Figure 4.5(a), DNA molecule A, which is closer to the centerline was stretched to a longer length (close to 9 μm) compared to DNA B, which is away from the centerline, although they experienced almost the same length of residence time. This is because DNA A has an unfolded initial conformation, while DNA B is initially in the folded shape, which is harder to be stretched as reported in [Perkins97, SmithD99].

At mixed-shear flow regions, sheared DNA molecules experienced different configurational changes in both size and orientations, depending on their initial conformations and flow paths. As shown in Figure 4.5(b), the DNA molecules C and D can only be stretched to 3–5 μm (Weissenberg number is ~ 1.74 to 2.1).

There are two problems we need to solve before doing the Brownian dynamics simulation to study the dynamics of single DNA molecules in this five-cross extensional/shear flow.
Figure 4.5: Observed and simulated \( \lambda \)-DNA stretching in (a) EO extensional flow in the center cross, and (b) extension dominated mixed-shear flow in the side cross.
(1) First, we used in the experiments a scratch tape (highly negatively charged) to seal the PMMA device (have a weakly charged surface) and somehow it can increases the surface zeta potential of the device (we guess that is because the negative charges moves from scratch tape to the PMMA surface to make the whole system charge-balanced). Thus in the simulation, we need to figure out the “effective” EO mobility for the surface wall. In the Chapter 3, we determined the “effective” EO mobility by comparing the experimental data with the analytical solution. Now we have to use another method to get it because there is no analytical solution for the five-cross device. We turn to the help of the simulation. Since the electric field can be calculated by the simulation, we can get the EP velocity for a charged particle once its EP mobility is known. The problem is that we can’t get the EOF velocity since the surface zeta potential is unknown. By using the particle visualization method, which we carried out for the five-cross extensional/shear flow experiments, we can get the particle velocity $u_p$. By subtracting the EP velocity from the particle’s velocity, we can get the EOF velocity $u = u_p - \mu_{EP}E$, which increases in magnitude as EO mobility increases. In simulation, we assume an initial value of EO mobility (or zeta potential), and by comparing the calculated EOF velocity with that obtained indirectly from the experiments (on one path line of charged particles), we know whether the assumed EO mobility is larger or smaller than the correct value. Then we can adjust its value until the calculated EOF velocity matches the experiment data.

(2) Second, the dynamics of DNA can be captured by the video in experiments, but locations of these DNA molecules are unknown and it is almost impossible to use the microscopy to find their location. In this five-cross device, it is probably easier for us to get the location of the DNA molecules because the stagnation point is the center of the
device and we know the size of our captured images. But it is very hard to use the same method in the shear flow because we don’t know the location of the saddle point in the shear flow beforehand. To solve this problem, we need to use the finite element simulation. Once we get the surface EO mobility and DNA EP mobility, we can draw the pathlines for the center of mass of the DNA molecules by simulation (because the electroosmotic flow and the electric field have been calculated). By fitting the locations of the center of mass of the DNA molecules (at different time) obtained in experiments with that pathlines calculated by the simulations, we can locate these DNA molecules and the initial locations are used for the Brownian dynamics simulations.

The measured EP mobility $\mu_{EP}$ (using a zeta potential analyzer (ZetaPALS, Brookhaven Instrument) for $\lambda$-DNA molecules in DNA buffer solution are $-0.4 \, (\mu m/s)/(V/cm)$ (the EP mobility is dependent on the pH value and ion strength of the solution). The calculated effective EO mobility $\mu_{EO}$ around the center plane (in the Z direction) inside the microchannel where the particle visualization was carried out is $0.8 \, (\mu m/s)/(V/cm)$ for the DNA buffer solution.

We still use the bead-spring worm-like chain for the Brownian dynamics simulation. The same procedures were taken as [Juang04] except we added the contribution from the electroosmotic flow.

For both extensional flow and mixed-shear flows, the calculated configurational changes from our coarse-grain molecular simulation could match the experimental results well with appropriate initial DNA conformations as shown in Figures 4.6(a) and (b).
4.3 DNA Stretching in Converging/Diverging Channel with Electrophoresis

Figure 4.6 shows the dimensions of this 2D converging/diverging channel. The distance between the two reservoirs is around 1.5 cm, while the width of the small end is only 20 μm. The aspect ratio is 750, which is too large for our finite element simulation because the number of elements for this domain becomes too large.

