OPTOFLUIDIC MANIPULATION AND SORTING OF NANOPARTICLE AND BIOMOLECULES

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OPTOFLUIDIC MANIPULATION AND SORTING
OF NANOPARTICLE AND BIOMOLECULES

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# TABLE OF CONTENTS

Acknowledgement ................................. i
Summary ............................................ iii
Table of Contents ................................ v
List of Figures ................................... ix
List of Tables ................................... xvii
Nomenclature ................................... xviii

## 1. Introduction ........................................... 1

1.1 Motivation .......................................... 1
1.2 Objectives .......................................... 7
1.3 Major contributions ................................. 9
1.4 Organization ....................................... 11

## 2. Literature survey ....................................... 13

2.1 Light-fluid interaction in optofluidics ................. 14
2.1.1 Types of light-fluid interaction ....................... 14
2.1.2 Diffusion-controlled optofluidics ....................... 15
2.2 Optofluidic waveguide ............................... 16
2.2.1 Concept and configuration ........................... 16
2.2.2 Light propagating behaviour ....................... 18
2.2.3 Application in integrated optofluidic systems .......... 19
2.3 Optofluidic lens ................................... 23
4. Optofluidic hyperbolic secant lens ........................................... 82

4.1 Design of the optofluidic hyperbolic secant lens ...................... 83

4.1.1 Optical aberrations in optofluidic lenses .............................. 83

4.1.2 Index profile derivation ..................................................... 85

4.1.3 Microfluidic gradient generator .......................................... 88

4.1.4 Theoretical analysis and simulation ...................................... 90

4.2 Fabrication processes and experimental setups .......................... 98

4.2.1 Fabrication processes ....................................................... 98

4.2.2 Preparation of fluids ....................................................... 101

4.2.3 Experimental setup .......................................................... 101

4.3 Experimental results and discussions ..................................... 103

4.3.1 Index profile measurement ............................................... 103

4.3.2 Light propagation vs divergence angles ............................... 105

4.3.3 Light propagation vs off-center positions ............................. 109

4.3.4 Light focusing for multiple light sources ............................. 112

4.4 Summary ............................................................................ 115

5. Nanoparticle manipulation in near-field optics ......................... 117

5.1 Design of the optofluidic system ......................................... 118

5.1.1 Design of the microfluidic subsystem ................................. 119

5.1.2 Design of the photonic subsystem ..................................... 123
SUMMARY

Optofluidic technology exploits the light and fluids interaction to create versatile systems. It is a burgeoning field with broad applications in biotechnology, analytical chemistry, medicine, etc. This doctorate thesis focuses on integrated Lab-on-a-chip functionalities stimulated by the unprecedented light-matter interaction in optofluidics. Specifically, three aspects of this subject have been investigated: fluid-fluid interaction-induced light propagation change for biochemical detection, i.e. optofluidic waveguide-based chemical sensor, light-fluid interaction to control lightwave, i.e. optofluidic hyperbolic secant (HS) lens, and light-matter interaction to manipulate nanoscale samples, i.e. nanoparticle and biomolecule separation.

An optofluidic waveguide sensor to monitor chemical reaction and measure diffusion coefficient is developed based on the light focusing pattern in optofluidic waveguides. The index profile is studied theoretically. The influence of the contributing factors on the focal position is investigated theoretically and experimentally. A characterization experiment is designed to validate the use of the focal position as a sensing signal. In chemical reaction monitoring, the hydrolysis of sucrose is studied and the initial hydrolysis rate is determined. In diffusion coefficient measurement, simulation models are built up to quantify the focal length different as a function of the diffusion coefficient. The diffusion coefficient of ethylene glycol-DI water solution is measured experimentally.

An optofluidic HS lens is developed to improve the focusing power. The optical aberrations which deteriorate the optical performance are investigated. The optimized index profile is derived based on coordinate transformation and a microfluidic gradient generator is designed to generate the index profile. The chip
fabrication processes are developed for the fabrication of the optofluidic HS lens. Subsequently, simulations are conducted to verify the performance of the optofluidic HS lens. In the experiment, the performance of the lens is evaluated, including the focal length and beam waist at different divergence angles and off-center positions. The focusing experiment with multiple light sources is also demonstrated.

A photonic pillar array-based optofluidic manipulation system is developed based on waveguide-pair arrays for nanoparticle and bacteria manipulation. The design considerations and parameters of the optofluidic system are discussed in detail. The process flow is presented to fabricate the silicon-glass hybrid chip. The buffer solution and surface treatment are optimized to minimize the particle adhesion problem. In the nanoparticle separation experiment, the trajectory of individual 200-nm and 500-nm particiles are compared, followed by the separation of 500-nm polystyrene particles from particle mixtures. The statistical analysis of the particle distribution is also conducted. In the bacteria trapping and alignment, the principle and force analysis are studied based on FDTD simulation. The motions of a single Shigella are investigated experimentally. Then parallel trapping and alignment of Shigella are conducted and the trapping rate is analyzed.

The successful implementation of optofluidic waveguide-based chemical sensor provides a simple and efficient chemical sensing method for biochemical research. The development of optofluidic HS lens improves the optical performance of on-chip lenses for diverse Lab-on-a-chip applications. In addition, the photonic pillar array-based optofluidic manipulation system provides a powerful toolbox and is anticipated to facilitate the study of biomolecule purification, disease diagnostics, intercellular interaction, etc.
# LIST OF FIGURES

| Fig. 3.1 | Schematic illustration of optofluidic waveguides | 45 |
| Fig. 3.2 | Index profile comparison. 2D index profile of (a) optofluidic waveguide and (b) solid GRIN waveguide. (c) Transverse refractive index profile of solid GRIN waveguide (dashed black) and optofluidic waveguide at \( x = 0 \) (solid blue), \( x = 0.5 \) (solid red) and \( x = 1 \) (solid green). (d) Longitudinal refractive index of solid GRIN waveguide (dashed black) and optofluidic waveguide (solid blue) at \( y = 0 \) | 45 |
| Fig. 3.3 | Dimensionless model of the diffusion-induced index profile | 47 |
| Fig. 3.4 | Index profile when \( r = 0.3 \) and \( Pe = 100, 500, 1000 \) and 2000. | 48 |
| Fig. 3.5 | (a) Transverse index profile at \( x' = 1 \) and (b) longitudinal index profile at \( y' = 0 \) when \( r = 0.3, Pe = 100 \) (blue), 500 (red) and 1000 (green) | 49 |
| Fig. 3.6 | Index profiles when \( Pe = 1000 \) and \( r = 0.2, 0.25, 0.3 \) and 0.5 | 49 |
| Fig. 3.7 | (a) Transverse index profile at \( x' = 1 \) and (b) longitudinal index profile at \( y' = 0 \) when \( Pe = 1000, r = 0.2 \) (blue), 0.3 (green) and 0.5 (red) | 50 |
| Fig. 3.8 | Normalized pixel intensity as a function of the mass fraction of ethylene glycol. | 51 |
| Fig. 3.9 | (a) Fluorescent image of the ethylene glycol distribution in the optofluidic waveguide. (Scale bar: 30 μm) (b) The measured refractive index at \( x_1 \) (blue), \( x_2 \) (red) and \( x_3 \) (green). | 52 |
Fig. 3.10 Light trajectories along the microchannel with interface position of (a) $r = 1/3$, (b) $r = 1/2$ and (c) $r = 3/5$ when $Pe = 500$.

Fig. 3.11 Light trajectories along the microchannel with Péclet number of (a) $Pe = 1000$, (b) $Pe = 2000$ and (c) $Pe = 20000$ when $r = 1/3$.

Fig. 3.12 Light propagation patterns when $Pe = 500$ and interface position (a) $r = 0.1$, (b) $r = 0.2$, (c) $r = 0.3$ and (d) $r = 0.4$. (Scale bar: 100 μm)

Fig. 3.13 The relationship between the 1st focal length and the interface position $r$ when (a) $Pe = 500$ and (b) $Pe = 1000$.

Fig. 3.14 Light propagation patterns when $r = 0.23$ and Péclet number (a) $Pe = 375$, (b) $Pe = 500$, (c) $Pe = 750$, and (d) $Pe = 1000$ (Scale bar: 100 μm)

Fig. 3.15 The relationship between the 1st focal length and the Péclet number $Pe$ when (a) $r = 0.23$ and (b) $r = 0.14$.

