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Using Coriolis Force to Facilitate Molecular Transportation and Fluid Mixing in

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This Thesis is dedicated to my Mom and Dad.
ABSTRACT OF THE THESIS

Using Coriolis Force to Facilitate Molecular Transportation and Fluid Mixing in CD Microfluidics Platform

by

Dhruv Bharatkumar Patel
Master of Science in Aerospace Engineering
San Diego State University, 2012

This study investigates the influence of Coriolis force on transport and hybridization of DNA molecules and fluid mixing in compact disk (CD) microfluidic platform where centrifugal force is used as the driving force. While the effect of Coriolis force on fluid flow in CD microfluidic channels has been studied experimentally and numerically only recently, its influence on DNA molecule migration and hybridization and on fluid mixing has not been investigated so far. This study addresses this phenomenon through numerical simulation and demonstrates that for most practical geometrical configurations and angular velocity ranges reported in the literature, the Coriolis force introduces significant qualitative and quantitative spatial variations in the hybridization of DNA molecules, particularly at locations near the periphery. In a particular example investigated here, hybridization was observed to reach steady-state at some locations in about half the time required in the absence of Coriolis force. However, our results further indicate that the time frame for hybridization is so fast (< 1 sec) that the effect due to Coriolis force on the location of hybridization is more important than time of hybridization. Our results indicate that for low viscosity fluids, angular velocities as low as 25 rad/sec could introduce Coriolis force that is as high as at least 25% of the main driving centrifugal force. As for the fluid mixing under microchannel with and without obstacles significant amount of fluid mixing efficiency is observed for both kind of channel, the results demonstrates that at higher omega for channel with obstacle has more mixing efficiency then without obstacles.
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I also thank my Lab mates and friends for helping me to understand the things especially which were related to bioengineering.
CHAPTER 1

INTRODUCTION

1.1 WHAT IS MICROFLUIDICS?

Microelectronics was the most significant enabling technology of the last century. With integrated circuits and progress in information, microelectronic has changed the way we work, discover and invent. From its inception through late 1990’s miniaturization in microelectronics followed Moore’s Law doubling the integration density every 18 months. Presently poised at the limit of photolithography technology this pace will slow down to doubling integration density every 24 months.

In late 1970s the silicon technology was extended to machining mechanical microdevices, which later came to know as MEMS (Microelectronics and Mechanical System). With fluidics and optical in microdevices, Microsystem Technology (MST) is a more accurate description. The Development of microflow sensor, micropumps and microvalves in early 1980s dominated the early stages of microfluidics. Several competing term such as ‘Microfluidics’, ‘MEMS- fluidics’, ‘Bio- MEMS’ appeared for the research discipline which was dealing with the transport phenomena and fluid devices at microscopic level. (See Figure 1.1 [28]).

Microfluidics Devices need not to be silicon-based fabricated using silicon based machining technology. The main advantage of the microfluidics is to use scaling law for better performance and this can be derived by microscopic amount of fluid which a microfluidics device can handle. Regardless of the material and instrument used for machining the micro-device only the part where fluid is processed need to be miniaturized. Handling the fluid is the main key aspect of the microfluidics, miniaturizing the whole system is often beneficial but is not a requirement of the microfluidics devices. The term microfluidics does not necessarily means its fluid mechanics system but it rather refers to as the small scale causing change in the fluid behavior [28].

### 1.2 Basic Principle of Microfluidics

There are two common methods by which fluid actuation through microchannel can be achieved:

a. **Pressure Driven Flow:** In pressure driven flow, in which the fluid is pumped through the device via positive displacement pumps, such as syringe pumps. One of the basic laws of fluid mechanics for pressure driven laminar flow, the so-called no-slip boundary condition, states that the fluid velocity at the walls must be zero. This produces parabolic velocity profile within the channel [33] (as shown in Figure 1.2 [33]).

The parabolic velocity profile has significant implications for the distribution of molecules transported within a channel. Pressure driven flow can be a relative inexpensive and quite reproducible approach to pumping fluids through microdevices [33].

b. **Electrokinetic Flow:** Another common method for transferring fluid in microchannel is through electro-osmotic pumping in open microchannel. In such channel if the walls of the channel as the electric charge as most surface do then on applying the electric field the ion moves towards the electrodes of the opposite polarity in the open channel. This will create the motion of the fluid via viscous force into convective motion of the fluid in the channel; if the channel is open the velocity profile remains uniform along the width of the channel [33]. (See Figure 1.3 [33]).

If the channel is closed or back pressure exist in the channel the recirculation will appear in the channel causing the velocity profile at the center of the channel to move on the opposite direction to that of the flow [33]. (See Figure 1.4 [33]).

### 1.3 Modeling Diffusion

The diffusion process can be described as in terms of Fick’s first law and second law:

a. **Fick’s First Law:** Fick’s postulated that diffusion in one direction, the flow; $J$ of a substance through a plane perpendicular to the direction of the diffusion is directly

proportional to the rate of change of concentration with distance $\frac{dC}{dx}$, the concentration gradient and the equation is given as follows;

$$J = -D\frac{dC}{dx} \quad (1.1)$$

Where; $J$ is the flux (the rate of mass flow rate per unit area in direction x in g mol/cm$^2$/s), $D$ is the diffusion coefficient in cm$^2$/s and $C$ is the concentration of the solute in g mol/cm$^3$ [1].

b. Fick’s Second Law: For solving most of the diffusion cases the first law is insufficient because usually the diffusion value is unknown, and this can be better handled by the Fick’s second law, given as;

$$\frac{dC}{dt} = D\frac{d^2C}{dx^2} \quad (1.2)$$

Where; $C$ is the concentration and $t$ is the time.

According to the equation the time rate of change of concentration is equal to the spatial rate of change of direction of the concentration gradient. When both flow and diffusion occurs the time rate of change of concentration can be given as following equation;

$$\frac{dC}{dt} = D\frac{d^2C}{dx^2} = -v\frac{dC}{dt} \quad (1.3)$$

Where, $v$ is the velocity of the flow in x direction [1].