![Figure 4.6: Dimension for the converging/diverging channel in experiments.](image)

From Figure 3.25, we know that the electric field in the center line is nearly constant when the distance away from the diverging channel is around 10 times of the width of the small end of the converging channel. Thus we can use a shorter channel shown in Figure 4.7(a), which is nondimensionalized by the width of the small end of the converging channel. In this problem, the characteristic length is 20 μm, but the characteristic electric field is unknown because we use a different geometry instead of the one in experiment. Here we use a method shown in Figure 4.7(b) to determine the characteristic electric field.
Figure 4.7: (a) Dimensionless geometry of the converging/diverging channel for simulation; (b) Method to determine the characteristic electric field.

For the charged particle in an electric field (without any other forces and the surrounding fluid is stagnant), its velocity $\mathbf{u}_p = \mu_{ep} \mathbf{E}$. Thus $|\mathbf{u}_p|/|\mathbf{E}| = \mu_{ep}$, which is only dependent on the viscosity, pH value and ion strength of the solution. If we use the same buffer solution in two experiments: one in a straight channel and the other in a converging/diverging channel, and measure the particle velocity at a location far away from the converging channel. Thus we will get the following relation:

$$\frac{u_{p,1}}{u_{p,2}} = \frac{E_1}{E_2}$$  \hspace{1cm} (4.7)$$

where $u_{p,1}$ and $u_{p,2}$ are the particle velocity in the first and second experiments, and $E_1$ and $E_2$ are the dimensional electric field at these two experiments. Thus we can get the
electric field at a location far away from the small end in the converging/diverging channel:

\[ E_2 = u_{p,z}E_t / u_{p,1} \]  

(4.8)

We can define \( E_S \) as a simulated electric field (far away from the small end) using the new geometry with the finite element method. The characteristic electric field \( E_C \), can then be chosen as \( E_C = E_2 / E_S \), which will be used for the Brownian dynamics simulation for DNA stretching in this converging/diverging channel.

If we only consider the external electric field for the DNA dynamics in the converging/diverging channel, the governing equation for a bead-rod chain movement (4.3) would be changed to

\[
\frac{db_i}{dt} = E_0E_i + f_{i \text{random}} + f_{i \text{spring, total}}
\]  

(4.9)

where \( E_0 = qE_C \frac{b_K}{k_B T} = \frac{q}{\xi} \frac{E_C b_K}{k_B T} \) is the only parameter we need to know. Since \( \mu_{EP} = \frac{q}{\xi} \) is the EP mobility and can be measured in experiments and the drag coefficient \( \xi \) can be determined by the formula in [Larson05], the value of \( E_0 \) can be calculated as long as the characteristic electric field is known.

Figure 4.8 shows the experimentally measured stretching of a DNA molecule and its center of mass locations at 8 time points. The imposed electric field was around 60 V/cm. We can see that the DNA molecule was stretched gradually by the electric field to the length around 11 \( \mu \)m.
Since we did not measure the characteristic electric field, neither quantitative or qualitative comparison between the simulation and experiments can be carried out. In simulation, we choose $E_0 = -500$ and $-2000$.

Figure 4.9 shows the stretching of two bead-rod chains with the same initial configuration at $E_0 = -500$ (time step $\Delta t = 0.0001$). The $x$-axis is the $x$ location of the center of mass of the chains, and the $y$-axis shows the fractional visual stretch length (visual strength length divided by the contour length). These two DNA chains start on different electric lines. One starts at the point $(x_0, y_0) = (-4.9, 0)$ on the center line and the other starts on a higher location $(x_0, y_0) = (-4.9, 4.2)$. Both bead-rod chains are gradually stretched before approaching the small end, and then coil back outside the
converging channel. There are some slight differences in the configuration and length between these two chains. It seems that the chain on the center line (the solid line) is stretched to a length a little bit shorter than the one on a higher electric line (the dash line), but the maximum length of the DNA on the center line might not be recorded because of selected time period for data storage (i.e., data stored every 20,000 time steps).

![Figure 4.9: The stretching of two bead-rod chains on two electric lines (with the same initial configuration).](image)

Since the size of the small channel end is around 20 μm, much larger than the DNA persistence length of 67 nm. Thus we don’t consider any interactions between the beads and wall in our Brownian dynamics simulation.
In the next simulation, we keep the shape of the converging/diverging channel the same, but reduce the width of the small end to 200 nm. The conformations of a bead-rod chain at different time for $E_0 = -2000$ are shown in Figures 4.10(a)–(f) (dimensionless time are $t = 1, 1.5, 1.8, 2.0, 2.2, \text{and } 2.7$). The “coil-stretch-recoil” phenomenon is also observed in this electrophoretic driven nano-converging/diverging flow. The DNA chain is gradually stretched until it reaches the small end. It seems that the DNA chain is pulled out of the converging channel fragments by fragments. And the fragments outside the converging channel coils back quickly even other fragments inside the converging channel are still stretched.