Fig. 3.16 Illumination of chemical sensing using the light propagation pattern in optofluidic waveguides. (a) Schematic of the chip design. (b) Simulated concentration profile. Simulated (c) light propagation patterns and (d) the intensity profiles of two chemicals with different diffusion coefficients. ($\Delta x$: focal length shift)

Fig. 3.17 Diffusion coefficient of ethylene glycol (black, square), glycerol (red, triangle) and IPA (blue, circle) as a function of mass fraction.

Fig. 3.18 Light propagation pattern and light intensity in the under-mixed region with the core solution of (a) ethylene glycol, (b) glycerol, (c) IPA and (d) the equal mixture of the three chemical solutions. (Scale bar: 100 μm)
Fig. 3.19  Light propagation pattern and light intensity in the over-mixed region with the core solution of (a) ethylene glycol, (b) glycerol, (c) IPA and (d) the mixture of the three chemical solutions. (Scale bar: 100 μm)........ 67

Fig. 3.20  The focal length shift for different chemical compositions when the overall flow rates are 2.25 μL/min (blue) and 6 μL/min (red). ........... 68

Fig. 3.21  Light propagation pattern and light intensity along the central line of the optofluidic waveguide for the reaction products after (a) 0, (b) 40 min, (c) 80 min and (d) 120 min. (Scale bar: 100 μm) ......................... 72

Fig. 3.22  The 1st focal shift as a function of (a) reaction time and (b) the concentration of hydrolyzed sucrose. ................................. 73

Fig. 3.23  The concentration of hydrolyzed sucrose as a function of the reaction time......................................................... 75

Fig. 3.24  Simulated concentration profile where the diffusion coefficient is set to be (a) 2.0, (b) 5.0, (c) 8.0 and (d) 10.0×10⁻¹⁰ m²/s and (e-h) the corresponding focal length difference (Δ)........................................ 76

Fig. 3.25  Simulated focal length difference as a function of diffusion coefficient. ................................................................. 77

Fig. 3.26  (a) Captured light propagation image (Scale bar: 100 μm). (b) Measurement of the focal length difference based on the normalized intensity profile along the central line of the microchannel........... 78

Fig. 4.1  Schematic illustration of (a) spherical aberration and (b) field curvature in optofluidic GRIN lenses; and optofluidic fisheye lens without (c) spherical aberration and (d) field curvature.............................. 84
Fig. 4.2  Light propagation in (a) Maxwell’s fisheye lens and (b) optofluidic hyperbolic secant lens…………………………………………………………. 87

Fig. 4.3  The spatial relationship of the discarded region between (a) Maxwell’s fisheye lens and (b) the optofluidic HS lens. (c-d) Illustration of the light propagation in the two lenses with index approximation……………… 89

Fig. 4.4  (a) Gradient generator using complex microfluidic network. (b) Analysis of the splitting ratio in the highlighted microchannel………………… 90

Fig. 4.5  Numerical simulation of the index profile in the optofluidic lens……… 90

Fig. 4.6  (a) Index profile of the optofluidic lens under different core/cladding flow rates (Solid lines: simulated profiles, dashed-lines: fitted ideal profiles). (b) Maximum (Solid lines) and minimum (Dashed lines) refractive index at x1 as a function of flow rate ratio when the cladding flow rate is 1.0 μL/min (red) and 10 μL/min (blue), respectively………………… 91

Fig. 4.7  Ray-tracing simulation of the optofluidic fisheye lens when the light source is placed (a) at the center and (b) 30 μm above the center. (c) The focal length and divergence angle as a function of flow rate ratios……… 93

Fig. 4.8  (a) Ray tracing simulation of light beams with different channel widths. (b) Simulated focal length as a function of channel widths with the core/cladding ratio of 2.25…………………………………………………………. 94

Fig. 4.9  Ray tracing simulation of light beams with different divergence angles (θ) in the (a) optofluidic GRIN lens and (b) optofluidic HS lens…………… 95

Fig. 4.10  Ray tracing simulation of light beams with different off-axis positions (Δy) in the (a) optofluidic GRIN lens and (b) optofluidic HS lens…… 96
Fig. 4.11  (a) Simulated spherical aberration as a function of divergence angle. (b) Focal position as a function of light source positions. (Red: optofluidic GRIN lens, Blue: optofluidic HS lens) ........................................... 97

Fig. 4.12  Fabrication flow of PDMS chips. (a) Silicon wafer cleaning, (b) photoresist coating, (c) lithography exposure, (d) photoresist develop, (e) PDMS molding and (f) chip bonding........................................... 99

Fig. 4.13  Photograph of the fabricated PDMS microchip.............................. 100

Fig. 4.14  Experimental setup of the optofluidic HS lens............................. 102

Fig. 4.15  Captured image of the beam profile from the single-mode fiber....... 102

Fig. 4.16  Fluorescent image of the branch channels, the mixing chamber and the optofluidic chamber. (Scale bar: 100 μm)................................. 104

Fig. 4.17  Measured refractive index along the microchannel at the position of $x_1$, $x_2$ and $x_3$................................................................. 104

Fig. 4.18  Light propagation images with the divergence angle of (a) 12, (b) 20, (c) 30 and (d) 45 degrees, respectively. (Scale bar: 50 μm).............. 106

Fig. 4.19  Light intensity profiles along the central line of the microchannel when the divergence angles are 12, 20, 30 and 45 degrees, respectively....... 107

Fig. 4.20  Focal positions and spherical aberration as a function of divergence angles. ................................................................. 107

Fig. 4.21  Schematic illustration of spherical aberration measurement........... 109

Fig. 4.22  Light propagation images when the light source is placed with the off-axis position of (a) 0, (b) 15 μm, (c) 30 μm and (d) 45 μm, respectively. (Scale bar: 50 μm)................................................................. 110
Fig. 4.23 Normalized light intensity on the focal plane when the light source is placed at different off-axis positions……………………………………111
Fig. 4.24 The longitudinal (blue) and transverse (red) focal position as a function of the off-axis position…………………………………………………..112
Fig. 4.25 Schematic illustration of the potential application in multiplexed detection………………………………………………………………..113
Fig. 4.26 (a) Light propagation image with two sources. (Scale bar: 100 μm, vertical direction is magnified by 1.5-fold) (b) FWHM of the two focal points……………………………………………………………………………..114
Fig. 5.1 Illustration of the optofluidic system for nanoparticle and bacteria manipulation……………………………………………………………..118
Fig. 5.2 Schematic illustration of the microfluidic subsystem…………………120
Fig. 5.3 The equivalent hydraulic circuit of the microfluidic subsystem……120
Fig. 5.4 The flow velocity in the main channel as a function of the branch channel dimensions…………………………………………………………..121
Fig. 5.5 The relative width of the particle streams, $w_{\text{particle}}/w_0$, as a function of the inlet flow rate ratio, $Q_1/Q_2$…………………………………………………..123
Fig. 5.6 (a) Top view and (b) cross-sectional view of the photonic subsystem..124
Fig. 5.7 (a) Design of the improved beam splitter. (b) Simulation result of the E-field distribution at 1550 nm………………………………………………125
Fig. 5.8 (a) Schematic illustration of coupling length ($L_c$). (b) Coupling length as a function of the waveguide width and gap…………………………126
Fig. 5.9 Fabrication process flow of the silicon-glass hybrid chip………………130
Fig. 5.10  SEM image of the fabricated silicon photonic chip: (a) beam splitter, and (b) the waveguide array………………………………………………………… 131

Fig. 5.11  Schematic illustration of the chip holder……………………………………………… 132

Fig. 5.12  The photography of the assembled chip holder…………………………………… 133

Fig. 5.13  Illustration of the experimental setup……………………………………………. 134

Fig. 5.14  Illustration of the laser coupling procedure……………………………………….. 134

Fig. 5.15  Image of the sticked particles for different buffer solutions…………………. 136

Fig. 5.16  Images of the sticked particles for solutions (a) without surfactant and with surfactant of (b) Hyamine 1622, (c) SDS, (d) SPAN 80, (e) Tween 20 and (f) Triton X-100………………………………………………………….. 137