1.4 CD MICROFLUIDICS

Microflow can be actuated by rotational (Centrifugal and Coriolis force) forces by spinning the microfluidic network on the Compact Disk. Such type of flow actuation is known as CD Microfluidics. CD Microfluidics has gained considerable attention owing to
biomedical application. Its prime advantages lies in handling large varieties of sample liquid, ability to gate the flow of the liquid, simple rotational motor requirement and large range of the flow rates can be attained. For low rotational speed (ignoring Coriolis force) the governing equation for the rotating frame can be described by using the pressure gradient [6].

\[
\frac{\partial P}{\partial x} = \frac{\partial p}{\partial x} - 2\omega x
\]  

(1.4)

Where; \(\omega\) is angular velocity of rotation and \(x\) is the distance from the center of the rotation, although the force is function of radial coordinate, the flow attains the fully developed condition and the parabolic velocity profile is attained. The discharge rate \(Q\) is obtained by integrating velocity profile over the cross-section area \(A\) [6].

\[
Q = \frac{\rho \omega^2 \overline{r} \Delta r AD^2 h}{32 \mu L}
\]  

(1.5)

Where, \(D_h\) is the hydraulic diameter of the channel, \(\overline{r}\) is the distance from the center of the CD, \(\Delta r\) is the radial extent of the fluid, \(L\) is the length of the liquid in the liquid channel, \(\rho\) is the density of the liquid and \(\mu\) is the dynamic viscosity of the liquid [6]. (See Figure 1.5 [6]).

1.5 Coriolis Effect

Coriolis force is felt by an observer who is on rotating frame of reference and moves inward or outward from its position or axis. It acts perpendicular to the motion of the observer or to that of rotating axis. In vector notation the Coriolis force can be determined as

$$ F_c = -2m \overline{\omega} \times \overline{V} $$

(1.6)

If body on the earth moves northern hemisphere then due to Coriolis force it drives toward the east and for southern hemisphere to moves toward west. The reason for the contrary deflection is the body moving towards the north always falls ahead of the earth circumferential velocity and body travelling towards the south fall behind the earth circumferential velocity [2]. (See Figure 1.6 [2]).

CHAPTER 2

LITERATURE SURVEY

Over the past several years, research and commercial development interest in CD microfluidic platforms has experienced a significant increase [13, 20, 24, 25, 27, 34]. Further, there has been a noticeable expansion of the reported application of such platforms to new areas such as complete sample-to-answer systems in molecular clinical diagnostics, blood separation, gene sequencing and gene profiling systems [20, 23, 26, 32]. The most important driving force for this increased interest in the platform is the absence of moving parts that simplify fabrication as well as operation of devices. The physics of fluid flow in such platforms through centrifugal force that provides the driving pressure gradient has been studied extensively through experiments and numerical models by several researchers [20, 24, 34]. However, it was only recently that the effect of Coriolis force on fluid flow was demonstrated and quantitatively determined by Brenner, Zengerle, and Ducrée [5] and Ducrée et al. [12] who used a rotating frame of reference for a CD platform rotated by an angular velocity. The work of Brenner, Zengerle, and Ducrée [5] as well as Ducrée et al. [12] showed that Coriolis force introduces a significant change in fluid velocity which is conveniently adopted as a fluid flow switch [5] and mixer [12].

Figure 2.1 illustrates typical geometry parameters and forces acting on a CD microfluidic platform. Centrifugal force creates an artificial gravity - and hence a pressure gradient - pointing in the radial direction of the channels. This force scales with the square of the frequency of the angular velocity at which the channel is rotated. Coriolis force, on the other hand, is induced when the resulting fluid flow is observed from a rotating non-inertial reference frame. This apparent force acts perpendicular to the plane of the flow channel and the angular velocity. As a result, the fluid experiences pumping in a radial direction due to centrifugal force but its direction and magnitude are further modified by the radial and tangential components of Coriolis force. As will be shown later in section 2, Coriolis force depends linearly on the angular velocity ($\omega$) and varies with the square of the channel width. For a fluid of dynamic viscosity ‘$\eta$’ and density ‘$\rho$’ flowing in a channel of width ‘$b$’ on a
CD platform rotating at angular velocity of \( \omega \)', it can be shown that the ratio of Coriolis force to centrifugal force can be approximated as \( \frac{F_{\text{Coriolis}}}{F_{\text{Centrifugal}}} = \frac{\rho b^2 \omega}{4h} \) [12].

This ratio is an important indicator of the potential effect Coriolis force has on fluid flow in a CD platform (see Figure 2.2 [12]). Figure 2.3 presents a family of curves corresponding to different angular velocities demonstrating the effect of channel width on Coriolis force. Figure 2.2 [12] demonstrates that even at lower angular velocities in the range of 25 rad/sec, Coriolis force could be significant (25% of the centrifugal force) if the channel widths are moderately wide (in the range of 200 microns).

To provide a perspective to the range of dimensions used in recently published works in CD microfluidic platforms, Table 2.1 summarizes some of the typical CD microchannel configurations reported along with angular velocities. The width of channels varies from 20\( \mu \)m [4] to 500\( \mu \)m [22, 25] whereas the depth of channels varies from 34\( \mu \)m [27] to 1000\( \mu \)m [31]. The variation of lengths is from 8.4mm [10] to 21 mm [4, 11]. Angular velocity variations from 40 rad/sec (~400 rpm) [25] to 950 rad/sec (9500 rpm) [10] have been reported. Table 2.1 suggests that the variations in dimensions of microchannels, particularly width and depth, used by different researchers are in the order of 25 times or more. This, in turn, translates to substantial variations in fluid velocities. Figure 2.2 plots these results reported in the literature on a graph of angular velocity vs. width and depicts which results fall in a region where Coriolis force exceeds the driving centrifugal force (i.e. region A). Ranges where the Coriolis force is more than 50% and 25% of the main driving
Figure 2.2. The ratio of Coriolis to centrifugal force for various widths of channel ($F_{\text{Coriolis}}/F_{\text{Centrifugal}} = \rho b^2 \omega/4$). For a case of $\nu = 1e^{-3}$ Pa-s and $\rho = 1000$Kg/m$^3$, $F_{\text{Coriolis}}/F_{\text{Centrifugal}} = 2.5e5 \, b^2 \omega$. Source: Ducrée, Jens, Thilo Brener, Thomas Glatzel, and Roland Zengerle. “Coriolis-Induced Switching and Mixing of Laminar Flows in Rotating Microchannels.” Paper presented at the Proceedings of Micro Technology, Munich, Germany, October 2003.