(Figure 4.10 continued)
(Figure 4.10 continued)
Figure 4.10: DNA conformation in the electrophoretic driven nano-converging/diverging flow at different time.
CHAPTER 5

CONCLUSIONS AND RECOMMENDATIONS

In this chapter, we will summarize the major issues and results in the previous chapters and give some suggestions on the future work.

5.1 Conclusions

In this dissertation, the dynamics (conformation change and movement) of single DNA molecules in both hydrodynamic and electrokinetic flows are studied. The electrokinetically induced flow profiles in the complex geometries are obtained by solving the governing equations using the finite element method. The solutions are used as the input for the Brownian dynamics simulations on the dynamics of single DNA molecules. We have reached the following conclusions:

(1) Electrokinetic forces are more suitable for driving the fluid flow or controlling (moving, trapping, separating, and mixing, etc.) the motions of charged or uncharged particles in micro/nano-scales than the hydrodynamic forces.

(2) The finite element method has been used to solve the Poisson-Boltzmann equation and the Navier-Stokes equations for the EOF velocity and electric field. The simulation results agree well with the analytical solution and experiments in different microfluidic channels or devices.
(3) In the electrokinetic flows, the electrokinetic interactions affect the movement of the charged particles. The conventional surface charge patterning method can not always control the movements of the charged particles the same way as the uncharged particles. The five-cross design without any charge patterning on the surface, however, can generate different flow patterns to control the motion of charged particles.

(4) Understanding of the dynamics of single DNA molecules is very important both in the academic research and for the biomedical applications. As a coarse-grained method, the Brownian dynamics simulation can be used to simulate the motion of long chain DNA molecules in an affordable and efficient way. Both the bead-spring and bead-rod chain models can capture the dynamics of single DNA molecules in either the hydrodynamic flow or the electrokinetic flow. The simulation results agree qualitatively with the experiments in the cross-slot and five-cross flows.

5.2 Recommendations

In this section, we will discuss some issues which haven’t been considered or fully explored in the previous chapters. More basic analysis in these areas are very important in both academic research and real applications.

5.2.1 Hydrodynamic Interactions

In the previous work, we neglected the bead-bead and bead-wall hydrodynamic interactions (HI) in the Brownian dynamics simulation. But when the distance between any two beads or between the bead and wall is comparable with the persistence length,
we need to consider the hydrodynamic interactions to fully understand the behavior of DNA molecules in the highly confined geometry.

The Brownian dynamics simulations considering the analytical solutions for the hydrodynamic interactions have been carried out by [Ermak78, Hiesh03, Larson05]. As mentioned in Chapter 2, the analytical solutions for HI only exist for the simple flows (such as the flow in the bulk or the flow past a flat plane). For the flows in more complicated geometry, we need to use the numerical method to calculate the hydrodynamic interaction. Here, we only address the HI effect on the particle flow and the similar approach can be extended to the Brownian dynamics simulation of DNA chain considering the hydrodynamic interactions.

First, let us review the original description of the HI of a moving spherical particle to the surrounding stagnant bulk fluid. Since the flow domain is infinite, we can set up a coordinates at the center of the particle and then the fluid far away from the particle is moving with the same speed as the particle, but in the opposite direction (assuming a uniform flow velocity in the far-away domain is $u_\infty$). The velocity profile near the spherical object is not constant because the flow cannot penetrate the object. The velocity distribution can be obtained by solving the Stokes equation (since the Reynolds number is very small). By following the textbooks [Batchelor67, Happel83, Bird77a, Dhont96], we have the flow velocity

$$u = u_\infty + \Theta \cdot F$$

(5.1)

where $\Theta = \frac{1}{8 \pi \eta} \left( \frac{1}{r} - \frac{rr}{r^3} \right)$ is the so-called Oseen tensor, $r$ is the location vector in the fluid, $I$ is the unit tensor, and $F = 6 \pi \eta a U$ is the Stokes friction force acting on the
particle by the flow field (also we need exert an opposite force on the particle to keep the particle from moving), where $a$ is the radius of the spherical particle.