Fig. 5.17  Images of the sticked particles (a) without surface treatment and with different surface treatments of (b) 1% BSA, (c) 5% BSA, (d) 1% DOPC, (e) 1% PEG, and (f) 1% APTES………………………………………………………….. 138

Fig. 5.18  Time-lapse images of particle movements on a single waveguide with a diameter of (a) 500 nm, (b) 1.0 μm, and (c) 2.0 μm. (Scale bar: 10 μm).140

Fig. 5.19  Measured optical force as a function of guided power for particles of different diameters…………………………………………………………. 140

Fig. 5.20  Schematic illustration of (a) the chip design and (b) the separation of different-sized particles in the PPA…………………………………………………143

Fig. 5.21  Simulated light intensity in a waveguide-pair. (Vertical direction is magnified by 5-fold).………………………………………………………… 143

Fig. 5.22  Calculated (a) x-component and (b) y-component of the resultant force distribution for 200-nm particle. (Dashed box: the trapping region)… 144
Fig. 5.23  Calculated (a) $x$-component and (b) $y$-component of the resultant force distribution for 500-nm particle. (Dashed box: the trapping region)… 145

Fig. 5.24  Schematic illustration of the particle trajectory when the particle enters the optical field from different positions…………………………………… 147

Fig. 5.25  Width of trapping region ($D$) as a function of the particle diameter under different guided powers……………………………………………… 147

Fig. 5.26  Trajectories of 200-nm and 500-nm particles………………………… 149

Fig. 5.27  The particle displacement in the $y$-direction as a function of time….. 150

Fig. 5.28  The particle displacement in the $x$-direction as a function of time……… 150

Fig. 5.29  Superposition image of the 200-nm, 300-nm and 500-nm particles when flowing through the waveguide-pair array. (Scale bar: 20 μm)……………… 151

Fig. 5.30  Statistical analysis of the particle distribution (a) before and (b) after the optical field…………………………………………………………… 152

Fig. 5.31  (a) Schematic illustration of bacteria trapping and alignment in the optofluidic system. The bacterial motion can be decomposed into: (b) out-of-plane rotation, (c) in-plane rotation, and (d) translation motion…….. 155

Fig. 5.32  Simulated (a) $x$-component, (b) $y$-component and (c) $z$-component of the optical force distribution for the bacteria…………………………………… 156

Fig. 5.33  Simulated torque as a function of the rotation angle in the (a) $x$-$y$ plane and (b) $x$-$z$ plane at different positions…………………………………….. 157

Fig. 5.34  Out-of-plane ($x$-$z$ plane) rotation of a single *Shigella*……………… 159

Fig. 5.35  In-plane ($x$-$y$ plane) rotation of a single *Shigella*…………………... 160

Fig. 5.36  Translation motion of a single *Shigella* in the $x$-$y$ plane…………... 160
Fig. 5.37  Images of (a) parallel trapping and alignment of *Shigella*, and (b) release the trapped *Shigella*………………………………………………………… 161

Fig. 5.38  Number of trapped *Shigella* as a function of flow velocity and guided power……………………………………………………………………………… 162
LIST OF TABLES

Table 2.1: Typical value of difference forces on particles............................ 34
Table 3.1: Chemical properties of ethylene glycol, glycerol and IPA............... 66
Table 5.1: Summary of the dimension and hydraulic resistance...................... 122
Table 5.2: Design parameter of the improved beam splitter......................... 125
Table 5.3: Design parameters of the photonic subsystem............................. 128
Table 5.4: pH and conductivity of buffer solutions..................................... 136
Table 5.5: Summary of the buffer solutions and the surface treatment............ 139
Table 5.6: Sorting resolution under different guided powers......................... 148
## NOMENCLATURE

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>GRIN</td>
<td>Gradient index</td>
</tr>
<tr>
<td>CV</td>
<td>Coefficient of variance</td>
</tr>
<tr>
<td>DI</td>
<td>Deionized</td>
</tr>
<tr>
<td>HS</td>
<td>Hyperbolic secant</td>
</tr>
<tr>
<td>FDTD</td>
<td>Finite-difference time-domain</td>
</tr>
<tr>
<td>TIR</td>
<td>Total internal reflection</td>
</tr>
<tr>
<td>ARROW</td>
<td>Antiresonant reflecting optical waveguide</td>
</tr>
<tr>
<td>DEP</td>
<td>Dielectrophoresis</td>
</tr>
<tr>
<td>RI</td>
<td>Refractive index</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>PDMS</td>
<td>Polydimethylsiloxane</td>
</tr>
<tr>
<td>NA</td>
<td>Numerical aperture</td>
</tr>
<tr>
<td>PPA</td>
<td>Photonic pillar array</td>
</tr>
<tr>
<td>BSA</td>
<td>Bovine serum albumin</td>
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CHAPTER 1

INTRODUCTION

1.1 Motivation

This PhD research topic is motivated by the potential optofluidic functionalities stimulated by the unprecedented light-matter interaction in applications such as biochemical detection, on-chip light manipulation, and biomolecule sorting.

Optofluidics aims to manipulate light and fluids at the chip level and exploits their interaction to create versatile systems [1-3]. Opto refers to the on-chip light manipulation and it brings various optical functionalities to Lab-on-a-chip applications [4, 5]. Fluidic refers to the fluidic manipulation and it brings fluidic features to microfluidic systems. There are several unique features in fluidics compared with its solid counterpart. First, fluidic medium is flexible in reconfiguring its properties such as shape and refractive index. Second, fluidic medium is naturally compatible with the fluidic environment where most organism are living. Third, fluidic medium could mix and react easily in a controlled fashion.

The marriage of opto and fluidic creates new level of optical and fluid interaction and promotes enormous optofluidic systems for broad applications. Optical and fluid interaction can be divided into two classes based on the role of the fluidic component. On the one hand, the fluidic component works as an alternative to the solid counterpart. The
introduction of the fluidic component makes the optical and fluid interaction occur at the place that is difficult, if not impossible, in the system with solid components. The feature facilitates many Lab-on-a-chip applications in biochemical detection and particle manipulation [6]. Meanwhile, the mobile nature of fluidic matters allows the dynamic control of the geometry and property of optofluidic systems, which fosters the emergence of many tunable optofluidic devices [7-9]. On the other hand, multiple fluidic components could interact with each other and bring in unprecedented optical functionalities. For example, the mass transport or reaction in the fluids will change the index profile and eventually lead to a distinct light propagation behavior.

Optofluidic waveguide is a fundamental component in optofluidic systems. It confines the light wave in the waveguide core by total internal reflection and can be divided into liquid-solid (LS) and liquid-liquid (L²) waveguides based on the configuration. The LS waveguide has a fluidic component in either the waveguide core or the cladding. The index distribution follows a step-index profile which is the same with solid waveguides. The introduction of the fluidic component allows the light-matter interaction to occur at the place that is difficult in solid waveguides. Such a configuration promotes the use of optofluidic waveguides in applications such as multiplexed detection [10], near-field particle manipulation [11], spectroscopic detection [12], etc. In comparison to the LS waveguide, the L² waveguide has the all-fluidic core and cladding. The all-fluidic configuration endows optofluidic waveguides with greater flexibility in reconfiguring the waveguide geometry. The waveguide geometry can be reshaped easily using electrical [13], hydrodynamical [14], or mechanical [15] approaches, which stimulates the development of optofluidic waveguide-based devices such as optical switch [15], and dye laser [16, 17].
In those applications, the optofluidic waveguide is treated as the fluidic counterpart to a solid waveguide and the light propagation in it is similar to the light behavior in solid single-mode or multimode waveguides. On the other hand, the all-fluidic configuration brings in additional fluidic-fluidic interactions to the light-mater interaction, i.e. the mass transport or reaction in fluids will change the index profile and eventually lead to a distinct light behavior. Tunable beam splitting [18], focusing [19, 20] and interference [21] have been demonstrated in optofluidic waveguides by controlling the fluidic diffusion.