Figure 2.3. Effect of width and angular velocity on the dominance of Coriolis force.
Table 2.1. Summary of Recent Results in Flow Rate and Velocity in CD Microfluidic Platform Reported in the Literature

<table>
<thead>
<tr>
<th>Authors</th>
<th>Width (µm)</th>
<th>Depth (µm)</th>
<th>Length (mm)</th>
<th>Ang. Velocity (rpm)</th>
<th>Ang. Velocity (ω) – rad/sec</th>
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<tbody>
<tr>
<td>Madou et al. [27]</td>
<td>150</td>
<td>34</td>
<td>--</td>
<td>524 – 1126</td>
<td>50 -100</td>
</tr>
<tr>
<td>Madou et al. [25]</td>
<td>20-500</td>
<td>16-340</td>
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<td>400-1600</td>
<td>40-160</td>
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<tr>
<td>Kim et al. [23]</td>
<td>50</td>
<td>40</td>
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<td>500</td>
<td>50</td>
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<tr>
<td>Ducree et al. [12]</td>
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<td>---</td>
<td>1000</td>
<td>100</td>
</tr>
<tr>
<td>Kim et al. [22]</td>
<td>500</td>
<td>50, 18 or 8</td>
<td>15</td>
<td>---</td>
<td>fixed velocity of 0.67 mm/s</td>
</tr>
<tr>
<td>Kim et al. [21]</td>
<td>215</td>
<td>80</td>
<td>13</td>
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<td>Riegger et al. [31]</td>
<td>30</td>
<td>1000</td>
<td>10</td>
<td>6300 – 9500</td>
<td>630-950</td>
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<td>Ducrée et al. [10]</td>
<td>250</td>
<td>150</td>
<td>8.4</td>
<td>3000</td>
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<td>Brenner, Zengerle, and Ducrée [5]</td>
<td>360</td>
<td>125</td>
<td>10.1</td>
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<td>Riegger et al. [30]</td>
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<td>400,800</td>
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<td>6000</td>
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<td>300-700</td>
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<td>Haeberle et al. [15]</td>
<td>300</td>
<td>85</td>
<td>32</td>
<td>2500</td>
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<tr>
<td>Brenner et al. [3]</td>
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<td>25</td>
<td>50</td>
<td>10000</td>
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<tr>
<td>Cho et al. [7]</td>
<td>127-762</td>
<td>60-800</td>
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<td>600-1500</td>
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force of centrifugal force are indicated as region B and C, respectively. It is instructive to note that a significant number of results reported in the literature fall in regions A, B, and C suggesting that their corresponding Coriolis forces are 25% - 100% of the centrifugal force.

As this CD fluidics platform is finding increasing research and commercial interests in molecular clinical diagnostics, an accurate understanding of the hybridization of single-stranded DNA molecules (ssDNA) as affected by all the body forces acting on the fluid medium such as Coriolis force becomes more important. There are currently several research publications that model the hybridization of ssDNA molecules in microarray format [8, 9, 19, 22]. However, research in the modeling of DNA hybridization phenomenon in CD microfluidic platform is extremely rare.

Further, to the best of our knowledge, the influence of Coriolis force on the migration and hybridization phenomenon of DNA molecules, particularly on the distribution of hybridization region, has not been reported in the literature yet. In this paper, therefore, we present a numerical model for the transport and hybridization of DNA in CD microfluidic platform. We demonstrate that as the angular rotation of the CD platform increases, the rate of hybridization experiences a qualitative as well as a quantitative change resulting in increased hybridization at the peripheries. This has implications in the design of the location of the probes as well as the detection system. The paper is arranged in the following fashion: section 1 presents introduction; section 2 presents the numerical model development; section 3 covers the solution of the developed model; section 4 presents numerical results and their discussion followed by section 5 which presents experimental results and section 6 which outlines concluding remarks.

Results reported in the literature are indicated in Figure 2.3 with their position on the graph corresponding to their respective angular velocity and channel width. Three different scenarios corresponding to cut-off values of 25, 50, and 100% are considered for $\frac{F_{\text{Coriolis}}}{F_{\text{Centrifugal}}}$ ratio to demonstrate where Coriolis force is significant enough to affect flow patterns in published results. Region C represents the range where Coriolis force is between 25%-50% of centrifugal force. Region B indicates the ranges where the Coriolis force is between 50% and 100% of centrifugal force, while Region A represents the region where the Coriolis force is more than 100% of centrifugal force.
CHAPTER 3

MULTIPHYSICS MODEL DEVELOPMENT

The modeling of migration and hybridization of single-stranded DNA molecules in CD microfluidic platform requires the consideration of multi-physics phenomenon. To illustrate our discussion, we consider a generic CD microfluidic platform shown in Figure 1.1.

The first physics is that of fluid flow that is described by the continuity equations and Navier-Stokes equation for incompressible flow (Eq. 3.1.a-b). However, the body force term in the conventional Navier-Stokes equation includes the centrifugal as well as the Coriolis forces as shown in Eq. 3.1.c and 3.1.d. The second physics involves the advective transport of DNA molecules through microchannels as described by Nernst-Planck equation (Eq. 3.2). The transport is enabled by Brownian diffusion and convective fluid flow. The third set of equations consists of hybridization model for ssDNA (single-stranded DNA) that in turn includes equilibrium equation of DNA association and dissociation and the transient first-order heterogeneous hybridization reaction rate equation (Eq. 3.1.a – b). To keep track of the concentration of hybridized double-stranded DNA (dsDNA) that accumulates on the capture surfaces, a diffusion-only model is added (Eq. 3.1.c) [18].