Now we turn back to the original problem, where the particle is moving with the velocity $-u_\infty$ and the fluid in infinity is stagnant. The near-field perturbed fluid flow velocity needs to add the particle’s velocity $-u_\infty$, thus the perturbed flow velocity is $u' = \Theta \cdot F$ and it is called the hydrodynamic interaction velocity in the bulk fluid. There is no analytical solution for the HI velocity in arbitrary geometry and we need to use the numerical method to calculate it.

However, the calculation of the HI velocity is very complicated. Ye and Li studied the EP motion of a charged spherical particle in a T-shaped rectangular channel [Ye04]. The movement of the particle (or the boundary of the particle) is unknown beforehand and the whole geometry is divided into the fluid domain and the particle domain. At each time step, the flow in the fluid domain needs to be calculated first, and then the pressure on the particle needs to be integrated to calculate the force and momentum on the particle. Finally, the movement of the particle is determined to get the new boundary for the fluid domain. This approach is essentially one of the Eulerian-Lagrangian methods and it needs to redraw the mesh at each time due to the moving particle boundary. Thus, this finite element method is very complicated. For a system consisting of thousands of such particles, this approach by directly simulation is nearly impossible. There is a need of new methods to simulate the HI velocity in a fast but still accurate way. A so-called the “Smoothed Profile Method” (SPM) with HI method [Nakayama05] may be a good choice. This method overcomes the problem of the interface tracking in the conventional Eulerian-Lagrangian method. It captures the interface (similar to the Level set method) in
an easy way and doesn’t need to reconstruct the mesh with time. By assuming a
smoothed profile (function) with finite thickness for the solid-liquid interface, the
positions of particles can be found by solving the continuous profile function
\[ \varphi(x,t) = \sum_{i=1}^{N} \varphi_i(x,t) \]
with time, which is the combination of all the particles’ profiles. At
the same time, we can get a continuous field for particle velocity \( u_p \) after introducing the
continuous profile function. And the total velocity \( u = (1 - \varphi)u_f + \varphi u_p \) is the ensemble
average of the particle and fluid velocity.

From the condition \( \nabla \cdot u_f = \nabla \cdot u_p = 0 \), the profile function satisfies the solid-fluid
impermeability condition:
\[ \nabla \cdot u = \nabla \varphi \cdot (u_p - u_f) \]  \hspace{1cm} (5.2)
where \( u_f \) is the velocity for fluid. If this equation is solved, we can solve the profile
function with time, thus getting the particle locations.

The governing equations (e.g., the N-S equation) on the fluid field can be rewritten
to the equations on the total velocity with the profile function (for more details, please see
[Nakayama05]). Then using the similar approach to [Ye04] but without reconstructing
the mesh, we can determine the particle location and the velocity field.

5.2.2 Excluded Volume (EV) Force

The hydrodynamic interactions between the beads and the wall should be considered
when the width of the small end is comparable to the DNA persistence length. Also the
repulsive excluded volume (EV) force between the bead and wall needs to be considered
when the distance between the bead and wall is comparable to the effective bead radius, which is given by the Stokes formula \( a = \frac{\xi}{6\pi \eta} \), where \( \xi \) is the drag coefficient, \( \eta \) is the viscosity of the fluid. The schematic of the repulsive EV force between a bead-rod chain and the wall is shown in Figure 4.11.

The repulsive EV force between the bead and the wall has been studied by several research groups [Deutsch89, Patel03, Streek04]. In general, there are two kinds of repulsive forces: one is obtained by the truncated Lennard-Jones model and the other is the hard core repulsive force.

Figure 5.1: Schematic for the EV force between a bead-rod chain and the wall.

(1) Truncated Lennard-Jones (L-J) potential [Patel03, Streek04]

For the EV force using the truncated Lennard-Jones model, the truncated Lennard-Jones potential \( U_{EV} \) (the conventional L-J potential has singularity points) is given as
\[ U^{EV}_d = \begin{cases} 
4 \varepsilon k_B T \left( \left( \frac{\sigma}{d} \right)^{12} - \left( \frac{\sigma}{d} \right)^6 + \frac{1}{4} \right), & (d/\sigma)^6 \leq 2 \\
0, & \text{otherwise} 
\end{cases} \]

where \( \varepsilon \) is the parameter on the energy, \( d \) is the distance between the bead and the wall surface, \( \sigma = 4a \) is L-J radius.