The light focusing in optofluidic waveguides is a useful yet unthoroughly discussed phenomenon. Several groups have observed the tunable light focusing in optofluidic waveguides and adapted it to a focusing lens [9, 22]. Our previous work reports the periodical focusing in optofluidic waveguides and finds that the first focal length is inversely proportional to the core flow rate in the studied flow rate range [20]. However, the general trends of focal length shift are not fully discussed, and the contributing factors to focal length are also unclear, which hinders its practical application in chemical sensing.

Optofluidic lens is an important component for on-chip optical systems. It has many advantages over a solid lens in terms of reconfigurable geometry and tunable refractive index. Optofluidic lens can be divided into two types: interface curvature-based [23, 24] and gradient index (GRIN) lens [22, 25]. The curvature-based optofluidic lens, similar to a solid lens, refracts light based on the curvature of air-liquid or liquid-liquid interface. On the other hand, the GRIN-based optofluidic lens uses the gradient refractive index profile to gradually bend light beams. In optofluidic imaging applications, curvature-based optofluidic lens is used to change the image plane by deforming the interface curvature using external pressure [26] or electrical field [27], etc. Whereas in microfluidic
applications such as detection and sample illumination [28, 29], both the interface curvature-based and GRIN-based optofluidic lenses are widely used to focus light beam for higher signal-to-noise ratio and enhanced light intensity. The focal length is tunable two-dimensionally in a range of several hundred micrometers by tuning the fluidic configurations.

An issue of most optofluidic lenses is the relatively poor optical performance is, which limits its use in some Lab-on-a-chip applications. The optical performance of optofluidic lenses is usually degraded by optical aberrations including spherical aberration and field curvature aberration [22, 24]. Spherical aberration describes the optical engineering problem where the incident light beams are focused at multiple points by a lens [30]. A reduced spherical aberration can increase the focusing power for highly localized excitation. In interface curvature-based optofluidic lenses, spherical aberration can be reduced by optimizing the inference curvature, for example using an aspherical polymer-liquid interface [26, 27]. However, the method necessitates control systems to precisely control the electric fields or pressure, which make it challenging for chip integration. In optofluidic GRIN-based lenses, the focusing power is determined by the index profile and the ideal profile to suppress spherical aberration is not discussed previously [22]. A reduced spherical aberration in optofluidic lenses can greatly improve the optical performance in on-chip flow cytometry and integrated optical detection. For example, in fluorescent spectroscopy, the limit-of-detection is increased 3-fold with a reduced beam waist of 80 µm [28]. In on-chip flow cytometry, a small beam waist ensures a single sample is excited at a time in the detection region, which allows for higher sample concentration, and better performance in signal-to-noise ratio, the coefficient of variance
(CV) and throughput [29, 31]. On the other hand, field curvature aberration describes the optical aberration when multiple light sources are placed at different off-axis positions, they are focused on different focal planes. Traditionally, multiple light sources are generated by using integrated beam splitter or lens array, which increases the footprint and configuration complexity [32]. With a suppressed field curvature, multiple light sources can be focused on the same focal plane by using a single optofluidic lens. The single optofluidic lens can be exploited in applications such as barcoded particle scanning [33], particle velocity measurement [32], flow cytometry [34], photobleaching quantification [35, 36], and so forth. However, neither the effort to reduce field curvature nor the influence of field curvature in optofluidic systems is discussed and investigated.

Optical manipulation grows enormously benefitting from the technical advance in nanofabrication [37], single molecule detection [38], etc. It utilizes the combination of optical force, fluidic drag force, and particle’s Brownian motion to achieve functionalities such trapping, sorting and patterning. Optical force can be divided into far-field and near-field approaches based on the optical configuration. Far-field manipulation exploits the optical force from propagating waves in free space, while near-field manipulation exploits the force from evanescent waves in guided modes. The near-field approach is more effective in dealing with nanoscale biomolecules due to the larger gradient force induced by the diffraction-limit-free evanescent wave. Biomolecule is the biological matter in living organisms which include nucleic acids, virus, microvesicle and cell. The size of biomolecule generally ranges from several tens of nanometers to several micrometers. The refractive index is generally close to the index of water, ranging from 1.355 -1.42 [39]. The parallel manipulation of biomolecules is of great interest in physical and life science.
However, the small molecular size and low index contrast significantly reduce the optical force and poses a challenge to optical manipulation. Near-field optical manipulation solves the issue by using sophisticated optical structures to enhance the optical field. Various implementations of near-field manipulation have been demonstrated in recent decades based on different configurations such as prism, optofluidic waveguide, resonator and plasmonics [40].

The reported near-field manipulation generally focuses on the trapping of biomolecules at a specific point [41] or on a single line [42]. Most of these works cannot be arrayed to a large trapping region for parallel optical manipulation or sorting. For example, the resonator-based manipulation requires the applied frequency to match with the resonant frequency of the cavity [41]. Due to the unavoidable fabrication error, the resonant frequency could be very different from cavity to cavity. For the plasmonic-based manipulation, a few works demonstrate the feasibility to achieve multiple trapping points [43]. But the distance between the adjacent plasmonic structures is deliberately large to avoid cross-talking issues. It is still challenging to massively manipulating biomolecules for sorting, intercellular interaction study, etc.

In summary, many opportunities exist across the field of optofluidics. The marriage of opto and fluidic creates new level of light-matter interaction and promotes enormous optofluidic functionalities for broad applications. Therefore, the thesis focuses on the novel optofluidic functionalities stimulated by the unprecedented light-matter interaction: fluid-fluid interaction-induced light propagation pattern for biochemical detection, light-fluid interaction for lightwave controlling, and light-matter interaction for nanoscale sample manipulation.
1.2 Objectives

The main objective of this research is to explore the integrated optofluidic functionalities stimulated by the unprecedented light-matter interaction. Specifically, three aspects of this subject are investigated. First, the liquid diffusion-induced light propagation pattern is used to measure diffusion coefficient and monitor chemical reactions. Second, light-fluid interaction is utilized to develop a focusing lens with low optical aberrations. Third, photonic pillar array is used to manipulate nanoscale biomolecules based on the light interference in silicon waveguides.

An optofluidic waveguide sensor to monitor chemical reaction and measure diffusion coefficient is developed based on the light focusing pattern in optofluidic waveguides. The index profile is studied theoretically. The influence of the contributing factors, including interface position and Péclet number, on the focal position is investigated theoretically and experimentally. A characterization experiment is designed to validate the use of the focal position as a sensing signal. In chemical reaction monitoring, the hydrolysis of sucrose is studied and the initial hydrolysis rate is determined. In diffusion coefficient measurement, simulation models are built up to quantify the focal length difference as a function of the diffusion coefficient. The diffusion coefficient of ethylene glycol – deionized (DI) water solution is measured experimentally.

An optofluidic hyperbolic secant (HS) lens is developed to improve the focusing power. The optical aberrations which deteriorate the optical performance are investigated. The optimized index profile is derived based on coordinate transformation and a microfluidic gradient generator is designed to generate the index profile. The chip fabrication processes are developed for the fabrication of the optofluidic HS lens.
Subsequently, simulations are conducted to verify the performance of the optofluidic HS lens. In the experiment, the performance of the lens is evaluated, including the focal length and beam waist at different divergence angles and off-center positions. The focusing experiment with multiple light sources is also demonstrated.

An optofluidic manipulation system is developed for nanoparticle and bacteria manipulation based on photonic pillar arrays. The design considerations and parameters of the system are discussed in detail. The optofluidic chip is fabricated by using the silicon photonic fabrication processes, and silicon-glass bonding techniques. The buffer solution and surface treatment are optimized to minimize the particle adhesion problem. In the nanoparticle separation experiment, the trajectory of individual 200-nm and 500-nm particlces are compared, followed by the separation of 500-nm polystyrene particles from particle mixtures. The statistical analysis of the particle distribution is also conducted. In the bacteria trapping and alignment, the principle and force analysis are studied based on FDTD simulation. The motions of a single *Shigella* are investigated experimentally. Then parallel trapping and alignment of *Shigella* are conducted and the trapping rate is analyzed.