For clarity, the physics and chemical equilibrium reactions considered in this study are grouped below under three classifications, namely, (i) fluid dynamic system, (ii) DNA migration physics, and (iii) DNA hybridization physics. Taken together, these equations developed below describe DNA molecule transport and hybridization processes that occur in CD microfluidic platforms under the combined effects of centrifugal and Coriolis forces. The model assumes 3-dimensional formulations as the capture probes in typical hybridization channels are placed on the bottom floor of the channel in a 2-dimensional plane with fluid flow passing over them in a 3-D fashion. Further, assumptions of 2-dimension are invalid as the Coriolis force is a function of two of the planar coordinates only whereas the fluid flow is 3-dimensional. Note that Coriolis force exists only in the plane of angular rotation. Here, as
can be seen clearly from Eqs. (3.1.c) and (3.1.d), centrifugal force scales with the square of the angular velocity while Coriolis force is a linear function of the angular velocity.

### 3.1 Fluid Dynamics System

The Navier–Stoke’s equations which are defined here to include the continuity equation and equation of momentum conservation are given as

\[ \nabla \cdot \mathbf{u} = 0 \quad \text{(Continuity Equation)} \quad (3.1.a) \]

\[
\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla p + \mu \nabla^2 \mathbf{u} - \rho \mathbf{\omega} \times (\mathbf{\omega} \times \mathbf{r}) - 2\rho \mathbf{\omega} \times \mathbf{\dot{r}} \quad \text{(Momentum Equation)} \quad (3.1.b)
\]

Centrifugal and Coriolis forces given by \( \rho \mathbf{\omega} \times (\mathbf{\omega} \times \mathbf{r}) \) and \( 2\rho \mathbf{\omega} \times \mathbf{U} \), respectively, from the total body forces on the bulk fluid, these forces can further be broken down to their x-, y-, and z-components.

\[
F_x = \rho \times \omega^2 \times x + 2 \times \omega \times v \quad (3.1.c)
\]

\[
F_y = \rho \times \omega^2 \times y - 2 \times \omega \times u \quad (3.1.d)
\]

\[
F_z = 0 \quad (3.1.e)
\]

Where,

- \( p \) – fluid pressure, \( t \) – time, \( \mathbf{U} \) – velocity field, \( \mu \) – viscosity, \( \rho \) – density of fluid, \( u \) – velocity in the x-direction, \( v \) – velocity in the y-direction, and \( \omega \) = angular velocity in the x-y plane.

### 3.2 Migration of DNA Molecules

The movement of ssDNA molecules in the domain is governed by convective-diffusive transport equation that accounts for diffusion and convection and is given as:

\[
\frac{\partial c_{\text{DNA}}}{\partial t} + \nabla \cdot (-D_{\text{DNA}} \nabla c_{\text{DNA}}) = R - u \cdot \nabla c_{\text{DNA}} \quad \text{(Nernst-Planck Equation)} \quad (3.2)
\]

Where \( C_{\text{DNA}} \) is concentration of ssDNA molecules in the microarray and \( D_{\text{DNA}} \) is diffusion rate of DNA molecules. \( R \) is reaction term representing ssDNA species generated in the domain due to reaction (it is zero in this case).

### 3.3 DNA Hybridization Kinetics

DNA hybridization kinetics:

- The Non-specific Hybridization (also known as Non-specific binding or Non-specific absorption) takes place between the low affinity target and probe which does not have exact complementary sequence and this can lead to false signal on DNA array. But
still this non-specific absorption is very important as far as numerical modeling is concerned because DNA hybridization on the probe sites will be combination of specific and non–specific hybridization (Eq. 3.3.b and Eq. 3.3.c) (see Figure 3.1 [14]).

b. Hybridization of ssDNA Molecules: The binding of oligonucleotides (DNA, in our case) is governed by a chemical equilibrium reaction equation. The rate of this hybridization reaction is a function of all the concentrations of all species present in the overall chemical reaction at any given time and is given by the rate law (Eq. 3.3.a) [14]. Target ssDNA molecules from the sample immediately above the capture probe elements may hybridize with the immobilized DNA molecule directly [22] or may first be adsorbed onto the solid surface followed by diffusion over the surface and hybridization [14]. Taking into account only the direct DNA hybridization, the DNA heterogeneous hybridization reaction can be described by considering the chemical reaction given by Eq. 3.3.a. In this equation, the symbol $C_{DNA, Probes}$ represents single stranded DNA molecules immobilized on the solid surface that are available for hybridization (Figure 1.4). The target DNA molecules in the sample above the capture probes (represented by $C_{DNA}$) bind specifically to the DNA capture probes and form hybridized double-stranded DNA molecules (whose concentration is represented by $C_{DNA, Hybridized}$) on the surface of the capture elements [19].

$$
C_{DNA, Probes} + C_{DNA} \xrightarrow{K_a, DNA} C_{DNA, Hybridized} \xleftarrow{K_b, DNA} C_{DNA, Hybridized}
$$

(3.3.a)

Where $K_a, DNA$ is the forward reaction rate constant which governs the hybridization reaction rate and $K_b, DNA$ is the reverse reaction rate constant that determines the disassociation reaction rate.

The temporal variation of the concentration of hybridized double-stranded DNA molecules is given by a transient first-order reaction rate equation as shown below:

$$
\frac{dc_{DNA, Hybridized}}{dt} = K_b, DNA_S \times c_{DNA, Hybridized_S} - K_a, DNA_S \times c_{DNA_S} (c_{DNA, Initial} - c_{DNA, Hybridized_S})
$$

(3.3.b)

The term $C_{DNA, Initial}$ represents the initial concentration of the capture probes before hybridization.

Finally, a diffusion-only model is required to keep track of the hybridized double-stranded DNA (dsDNA) that accumulates on the capture surfaces as given in Eq. 3.3.c.

$$
\frac{dc_{DNA, Hybridized_Ns}}{dt} = K_b, DNA_{Ns} \times c_{DNA, Hybridized_{Ns}} - K_a, DNA_{Ns} \times c_{DNA_{Ns}} (c_{DNA, Initial} - c_{DNA, Hybridized_{Ns}})
$$

(3.3.c)

Where $\frac{dc_{DNA, Hybridized}}{dt}$ and $\frac{dc_{DNA, Hybridized_Ns}}{dt}$ represents the specific and non-specific rate of change of concentration with time, $D_{DNA, Hybridized}$ is the diffusion constant of hybridized double-stranded DNA (dsDNA) molecule and $R_{DNA}$ represents the reaction rate producing the hybridized double-stranded DNA molecule on this capture surface.
c. Introducing Dimensionless Variable [29]: The Chemical equilibrium equation is as follows:

\[
C_{DNA,Pr obes} + C_{DNA} \xrightarrow{K_{a, DNA}} C_{DNA,Hybridized} \leftarrow K_{b, DNA} \]