(2) Hard core repulsive force [Deutsch89]

\[ F^{EV}_d = \begin{cases} 
Ad \left[ \frac{1}{d^2 - d_c^2} - \frac{1}{3d_c^2} \right]^2, & d \in (d_c, 2d_c) \\
0, & d > 2d_c 
\end{cases} \]

where \( A \) is the strength of the EV potential and \( d_c \) is the critical distance.

The EV force can be obtained by solving the derivative of the EV potential, i.e.,

\[ F^{EV} = -\nabla U^{EV}. \]

Both EV force models have been successfully used for the simulation of the DNA separation in gel electrophoresis. Thus we can use them for the repulsive force between the bead and wall in the future.

5.2.3 DNA Stretching on Patterned Surface

Molecular combing has been used to stretch and align DNA molecules on a flat or pattern surface by the dewetting of DNA solution on the hydrophobic surface [Ondarçuhu99, Otobe01, Petit03]. Recently, Guan and Lee [Guan05] demonstrated that by using the patterned micro-well arrays (diameter for each well is 5 \( \mu m \) and the center to center distance is 10 \( \mu m \)), the DNA molecules can be stretched and aligned regularly to form the DNA nanowires as shown in Figures 5.2(a) and (b).
The procedures to create these two different DNA nanowires are shown in Figure 5.3. First, the PDMS microwell stamp is pressured to a drop of DNA solution on a flat glass substrate to make each well filled with the DNA solution. Then the stamp is peeled from the substrate. If the peeling speed is slow, the short DNA nanowires can be obtained; and if the peeling speed is fast enough, the long DNA nanowires (two neighboring DNA molecules connect together to form a bundle) are formed. The patterned DNA nanowires can be transferred to glass or mica for gene mapping or genetic analysis or diagnosis.
Figure 5.3: Procedures to get the short and long DNA nanowires (reprinted permission from [Guan05]).

The mechanism of the formation of the DNA nanowires on the patterned microwell arrays can be inferred from Figure 5.4. Since the PDMS stamp is hydrophobic, the contact line outside the microwell recedes faster than that inside the microwell, thus squeezing the DNA molecules in the microwell together (steps 1 to 3). With the meniscus breaks after the contact line touches the right edge of the microwell, one end of the DNA
molecule is attached in one microwell, while the other end is still free to move temporarily. The velocity gradient near the contact line is very large and it will stretch the DNA molecules (step 4). The contact line is still moving and the other end of the DNA molecule will finally attach to another microwell (step 5), thus forming a DNA nanowire.

Figure 5.4: Mechanism of the formation of DNA nanowires (reprinted permission from [Guan05]).
To simulate the stretching and alignment of the DNA molecules in the microwell arrays is not an easy task. There are several issues to be solved:

(1) First, we need to solve a free surface problem for this 3D complicated system. The shape of the moving contact line and the flow field are very difficult to calculate using the finite element or finite difference method. But some finite volume based methods such as the VOF (volume of fluid) [Scardovelli99] and the level set methods [Sethian99] can solve this problem in an easier way. We may also use commercial software to calculate the flow field and the location and the shape of the contact line at each time step.

(2) Second, DNA dynamics near the breakage of the contact line needs to be handled carefully. Theoretically, the thickness of the DNA solution film is nearly zero before it breaks. But in the simulation of a free surface, the shape of the contact line near the break point couldn’t be captured so accurately as at other locations. Also the flow field near the break point cannot be calculated precisely. Thus, we should be careful about the unrealistic behaviors of the DNA molecules near the break point. To describe the attachment of the DNA molecules on the solid surface, probably we need to use the similar method as that in [Chopra03]. That is, when the distance between a DNA molecule and the surface wall is less than a prescribed critical distance, we need to immobilize the DNA in the simulation and assume it has been attached.

(3) Third, interactions between the wall and the DNA molecules need to be properly simplified in the simulation in order to save the computational time. There are many interactions between the beads and the solid wall. Hydrodynamic interaction and the excluded volume force coming from the solid wall need to be considered in an indirect
way. That is, we might incorporate these interactions into other terms such as the drag force by increasing the effective drag coefficient. To directly simulate the hydrodynamic interaction or the excluded volume force in this problem will make the simulation more time-consuming and complicated, while it might not improve the accuracy. Although the quantitative comparison between the simulation and the experiments may not be achievable, the qualitative results may be obtained in simulation by properly adjust some parameters.