The above three topics are in the context of light-matter interaction in optofluidics. The study on the light propagation in optofluidic waveguides is used as a chemical sensor in the first topic, and then adapted into a focusing lens in the second topic. The third topic, the optofluidic manipulation system, involves many factors such as the Brownian motion, drag force and optical force. The fundamental understanding of diffusion, advection and light propagation from the first two topics is an indispensable link in developing the third topic.
1.3 Major contributions

The major contributions of this PhD thesis lie in the development of novel optofluidic functionalities in biochemical detection, optofluidic lens and particle manipulation. The details are listed below:

(1) The light propagation pattern in optofluidic waveguides is studied comprehensively, including the contributing factors, sensitivity, etc. The study provides a useful guidance on the design of the subsequent chemical sensing experiment. (See chapter 3)

(2) Chemical reaction monitoring is demonstrated based on the light focusing pattern in optofluidic waveguides. The proposed optofluidic method overcomes the integration problem of the traditional spectroscopy method and can be easily integrated in Lab-on-a-Chip systems. (See chapter 3)

(3) Diffusion coefficient measurement is demonstrated using a single optical image. It is simple and rapid compared with the conventional point-to-point measurements using interferometers. (See chapter 3)

(4) An optofluidic HS lens with low optical aberrations is developed by optimizing the index profile. The beam waist is reduced to $< 10\, \mu m$, which is twice better than the prior art. (See chapter 4)

(5) Coordinate transformation is used in the design of optofluidic HS lens to make the configuration of optical devices easier for microfluidic realization. It shows an example to design an optofluidic component from its solid counterpart. (See chapter 4)
Chapter 1 Introduction

(6) The focusing of multiple light sources is demonstrated. Thanks to the suppressed optical aberrations, this work can focus multiple light sources using a single optofluidic HS lens and in the meanwhile doesn’t compromise the focusing power. (See chapter 4)

(7) A near-field approach is proposed to sort nanoscale biomolecules in waveguide-pair array. The separation of 500-nm particles is demonstrated with a recovery rate of 94.76%. (See chapter 5)

(8) The photo-damage to the sample molecules is reduced in the near-field manipulation platform. Light energy is distributed in a large area and an accumulated optical force effects is obtained for particle manipulation. The guided power in each waveguide pair is only ~3 mW. (See chapter 5)

(9) The near-field manipulation platform can be used in broad biological applications such as optical mapping, biophysical characterization, cell-cell interaction, etc. Meanwhile, the platform is ready to be integrated with other microfluidic components or silicon photonic sensors to achieve more complex functionalities. (See chapter 5)
1.4 Organization of the thesis

The thesis is organized into six chapters. The introduction of the thesis covers the motivation, objective, and major contributions as presented in this chapter. The motivation section explains the background of the PhD research. The objective states the main focus of this thesis, and the contribution section lists the innovations and important findings.

In Chapter 2, literatures of light-fluid interaction, optofluidic waveguide, optofluidic lens, and near-field manipulation are reviewed. This chapter first reviews the light-fluid interaction and diffusion-controlled components in optofluidics. Then the chapter focuses on the concept and microfluidic configurations of optofluidic waveguides. The light propagation behavior and its application in integrated optofluidic systems are discussed. Afterwards, the principle and implementation of optofluidic lenses, as well as the application in Lab-on-a-chip systems, are introduced. Subsequently, the state-of-the-art near-field manipulation techniques, including the basic force analysis, experimental implementations, and the application in biological research, is reviewed. All such important background work provides the guidance and impetus for the research, and also lays the technological foundations on which the work of this thesis is built.

In Chapter 3, the light propagation behavior in optofluidic waveguides is studied. The index profile of optofluidic waveguides is investigated, including the comparison with solid gradient index waveguide, an analytical model, and the index profile measurement. Subsequently, the light propagation pattern in optofluidic waveguides is studied, including an analytical model and the light pattern as a function of the Péclet number and interface
positions. Finally, the optofluidic waveguide is used as a sensor for chemical reaction monitoring and diffusion coefficient measurement.

In Chapter 4, an optofluidic hyperbolic secant (HS) lens is developed to improve the focusing power. The optical aberrations which deteriorate the optical performance are investigated. Then the optimized index profile is derived based on coordinate transformation and a microfluidic gradient generator is designed to generate the index profile. Subsequently, simulations are conducted to verify the performance of the optofluidic HS lens. In the experiment, the performance of the lens is evaluated, including the focal length and beam waist at different divergence angles and off-center positions. The focusing experiment with multiple light sources is also demonstrated.

In Chapter 5, a photonic pillar array-based optofluidic manipulation system is presented for nanoparticle and bacteria manipulation. The design of the optofluidic system, including the microfluidic subsystem and the photonic subsystem, is discussed. Then the experimental preparation and setup are presented in detail, including the optimized buffer and surface conditions, the fabrication process, the experimental setup and the optical force calibration using a single nano-waveguide. In the experiment, the separation of 500-nm nanoparticle from particle mixtures is demonstrated, including the force analysis, the trajectory analysis, and the statistical analysis of the particle distribution. Finally, the trapping and alignment of Shigella are demonstrated in the optofluidic system.
CHAPTER 2
LITERATURE SURVEY

This chapter is divided into four parts. The first part briefly reviews the light-fluid interaction in optofluidics and the diffusion-controlled optofluidic components. The second part presents a review of the optofluidic waveguide which consists of the concept, microfluidic configurations, and the light propagating behavior. The review is then focused on its application in integrated optofluidic systems such as on-chip optical devices, biochemical detection, and particle manipulation. The third part focuses on the principle and implementation being employed to develop optofluidic lenses. Their application in Lab-on-a-chip systems is discussed in detail subsequently. The fourth part presents the state-of-the-art near-field manipulation techniques which include the basic force analysis, experimental implementations, and the application in biological research. All these works lay the foundation for the contributions of this thesis in the development of Lab-on-a-chip system for light manipulation and particle sorting.
2.1 Light-fluid interaction in optofluidics

2.1.1 Types of light-fluid interaction

Optofluidics is a technology that exploits the synergistic integration of optics and fluidics to create highly versatile devices and integrated systems [1, 44]. The integration of optical components brings in various optical functionalities such as imaging, light manipulation and optical detection to optofluidic systems. While the integration of fluidic components brings in the unique fluidic features such as reconfigurable, miscible and bio-compatible to the systems. The combination of optical and fluidic components facilitates their interaction in an unprecedented level, which promotes enormous optofluidic systems for broad applications.

The light-fluid interaction can be divided into two types based on the role of the fluidic component. Firstly, the fluidic component works as an alternative to the solid counterpart, i.e. the light interacts with the fluidic component in the same way as a solid component. However, the introduction of the fluidic component makes the optical and fluid interaction occur at the place that is difficult, if not impossible, in solid component-based systems. The feature facilitates many Lab-on-a-chip applications in biochemical detection and particle manipulation [6]. Meanwhile, the mobile nature of fluidic matters allows the dynamic control of the geometry and property of optofluidic systems, which fosters the emergence of many tunable optofluidic devices [7-9]. Secondly, multiple fluidic components could interact with lightwave and with each other simultaneously. The new level of light-fluid interaction creates novel optofluidic functionalities in biochemical detection and integrated optical components [25]. For example, the fluidic interactions such as molecular diffusion, chemical reaction, or biomolecule conjugation will lead to a distinct light
propagation behavior, which can be used for diffusion coefficient measurement and reaction monitoring.

### 2.1.2 Diffusion-controlled optofluidics

Diffusion is the physical process that molecules move from a high concentration region to a low concentration region. It plays a vital role in microfluidics because it is the primary process for liquid mixing in the laminar flow regime [45]. Diffusion, as an important method of fluid-fluid interaction, is used to create novel optofluidic components. Gradient index profiles are generated and reconfigured by controlling the liquid diffusion in microchannels. Light in the index profile shows specific propagating behaviours such as focusing, diverging, etc.