The Rate of Change of Concentration can be given as:

\[
\frac{\partial C}{\partial t} = K_{a, DNA} \times C_{DNA,Probes} (C_{DNA,Probe} - C_{DNA,Hybridized}) - K_{b, DNA} \times C_{DNA,Hybridized}
\]

Nernst Plank Equation:

\[
\frac{\partial C}{\partial t} + \nabla \cdot (-D_{DNA} \nabla C_{DNA}) = R - u \cdot \nabla C_{DNA}
\]

If the rate of reaction \(R=0\) and there is no convective flow, the change in concentration in cylindrical co-ordinate can be given as (see Figure 3.2 [29]);

\[
\frac{\partial C}{\partial t} = D \left[ \frac{\partial^2 C}{\partial r^2} + \frac{1}{r} \frac{\partial C}{\partial r} + \frac{\partial^2 C}{\partial y^2} \right]
\]

Where; \(D\) = diffusion constant; \(r\) = radial distance, \(d\) = thickness of the cylindrical co-ordinate and \(a\) = hybridized spot radius.
Let’s introduce the dimensionless parameter;

\[
y' = \frac{y}{d}; \quad r' = \frac{r}{a}; \quad C' = \frac{C}{C_0}; \quad C_{DNA} = \frac{C_{DNA}}{C_{DNA,\text{max}}}
\]

So it becomes the following equation

\[
\frac{\partial C'}{\partial t'} = D \left[ \frac{1}{2} \left( \frac{\partial^2 C'}{\partial r'^2} + \frac{1}{r'} \frac{\partial C'}{\partial r'} \right) + \frac{\partial^2 C'}{\partial y'^2} \right]
\]

If \( \frac{\partial C'}{\partial y'} \bigg|_{y'=0} = \frac{1}{C'} \frac{\partial C_{DNA}}{\partial t'} \)

Therefore, the rate of change of concentration can be given as;

\[
\frac{\partial C_{DNA}}{\partial t'} = \frac{D_a C_0'}{\gamma_a} \left( \gamma_a C_{y'=0} (1 - C_{DNA}) - C_{DNA} \right)
\]

Where; \( D_a = \text{Damkohler number}, \quad \gamma_a = \frac{K_a C_0}{K_b}, \quad C_0' = C_0 \frac{d}{C_{DNA,\text{max}}}, \quad = \frac{a}{d} \)
CHAPTER 4

SOLUTION OF NUMERICAL MODEL

The 3-dimensional generalized equations developed here (i.e., Eqns. 3.1.a-e, 3.2, 3.3.a-c) for this numerical framework of DNA molecule hybridization in the presence of centrifugal and Coriolis forces are conveniently solved using any finite element discretization approach. FEMLAB (COMSOL, 2010) multi-physics FEA modeling software is used here for the solution of these equations (see Figure 4.1 [22]). The mesh sizes differ depending on the geometry under consideration; however quadratic 3D elements are used with enough refinement for convergence. Most of the runs involved a mesh of approximately 62168 elements (see Figure A.1 in Appendix). Due to the coupling between these sets of equations, a nonlinear solution approach is used. The main coupling is between the equations for DNA molecule transport and its absorption reaction at the surface of the channel. The coupling between DNA molecule transport and fluid flow is weak and, therefore, neglected in this study. This suggests that the Navier-Stokes equations can be solved independently for nonlinear steady-state conditions under the body forces due to centrifugal and Coriolis forces. It is to be noted, however, that the Navier-Stokes equations have to be solved nonlinearly since the Coriolis forces are a function of the velocity terms which are themselves the primary unknowns. Once the flow velocities are determined, the transient DNA transport and hybridization phenomenon represented by the nonlinear equations, Eqns 3.2 and 3.3.a-c, respectively are solved simultaneously.

Boundary conditions for all the equation systems as well as the most important constants used in the numerical model are summarized in Table 4.1. The reaction term ‘R’ that defines the coupling of generation and consumption of DNA molecules is also given in Table 4.1.
### Table 4.1. Summary of the Boundary Conditions and Constants Used in the Numerical Model for DNA Hybridization in Straight Channel

<table>
<thead>
<tr>
<th>Physics</th>
<th>Bound. Cond.</th>
<th>R (Reaction Term)</th>
<th>Constants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid Flow (Navier- Stokes Equation)</td>
<td>No slip at all walls.</td>
<td>-----</td>
<td>(\rho = 1030 \text{ kg/m}^3) (\eta = 6 \times 10^{-4} \text{ Ns/m}^2)</td>
</tr>
<tr>
<td>Inlet</td>
<td>(P = 0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outlet</td>
<td>(P = 0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body force = (F_{\text{centrifugal}} + F_{\text{Coriolis}})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Migration of ssDNA Molecules (Eq. 3.3.b)</td>
<td>@ walls Insulated (zero flux).</td>
<td>Specific Inward flux (N) = (K_{B,\text{DNA}} S \times C_{\text{DNA,Hybridized}} ) (- K_{a,\text{DNA}} S \times C_{\text{DNA,Initial}} - C_{\text{DNA,Hybridized}} )</td>
<td>(D_{\text{DNA}} = 6.8 \times 10^{-11} \text{ m}^2/\text{s}) (K_{a,\text{DNA}} = 18 \text{ m}^3/\text{mol.sec}) (K_{b,\text{DNA}} = 10 \text{ m}^3/\text{(mol.sec)}) (K_{b,\text{DNA}} = 6 \times 10^{-2}/\text{sec}) (K_{b,\text{DNA}} = 1 \times 10^{-1}/\text{sec})</td>
</tr>
<tr>
<td></td>
<td>@ all domain constant (C_{\text{DNA}} (50\text{mM})) injected at entrance</td>
<td>Non-Specific Inward flux (N) = (K_{b,\text{DNA}} S \times C_{\text{DNA,Hybridized}} ) (- K_{a,\text{DNA}} S \times C_{\text{DNA,Initial}} - C_{\text{DNA,Hybridized}} )</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(This couples the migration and hybridization equations, Eq. 3.3.b and 3.3.c)</td>
<td></td>
</tr>
<tr>
<td>Hybridization of ssDNA Molecules (Eq. 3.1.a-c)</td>
<td>@ walls Insulated (zero flux).</td>
<td>@ Probes (RDNA,<em>{s} =) (RDNA,</em>{NS} =) Everywhere else (RDNA = 0)</td>
<td>(D_{\text{DNA,Hybridized}} = 0.0 \text{ m}^2/\text{s})</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CHAPTER 5

NUMERICAL RESULTS AND DISCUSSION FOR
MOLECULAR TRANSPORTATION

To validate and establish the accuracy of the numerical framework developed here for transport and hybridization of DNA molecules in a CD microfluidic platform, we analyze a number of models of microfluidic channels under centrifugal and Coriolis forces.

a. Example from Ducrée et al. [10-12]. The first problem solved here to establish the accuracy of the equations is an example taken from Ducrée et al. [10-12] where the length of the channel is 10.1mm, its depth 125µm, and width 360µm. An angular velocity of 350 rad/sec is applied. The center of rotation of the channel is assumed to be 3.5cm away from the entrance of the channel. For this problem and all other numerical solutions reported here, the following properties are used for a low conductivity fluid (1M NaCl): density ($\rho$) = 1030 kg/m$^3$ and dynamic viscosity ($\eta$) = $6 \times 10^{-4}$Ns/m$^2$. A maximum velocity of 10 m/s is determined by the current study whereas Ducrée et al. [10-12] report a maximum calculated velocity of 10 m/s.

b. Rectangular 3-Dimensional Channel: The second set of models consists of a rectangular 3-dimensional channel of 10.1mm length and 360µm width and 125µm depth. This is a slightly modified version of Ducrée et al. reported in [10-12]. The angular velocity ($\omega$) varies from 25 rad/sec to 350 rad/sec applied in clockwise direction. Velocities are noted at two important locations, i.e. at the center of the channel at mid-span (point A in Table 5.1) and at the exit (point B) and then compared. The ratios of these linear velocities corresponding to various angular velocities are also noted.

The results are summarized in Table 5.1; the first part of the results highlights the distribution of the centrifugal and Coriolis forces along the length of the channel indicating the region where centrifugal force and Coriolis forces dominate, respectively. It is noted that, the flow patterns are affected at the entrance and exit of the channels when the angular velocity is faster than 50 rad/second. The velocities turn to curl away from the direction of the angular velocity direction mostly at the entrance and exit. A family of curves representing the increase in velocity at the end of the channels for different channel widths and angular velocities are given in Figure 5.1. It is interesting to note that the overall velocity increases due to Coriolis force are significantly lower than the ratio of Coriolis force to centrifugal force given by Ducrée et al. [12] and summarized here in Table 5.1. The reason for this is that the relationship given by Ducrée et al. [12] is approximate and is valid only for the maximum Coriolis force that exists at the end of the channel.
Table 5.1 Summary of the Effect of Angular Velocity on the Coriolis Force Induced Velocity Pattern. Width = 360µm

<table>
<thead>
<tr>
<th>Omega (rad/s)</th>
<th>$F_{\text{Coriolis}} / F_{\text{Centrifugal}}$</th>
<th>Flow Pattern</th>
<th>Ave. Vel. (m/s)</th>
<th>Max. Vel. (m/s)</th>
<th>$V_{\text{max}} / V_{\text{ave}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>15.6</td>
<td></td>
<td>0.085</td>
<td>0.085</td>
<td>1.00</td>
</tr>
<tr>
<td>50</td>
<td>31.2</td>
<td></td>
<td>0.32</td>
<td>0.33</td>
<td>1.01</td>
</tr>
<tr>
<td>100</td>
<td>62.5</td>
<td></td>
<td>1.20</td>
<td>1.23</td>
<td>1.02</td>
</tr>
<tr>
<td>150</td>
<td>93.7</td>
<td></td>
<td>2.45</td>
<td>2.60</td>
<td>1.08</td>
</tr>
<tr>
<td>200</td>
<td>125</td>
<td></td>
<td>3.94</td>
<td>4.44</td>
<td>1.12</td>
</tr>
<tr>
<td>250</td>
<td>156.2</td>
<td></td>
<td>5.59</td>
<td>6.41</td>
<td>1.14</td>
</tr>
<tr>
<td>300</td>
<td>187.5</td>
<td></td>
<td>7.35</td>
<td>8.51</td>
<td>1.15</td>
</tr>
<tr>
<td>350</td>
<td>218.7</td>
<td></td>
<td>9.18</td>
<td>10.69</td>
<td>1.16</td>
</tr>
</tbody>
</table>

Figure 5.1. Effect of angular velocity on the Coriolis force and the ratio of the maximum velocity to the mean velocity of flow.
c. 3-D Channel under Various Rotational Speeds: In the third set of examples, we consider the same microchannel described (see Figure 5.2). The 3D microchannel is subjected to a series of angular velocities $\omega$ of magnitudes 25, 100, 150, 300, and 350 rad/sec. DNA of 50mM concentration is injected at the channel entrance continuously. There are five hybridization sites of 500µm width and 500µm depth along the length of the channel. These probe sites are placed at a spacing of 1mm. The results of DNA hybridization are shown in Figures 5.3-5.5. In Figure 5.3.a, we show the transient variation of hybridized DNA (dsDNA) at various locations in microchannel under $\omega = 300$ rad/sec. It is clearly shown that for point ‘C’ which is nearer the location of the maximum velocity (as affected by Coriolis force), dsDNA accumulates relatively faster, particularly for the first 0.4 seconds. Once equilibrium is reached, however, accumulations in all the four corner points seem to be approximately the same. Figure 5.3.b shows the effects of the magnitude of angular velocity on dsDNA accumulation on probe sites. As expected, there is a noticeable time lag of about 2 seconds in reaching equilibrium between higher angular velocities (300 rad/sec, for example) and angular velocity of 25 rad/sec.