The most classical example of diffusion-controlled optofluidic components is optofluidic liquid-core liquid-cladding waveguides [8]. In the configuration, liquids with high and low refractive indices are used as the core and cladding flow streams, respectively. Liquid diffusion occurs between the core and cladding streams and leads to a gradient index profile. Optofluidic focusing lens is demonstrated based on the configuration [46]. Similarly, large angle bending is presented by exchanging the position of high and low index liquids, i.e. apply the low index liquid as the core stream, and high index liquid as the cladding streams [47]. In another work, the diffusion in five flow streams is utilized for an optical beam splitter [25]. The splitting ratio is tunable by dynamically controlling the flow rates. A wavelength filter is also demonstrated by adding dye molecules to specific flow streams.
2.2 Optofluidic waveguide

2.2.1 Concept and configuration

Optofluidic waveguide is a fundamental component in optofluidic systems. Similar to a traditional solid waveguide, it consists of a waveguide core with high refractive index and a cladding with low refractive index. The electromagnetic wave is localized in the waveguide core by total internal reflection (TIR) [48] or wave interference [49, 50]. In contrast to the solid waveguide, the optofluidic waveguide has at least a fluidic component in the waveguide core or the cladding. The fluidic component not only brings in flexibility in tuning waveguide configurations, but also brings in new optical features that cannot be found in the solid counterpart.

The optofluidic waveguide can be divided into liquid-solid (LS) and liquid-liquid (L\textsuperscript{2}) waveguides based on the number of the fluidic component. The LS waveguide has a single fluidic component in either the waveguide core or the cladding. The liquid-core LS waveguide has a solid cladding material and a fluidic core carrying the target samples [51, 52]. Since the majority of the optical power is confined in the liquid core, the waveguide has a higher efficiency of the light-matter interaction and is expected to have better sensitivity in sample detection [53, 54]. However, the liquid-core configuration places constraints in the cladding material selection. The refractive index of the liquid medium in the core is relatively low (∼1.33) compared to that of solid materials. Therefore, fluorinated polymers, such as Teflon AF are used as the cladding material due to its low refractive index of 1.29 [55]. Due to the limitation in Teflon AF fabrication, the diameter of the liquid core is in the order of several hundred microns. Such large dimension of the waveguide core permits the higher order modes and will lead to high propagation loss [56]. In
comparison, the liquid-cladding LS waveguide has a solid core and a fluidic cladding carrying the target samples [57, 58]. The guided light interacts with the target samples through the evanescent wave. The configuration is a well suited for the detection of the molecule in the cladding liquid [59]. However, the typical penetration length is on the order of 100-400 nm, which results in a low light-matter efficiency. The deposition of a suitable layer, such as a thin porous or metal layer is demonstrated to increase the penetration length significantly [60, 61].

On the other hand, the L² waveguide has the all-fluidic core and cladding [7, 13]. The all-fluidic configuration allows the dynamic control of the waveguide geometry and the fluidic properties, and therefore enables the tuning of the optical performance or even the optical functionality [7, 13, 25]. Both single-mode and multimode waveguides have been demonstrated by proper control of the index contrast between the core and cladding streams [62]. Another merit of the L² waveguide is that the core-cladding interface is formed smoothly by fluidics and the waveguide is, therefore, inherently free of the propagation loss caused by the channel roughness. However, there are some issues in the L² waveguide. Firstly, the L² waveguide is somewhat more susceptible to the flow and environmental fluctuations, which poses higher demand in the future system integration. Secondly, the common L² waveguide is actually a two-dimensional waveguide [62], i.e. it forms the waveguide configuration only in a plane, typically the low-high-low index profile in the x-y plane, but is homogeneous in the other plane. The configuration will cause considerable light leakage in the unconfined direction. A three-dimensional waveguide is demonstrated by using the centrifugal Dean flow in curved channels [15, 63]. But the implementation complicates the flow control and requires high flow rate (1 mL/min) continuously to have the inertial effect. Thirdly, the cladding and
core liquids are mixing continuously in the microchannel and could cause unwanted effects in certain applications [9]. The diffusion effect could be reduced by increasing the overall flow rate, or by changing the core and cladding into immiscible liquids [64].

2.2.2 Light propagating behaviour

Light in optofluidic waveguides could exhibit a distinct propagating behavior depending on the role of the fluidic components. In LS waveguides, the fluidic component replaces either the waveguide core or the cladding of a solid waveguide. The index distribution follows the similar profile with the solid counterparts and as a result, the light behavior in LS waveguides is similar to that in solid waveguides. For example, the fluidic cladding in slab waveguides still functions as the low refractive index medium to reflect light waves, and the light in it shows the pattern of guided modes [56]. On the other hand, the fluidic components bring in a freedom to control the light propagation behavior by changing the fluidic properties. Tunable multi-mode interference and self-image effect are demonstrated in LS waveguides [21, 65]. The self-imaging period is reconfigurable in the range of 500 μm by changing the fluid indices. In addition, the introduction of the fluidic component makes the light-matter interaction occur at the place that is difficult, if not impossible, in solid waveguides. The light behavior change could work as an indicator of the biomedical events happening in the liquid or in the solid-liquid interface. The resonance wavelength presents red shift when the anti-BSA selectively binds to the activated waveguide surface. The detection limit of refractive index is measured to be $5 \times 10^{-6}$ RIU [66].
In L\(^2\) waveguides, both the waveguide core and the cladding are made of fluidic mediums. The all-fluidic configuration endows optofluidic waveguides with an additional freedom to reconfigure the waveguide geometry, in addition to the freedom to change the fluidic properties. A reconfigurable L\(^2\) waveguide is demonstrated by using dielectrophoresis to reshape the waveguide geometry [13]. The waveguide is used as an optical switch at a speed of up to 0.929 mm/s\(^{-1}\). Other approaches such as hydrodynamical [14] or mechanical [15] are also employed to reshape the waveguide geometry. In those demonstrations, the L\(^2\) waveguide is treated as the fluidic counterpart to a solid waveguide and the light propagation in it is similar to the light behavior in solid single-mode or multimode waveguides. On the other hand, the all-fluidic configuration brings in additional fluidic-fluidic interactions to the light-matter interaction. In the L\(^2\) waveguide made of miscible liquids, the light behavior is not only related to the interplay between the fluidic and light as in the LS waveguide and the L\(^2\) waveguide, but also influenced by the interplay between the fluidic-fluidic interaction, such as reaction, diffusion, etc. As a result, light could exhibit distinct propagating behaviors in L\(^2\) waveguide. Light splitting and wavelength filter are observed in a diffusion-controlled L\(^2\) waveguide [18]. Several groups report the tunable light focusing in optofluidic waveguides and adapted it to a focusing lens [9, 22]. Analogous discrete diffraction is also demonstrated in L\(^2\) waveguide based on the diffusion-induced bi-directional gradient index profile. [20]

### 2.2.3 Applications in integrated optofluidic system

Optofluidic waveguide is a fundamental component in integrated optofluidic systems. The introduction of the fluidic component not only makes the light-matter
interaction occur at the place that is difficult, if not impossible, in solid waveguides, but also brings in additional fluidic-fluidic interactions. The features promote the use of optofluidic waveguides in broad applications such as on-chip optical devices, biochemical detection, and particle manipulation.

The basic function of optofluidic waveguides is to confine the light energy in the waveguide core. The function is widely used for sample illumination. SU-8 waveguides are integrated into an on-chip flow cytometer to excite the target particles in the detection region [67]. Optofluidic waveguide is also employed to collect the scattered light efficiently [68, 69]. The signal-to-noise ratio is increased by 10-fold than the conventional method using a microscope objective [69]. The optofluidic waveguide also works with beam splitters for multiplexed detection [32].

Optofluidic waveguides have a reconfigurable geometry and index profile, which facilitates its use as the fundamental component in many tunable optofluidic devices. The low-high-low index configuration of optofluidic waveguides is adapted to a focusing lens [9, 22]. The focal distance is demonstrated to be variable two-dimensionally in a range of several hundred micrometers by tuning the fluidic configuration. Optofluidic dye laser is also reported based on a 3D optofluidic waveguide and the slope efficiency of the laser is increased at least 3-fold than its traditional two-dimensional equivalent. Many other integrated optofluidic components are also developed such as optical switch [62, 70], optical filter [71], evanescent coupler [72], etc.