The effect of channel width on hybridization is summarized in Figure 5.4. The maximum difference is about 10-15% between channels of widths of 500µm and 100µm. In general, the centrifugal force is dominant until the angular velocity reaches a value of 200 rad/sec after which its influence on hybridization is observed. The velocity patterns in most parts of the microchannel - particularly in the middle - do not seem to be affected by Coriolis force. However, at probe sites near to the exit of the microchannel a significant variation in hybridization is observed. For CD platform being rotated in a clockwise direction, the maximum hybridizations are located at the top of the probe sites nearer to the exit. This is expected as the velocities are higher at these regions as shown in the earlier examples.

Whereas, Figure 5.5 shows accumulation of the dsDNA on the zone 1 and zone 5 of the probe sites and from bar chart shows that as the ssDNA goes from zone 1 to zone 5 the accumulation of the dsDNA increases for the different omega ranging from 50 rad/sec to 350 rad/sec.
Figure 5.2. Geometry of a microchannel in a CD platform considered in this study. There are five hybridization sites of 360 µm width and 500 µm length along the length of the channel. These probe sites are placed at a spacing of 1 mm (clear span). L = 10.1 mm length and 360µm width and 125µm depth.
Figure 5.3. (a) Transient variation of hybridized DNA (dsDNA) at various locations in microchannel under $\omega = 100$ rad/sec., (b) effect of angular velocity on transient variation of hybridized DNA (dsDNA) at various locations in microchannel, and (c) effect of angular velocity on transient variation of hybridized DNA (dsDNA) at various locations in microchannel for $\omega = 100$ rad/sec and $\omega = 25$ rad/sec for non-specific and specific hybridization.
Figure 5.4. (a) Effect of channel width on transient variation of hybridized DNA (dsDNA) at various locations in microchannel, and (b) effect of channel width on transient variation of hybridized DNA (dsDNA) at Point 'C' for $\omega = 50$ rad/sec for non-specific and specific hybridization.
Figure 5.5. Accumulation ratios at the different capture probe locations as a function of the angular velocity.
CHAPTER 6

NUMERICAL RESULTS AND DISCUSSION FOR
FLUID MIXING

The mixing dynamics in the microchannel is simulated using the commercial finite element code, Comsol Multiphysics where the laminar Navier-Stoke’s equation is coupled with convection-diffusion equation for getting the transport of diluted species along the channel. We consider the two phase flow of NaCl with different concentration of 1 molar and 0 molar in one of the each channel. There are two different types of microchannel are used one with obstacles and one without obstacles, and the mixing efficiency is measured for each of the microchannel. The mixing patterns are visualized by the distribution of mixture fraction at various locations along the microchannel.

The velocity field and the pressure field in the microchannel are governed by the incompressible Navier-Stoke’s equation.

\[ \nabla \cdot \mathbf{U} = 0 \quad \text{(Continuity Equation)} \quad (6.1.a) \]

\[
\frac{\partial \mathbf{U}}{\partial t} + \mathbf{U} \cdot \nabla \mathbf{U} = -\nabla \mathbf{P} + \mu \nabla^2 \mathbf{U} - \rho \omega \times (\mathbf{U} \times \mathbf{r}) - 2\rho \omega \mathbf{r} \quad \text{(Momentum Equation)} \quad (6.1.b)
\]

Where, \( \rho \) is the density of the NaCl is 1030 kg/m\(^3\), \( \mathbf{U} \) is the velocity of the liquid, \( \mu \) is the dynamic viscosity of the liquid 6*10\(^{-4}\) and \( \omega \) is the angular velocity with which the microchannel is rotated.

Transportation of the molecular species in the microchannel is governed by the Fick’s second Law, assuming that there is no chemical reaction in the mixture.

\[
\frac{\partial C_i}{\partial t} + \mathbf{U} \cdot \nabla C_i = \nabla \cdot (D \nabla C_i) \quad (6.2)
\]

Where \( C_i \) is the concentration of the species and \( D \) is the diffusion coefficient of the liquid.

The schematics of the microchannel with obstacles and without obstacles are shown in the Figures 6.1 and 6.2 which carries the NaCl solution in one of the each channel having \( \rho \) of 1030 kg/m\(^3\) and \( \eta = 6*10^{-4} \), the boundary condition are show Table 6.1 and the number of mesh elements which are used for microchannel without obstacles are 10551 tetrahedral element.
Figure 6.1. Microchannel without obstacles.

Figure 6.2. Microchannel with obstacles.
and microchannel with obstacles have 21439 tetrahedral element (see Figures A.2 and A.3 in the Appendix). In the simulation the microchannel is rotated at angular velocity of $\omega = 50$ rad/s up to $\omega = 200$ rad/s.

### 6.1 Velocity Distribution in Microchannel

The Velocity in microchannel with and without obstacles is show in Table 6.2 with maximum velocity for different angular velocity varying from $\omega = 50$ rad/s to $\omega = 200$ rad/s.

### 6.2 Concentration Plots

The rate of change in the concentration with respect to time from 0 to 1 sec for microchannel with and without obstacles for angular velocity of 50 rad/s is show in Table 6.3.

As the angular velocity increase so as the mixing of the two fluid increase the only difference is that the mixing in the microchannel with obstacles will have faster rate of change of concentration in compare to the microchannel without any obstacles, and also this change depends on the speed of rotation which here varies from 50 rad/s to 200 rad/s and is shown in Figure 6.3 and Figure 6.4 respectively.
Table 6.2. Velocity Distributions for Different Omega

<table>
<thead>
<tr>
<th>Angular Velocity (rad/s)</th>
<th>Microchannel with obstacles velocity distribution(v1)</th>
<th>Microchannel with obstacles velocity distribution(v2)</th>
<th>Maximum Velocity (m/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ω = 200</td>
<td>v1 = 0.426</td>
<td>v1 = 0.445</td>
<td>v1 = 0.426 v2 = 0.445</td>
</tr>
<tr>
<td>ω = 150</td>
<td>v1 = 0.243</td>
<td>v1 = 0.241</td>
<td>v1 = 0.243 v2 = 0.241</td>
</tr>
<tr>
<td>ω = 125</td>
<td>v1 = 0.174</td>
<td>v1 = 0.169</td>
<td>v1 = 0.174 v2 = 0.169</td>
</tr>
<tr>
<td>ω = 100</td>
<td>v1 = 0.114</td>
<td>v1 = 0.112</td>
<td>v1 = 0.114 v2 = 0.112</td>
</tr>
<tr>
<td>ω = 75</td>
<td>v1 = 0.0652</td>
<td>v1 = 0.0657</td>
<td>v1 = 0.0652 v2 = 0.0657</td>
</tr>
<tr>
<td>ω = 50</td>
<td>v1 = 0.0291</td>
<td>v1 = 0.0300</td>
<td>v1 = 0.0291 v2 = 0.0300</td>
</tr>
</tbody>
</table>
Table 6.3. Rate of Change of Concentration with Time