Optofluidic waveguides could work as a sensor for biochemical detection benefiting from the easy light-matter interaction. Different detection mechanisms are employed in optofluidic waveguide sensors. A common approach is to detect the refractive index change caused by the presence of the target molecules. Since the
refractive index change is typically very small, optofluidic waveguide usually combines with resonant structures to obtain a high sensitivity. The detection limit in an antiresonant reflecting optical waveguide (ARROW) is measured to be $9 \times 10^{-4}$ RIU by measuring the resonance shift in the transmission spectrum [73]. The detection limit is decreased to $1 \times 10^{-7}$ RIU in a microsphere-based resonator [74]. Higher performance is reported based on more sophisticated resonators such as the whispering gallery mode resonator [75], ring resonators [76], etc. Another widely used approach is to detect the amount of absorbed light when passing through the target solution. The absorption occurs when the optical frequency matches the resonant frequency of the molecular structures. A bandgap liquid-core waveguide is demonstrated to detect ethyl chloride with a concentration limit of 30 ppb [77]. Hollow core fiber waveguide is also widely employed to detect chemicals due to its inherent advantage in fabricating long absorption channels [76]. However, the long absorption channel could be a problem in system integration. Resonant structures are exploited to maintain a long enough light-matter interaction length, and in the meantime make the sensor compact for on-chip integration [78]. A compact yet sensitive fiber sensor is developed based on localized surface plasmon resonance and the sensitivity is measured to 67.6 nm/RIU [79].

Another important application of optofluidic waveguides is particle manipulation based on the near-field evanescent wave. Evanescent wave is an electromagnetic field that decays exponentially outside the waveguide core. The shape decay of the light intensity induces a strong optical gradient force which makes it promising for nanoparticle manipulation. Solid SU-8 core and liquid cladding waveguide are presented to trap and transport microparticles. The particle velocity reaches 28 $\mu$m/s with a guided power of 53.5 mW [80]. The trapping of nano-sized
particles is demonstrated in waveguides with intensity enhancement structures. 75-nm nanoparticles and λ-DNA molecules are trapped in sub-wavelength slot waveguides. The trapping occurs along a line and provides the ability to handle extended biomolecules directly [42]. One merit of the optofluidic waveguide-based particle manipulation is that all the molecules are trapped on an image plane, which greatly facilitates the experimental observation and quantitative analysis. Parallel DNA molecule trapping is demonstrated in a controlled fashion based on the standing-wave evanescent field [81]. Besides, optofluidic waveguides can be integrated with more detection techniques, which make it more powerful for biomedical application [82]. However, one major issue of the waveguide-based particle manipulation is that the manipulation region is limited to 100-400 nm above the waveguide surface. To obtain a higher efficiency, shallow microchannels are needed to bring the target molecules to the optical interaction volume. But it complicates the fabrication process and the flow control. Another issue is that complexed hydrophobic and electrostatic interactions exist in the solid-liquid surface. The buffer solution and surface condition need to be prepared carefully to have obvious optical force effect [42, 81].
2.3 Optofluidic lens

2.3.1 Principle and design

Optofluidic lens is an important component for on-chip optical systems with apparent advantages over a solid lens such as tunable refractive index and reconfigurable geometry. Optofluidic lens utilizes the interaction between fluidic and light to manipulate light and is a promising candidate for broad applications ranging from sample illumination to biomedical detection. It can be categorized into interface curvature-based [23, 24, 83, 84] and gradient index (GRIN) lens [22, 85]. The curvature-based optofluidic lens uses the curvature of liquid-liquid interface, air-liquid interface or air-polymer interface to refract light beams based on the well-known Snell’s law. The liquid-liquid interface could be formed in both miscible and immiscible liquids. Optofluidic lenses made of miscible liquids are demonstrated based on the hydrodynamic focusing effect in an expanded microchannel [24] or circular-shaped chamber [84]. The light focusing position is reconfigurable by changing the liquid refractive index or changing the flow rate ratio to reshape the interface. The advantage of this configuration is that the liquid-liquid interface is inherently smooth and it will avoid the light scattering caused by sidewall roughness. There are some issues lies in the lens. Firstly, the liquid-liquid interface required the liquid pumping continuously at high flow rates. It will consume a large amount of solution, which is impractical in some applications. Secondly, the interface shape cannot be tuned accurately to eliminate optical aberrations such as spherical aberration. The optical performance is degraded as a consequence. Thirdly, the liquid-liquid interface is more vulnerable to flow fluctuations. Therefore, the lens mainly targets to applications such as sample illumination where the flow stability is
not very critical. On the other hand, tunable optofluidic lenses made of immiscible liquids are demonstrated. Since the liquids are immiscible, the interface shape can be maintained easily and tuned with various mechanisms such as electrowetting [86, 87], dielectrophoresis (DEP) [86, 87], stimuli-responsive hydrogels [88], etc. The air-liquid interface is also exploited in optofluidic lenses. The interface shape is determined by the air-liquid surface tension and the external forces such as pressure and electrostatic force [89]. The focal length can be tuned simply by changing the external force. Similarly, the deformable air-polymer interface is also employed to make tunable optofluidic lenses. The polymer is usually a transparent flexible membrane and deformable under external pressure [90].

Another type of optofluidic lenses is the GRIN lens. The lens uses the GRIN to bend light beams gradually in a large region, rather than refract them instantly at the interface. The light propagation in optofluidic GRIN lenses can be calculated using the ray tracing method. The GRIN profile can be generated by various methods. The most common method is based on the controlled liquid diffusion at low Reynold numbers. In the configuration, the liquids with different indices are pumped into the microchannel at low flow rates. The diffusion between the flow streams induces a GRIN profile which is used to focus [46] or split [47] light beams. Since low flow rates are needed to form the lens, the solution consumption in this configuration is much lower than that in liquid-liquid interface-based lenses. However, it is challenging to generate a three-dimensional gradient index, and as a result, the reported GRIN lenses are usually two-dimensional lens. The drawback greatly limits its use in imaging applications. Another method to generate the GRIN is based on the temperature-dependent nature of liquids. Light focusing is demonstrated in several thermal GRIN lenses with various configurations [85, 91, 92]. The major issue in the
configuration is the limited refractive index contrast caused by the low thermooptical efficient.

### 2.3.2 Microfluidic implementation

The apparent advantage of optofluidic lenses over a solid one is the great reconfigurability. The features are inherited from the flexible liquid and polymer material, as well as the sophisticated tuning mechanisms. Most liquid mediums are optical transparent and have a refractive index (RI) ranging from 1.29 to 1.64 [93]. The common liquids such as water (RI: 1.332), ethylene glycol (RI: 1.432), etc. are low in refractive index, while the high index liquids such as Benzyl alcohol (RI: 1.54) and benzothiazole (RI: 1.64) are usually volatile organic compounds, and raise health concerns. As a result, the commonly-used liquids in optofluidic lenses are the low refractive index liquids, namely water, ethylene glycol and CaCl₂ solution. Another liquid property that matters is the diffusion coefficient which describes the speed of liquid mixing. It is a vital parameter to maintain a clear liquid-liquid interface and to control the GRIN profile of optofluidic lenses. The liquid diffusion coefficient differs greatly from $0.2 \times 10^{-9}$ to $6.0 \times 10^{-9}$ m$^2$/s [94]. Regarding the polymer material, polydimethylsiloxane (PDMS) is widely used due to its excellent optical and mechanical performance. PDMS is an optically transparent material and has a refractive index of 1.4 [95]. It can be fabricated into thin membranes (~10 μm), and in the meanwhile maintain a strong enough mechanical strength. The PDMS membrane can be deformed in a controlled fashion and achieves tunable light focusing or diverging. Metal layers are also deposited onto the PDMS membrane to increase the reflectivity in some applications [96].
As discussed in Paragraph 2.2.1, optofluidic lenses can be categorized into interface curvature-based and GRIN lens. The two types of lenses can be tuned by different tuning mechanisms. In the interface curvature-based lens, the tuning mechanisms include hydrodynamic, electrical and mechanical techniques.