<table>
<thead>
<tr>
<th>Microchannel without Obstacles</th>
<th>Microchannel with obstacles</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Image](t=0.1 sec)</td>
<td>![Image](t=0.1 sec)</td>
</tr>
<tr>
<td>![Image](t=0.2 sec)</td>
<td>![Image](t=0.2 sec)</td>
</tr>
<tr>
<td>![Image](t=0.4 sec)</td>
<td>![Image](t=0.4 sec)</td>
</tr>
<tr>
<td>![Image](t=0.6 sec)</td>
<td>![Image](t=0.6 sec)</td>
</tr>
<tr>
<td>![Image](t=0.8 sec)</td>
<td>![Image](t=0.8 sec)</td>
</tr>
<tr>
<td>![Image](t=1 sec)</td>
<td>![Image](t=1 sec)</td>
</tr>
</tbody>
</table>
Figure 6.3. Change of concentration at different angular velocity for microchannel without obstacles.

Figure 6.4. Change of concentration at different angular velocity for microchannel with obstacles.
6.3 MIXING EFFICIENCY

Based on the visualization of the results from simulation here the mixing efficiency is calculated for both the microchannel at four different location from the entrance of the fluid which at 1mm, 2mm, 3mm and 4mm distance from the entrance of the channel having length of 5mm in x-direction using the below equation [16].

\[
M_{\text{eff}} = \left(1 - \frac{\int_{0}^{L} \left| \frac{C - C_0}{C_0 - C_e} \right| \, dx}{L} \right) \times 100\% \tag{6.3}
\]

Where, \( M_{\text{eff}} \) is the mixing efficiency of the two fluids, \( C \) is the mass concentration of the two fluids at outlet, \( C_\infty \) is the concentration of complete mixing and \( C_0 \) is the initial distribution of the concentration of the liquid [16] (see Figure 6.5).

![Figure 6.5. Mixing efficiency of microchannel without obstacles.](image)

The below plots show the mixing of the two fluid at different location for angular velocity changing from 50 rad/sec to 200 rad/sec and as the results shows, as the speed increase so as the mixing of the two fluid due to Coriolis force but in case of microchannel with obstacles the mixing efficiency is higher than one without the obstacles because in this even the obstacles also influence the mixing rate of the two fluid [16] (see Figure 6.6, 6.7 and 6.8).
Figure 6.6. Mixing efficiency of microchannel with obstacles.

Figure 6.7. Mixing efficiency plot of microchannel without obstacles.
Figure 6.8. Mixing efficiency plot of microchannel with obstacles.
CHAPTER 7

CONCLUSION

In our first study we investigate, through numerical modeling, the influence of Coriolis forces on the transport and hybridization of DNA in CD microfluidic chips where centrifugal force is used as the driving force. While the effect of Coriolis force on the fluid flow in CD microfluidic channels has been studied experimentally and numerically only recently, its influence on DNA hybridization has not been investigated so far. This study addresses, therefore, this phenomenon through numerical simulation and demonstrates that for most practical geometrical configurations and angular velocity ranges reported in the literature, the Coriolis force introduces significant qualitative and quantitative variations in DNA hybridization, particularly at locations near the periphery.

In general, the following conclusions are made based on results from this study:

1. This effect is observed to be significantly influenced by channel width and length and angular rotations larger than 100 revolutions per minute. Further, the velocity patterns in the most part of the microchannel, particularly in the middle, do not seem to be affected by Coriolis force.

2. However, at probe sites near to the exit of the microchannel a significant spatial variation in hybridization is observed.

3. For CD platform bring rotated in a clockwise direction, the maximum hybridizations are located at the bottom of the probe sites nearer to the exit.

4. Our results further indicate that the time frame for hybridization is so fast that the effect due to Coriolis force on the location of hybridization is more important than time of hybridization.

5. Our results indicate that for low viscosity fluids, angular velocities as low as 25 rad/sec could introduce Coriolis force that is as high as at least 25% of the main driving centrifugal force. If the channel widths are moderately wide (in the range of 200 microns).

Whereas in our second study for the influence of the Coriolis force on the mixing of two fluid for microchannel with obstacles and without obstacle shows significant amount of mixing taking place in microchannel with obstacle in compare to microchannel without obstacles because over here obstacle also influences the mixing along with the Coriolis force and centrifugal force. As the speed at which the microchannel is rotated is increased the mixing taking place between two liquids also increases. By the results obtain one can clearly
see the amount of mixing efficiency obtain at the higher speed then at lower speed even though the obstacles in the microchannel will have different effect on the system.
BIBLIOGRAPHY


APPENDIX

MESHED GEOMETRY FOR STRAIGHT CHANNELS
A.1 CO RIOLIS INDUCED HYBRIDIZATION

Figure A.1. Straight channel ~10mm length.

Grid of DNA Hybridization in straight channel
View- Isometric view of straight channel of 125µm height with grids
Grid Size- 62158 tetrahedral elements
Solver- Direct (UMFPACK)
A.2 Coriolis Induced Mixing in Straight Channel without Obstacles

Figure A.2. Straight channel ~5mm length.

Grid view of straight channel without obstacles
View- Isometric view of straight channel without obstacle of 150μm height with grids
Grid Size- 10551 tetrahedral elements
Solver- Direct (UMFPACK)
A.3 CORIOLIS INDUCED MIXING IN STRAIGHT CHANNEL WITH OBSTACLES

Figure A.3. Straight channel with obstacles.

Grid view of straight channel with obstacles
View- Isometric view of straight channel with obstacle of 150μm height with grids
Grid Size- 21439 tetrahedral elements
Solver- Direct (PARDISO)