The interface curvature can be formed at the liquid-liquid interface and tuned by hydrodynamic force. The first hydrodynamically tuned optofluidic lens is demonstrated by the laminar flow of three flow streams in an expanded microchannel [24]. The interface is reshaped from biconvex to meniscus by simply tuning the core and cladding flow rate ratio. The similar concept is demonstrated in circular and hexagonal channels [84, 97]. Biconcave lens is demonstrated by using a two-inlet and two-outlet design. The design allows light focusing using low RI liquids. The curved liquid-liquid interface is also formed in a curved channel due to a centrifugal effect [23]. The interface shape is determined by the ratio of centrifugal force to viscous force and can be conveniently reshaped by changing the flow rate. The functionality of the optofluidic lens is not limited to optical focusing. A tunable optofluidic prism is reported based on the liquid-liquid interface of two flow streams in a triangular chamber [83]. The apex angle is tuned from 75° to 135° by controlling the flow rate ratios. The lens shows high potential in continuous beam steering and on-chip spectroscopy.

The interface curvature can also be tuned by electrical force. Electrowetting effect describes the contact angle change at the solid-liquid interface when an external electrical field is applied. It is used to tune the interface shape in optofluidic lenses. The first proof of concept is demonstrated using a liquid electrolyte on a gold electrode. The contact angles changes from $128 \pm 2^\circ$ to $37 \pm 2^\circ$ with a voltage change of -1.7 V [98]. Similar works are reported with different electrode designs [99, 100].
Dielectrophoresis (DEP) effect is another phenomenon to tune the interface shape. It exploits the electrostatic force in a gradient of electric field. The power consumption is usually an order of magnitude smaller than in electrowetting-based lenses. A liquid crystal droplet lens is demonstrated [101]. The focal length changes from 1.6mm to 2.6mm tuning by the DEP forces in an alternating current (AC) electrical field.

An alternative way to tune the interface curvature is based on mechanical force. The pressure inside liquids is utilized to deform PDMS membranes. Biconcave and meniscus lenses are demonstrated by pumping liquids in or out the fluidic chamber. A lens array is fabricated based on the simple soft-lithography technique [102]. Another tunable optofluidic lens is demonstrated with variable aperture [103]. An actuator level is used to control the lens aperture and the curvature of the PDMS membrane at the same time. The interface curvature is also tuned mechanically by using stimuli-responsive hydrogels. A fluidic lens with autonomous focusing is demonstrated based on temperature and pH-responsive hydrogels [88]. The temperature-responsive hydrogel transits from expansion to contraction when the temperature increases from low to high. The focal length is demonstrated to be tunable from divergent and convergent. Similarly, chemical-responsive hydrogel is utilized in a tunable lens in another work [104]. The hydrogel swells or shrinks in response to a chemical stimulus. The feature endows the lens with great potential in optical detection and biosensing.

The GRIN-based lens utilizes the gradient index profile generated by various methods such as diffusion-induced concentration gradient, thermal gradient, etc. A diffusion-induced GRIN lens is demonstrated using CaCl₂ and di-ionized water. The focal length is variable two-dimensionally in a range of several hundred micrometers by tuning the fluidic configuration [22]. In another work, the index profile is
optimized to suppress spherical and field curvature aberrations [9]. The spot size is measured to be smaller than 10 μm, which is twice better than the prior art. Similarly, the thermal-induced GRIN lens can be tuned by controlling the thermal gradient. The thermal gradient is generated by shining laser beams onto two chromium strips [85]. Benzyl alcohol solution is heated up by the metal strips and creates a two-dimensional gradient. The focal length changes from infinity to a minimum of 1.3 mm. Another thermal-induced GRIN lens is also demonstrated based on co-flowing streams with different temperatures [91].

2.3.3 Lab-on-a-chip Applications

Optofluidic lens shows advantages over a solid lens in several aspects. First, optofluidic lens has great flexibility in reconfiguring the refractive index and geometry. The focal length is tunable three-dimensionally based on various driving mechanisms. Second, optofluidic lens is generally compact in size. The lens is fabricated using microfabrication technique, which allows the integration of multiple lenses in a small space. Third, optofluidic lens is inherently compatible with microfluidic systems. It avoids the necessary assembly and alignment in solid lenses. Optofluidic lens caters the growing demand posed by Lab-on-a-chip systems, and has been used in various areas such as imaging, sample illumination, optical detection, particle manipulation, and so forth.

Optical imaging is a common function for both solid and optofluidic lenses [105-107]. Optical imaging poses high requirement on the lens performance such as stability, fast response time and small optical aberrations. A tunable lens array is demonstrated using soft lithographic techniques [108]. PDMS membrane is bonded
with the underlying microfluidic network. The imaging plane is tunable in a range of several hundred micrometers by controlling the external pressure. The optical resolution can reach 3 μm with a pressure of 20 KPa. The optofluidic lens cannot correct optical aberrations by using additional compensation lenses as in solid optical systems [109, 110]. To obtain an improved imaging quality, optical aberrations should be suppressed deliberately in another way. An optofluidic lens with tunable focal length and asphericity is demonstrated to reduce spherical aberration [111]. The interface between a conductive fluid and a non-conductive ambient fluid is controlled by varying both the hydrostatic pressure and electric fields. The focal lengths and spherical aberrations are tunable in a range of 8 - 20 mm, and -1.79 - +1.13 mm, respectively.

Optofluidic lenses are also used for sample illumination in flow cytometer [112-114], optical detection [28], etc. An improved on-chip flow cytometer is demonstrated by integrating a liquid-liquid lens to reduce the laser beam size. The laser beam size is 23 μm after the lens and the coefficients of variation (CV) is reduced to 20% for 5-μm particles. Another GRIN lens with reduced spherical aberration and field curvature is demonstrated to further improve the focusing power [9]. The beam waist is reduced to 7.8 μm, which is expected to improve the throughput, signal-to-noise ratio and CV in flow cytometers. More applications have been demonstrated in particle velocity measurement [32], barcoded particle scanning [33], photobleaching quantification [35, 36], etc.

Optofluidic lens can not only excite the sample, but also collect the fluorescent or scattering signal from the detection region [115-117]. A droplet-based lens array is integrated into a microfluidic device to enhance the fluorescent intensity [116]. The fluorescent and spatial resolution are increased by 8-fold compared with
the device without the lens array. In an on-chip flow cytometer, a fluidic lens is used to collect the light scattering signal at predefined angular regions to achieve angularly resolved measurement [113].

Another important application of optofluidic lenses is integrated optical tweezer [118-121]. A tunable thermal GRIN lens is demonstrated to trap a single living cell in flowing environments [118]. The focal length is tunable from 430 μm to 930 μm with a beam waist of 4 μm. Cell manipulate is realized in a rapid and simple fashion by tuning the focal length. The configuration avoids the complex optical setup in the traditional bulk system. The issue of integrated optical tweezer lies in the challenge in manipulating nano-sized biomolecules. Highly focused light beam is needed to trap small biomolecules such as DNA and exosome [122, 123]. Due to the limitation in eliminating optical aberrations, the focusing power of optofluidic lenses is still low compared with solid lenses.

Optofluidic lens can also work as a sensor for biomedical detections [124-126]. The focal length of optofluidic lenses is sensitive to external conditions such as pH, temperature, protein, etc. In the protein-responsive hydrogel-based lens, the image pattern produced by the lens changes with the presence of target molecules. Similarly, the thermal lens effect is utilized to detect the molecule distribution [127] or a single nanoparticle [92].
2.4 Optical manipulation in a near-field lattice

2.4.1 Forces in optical manipulation

Optical manipulation utilizes the combination of optical force, fluidic drag force, and particle’s Brownian motion to achieve manipulation functionalities such as trapping, sorting, patterning, etc [128-130]. The phenomenon that particle movement could be affected by light has been observed 400 years ago by Johanne Kepler [131]. He proposes that it is the solar ray that deflects a comet’s tail away from the Sun. In the 1970s, Ashkin et al. demonstrate the trapping of a dielectric particle by single-beam gradient force [132]. In recent years, optical manipulation has grown enormously benefitting from the advance in other optics-related areas [37]. The development of optical manipulation boosts the research in many areas such as cell biology [133, 134], atom physics [135], microscopy [136], and many others [137-139].

Optical force origins from the photon momentum change when the photon is absorbed or scattered by the object in the optical field [140]. The notion suggests the most general method to calculate the optical force:

\[
\langle \vec{F} \rangle = \iiint (\vec{T}) \cdot \vec{n} dA
\]  

(2.1)

Where \( \vec{T} \) is the Maxwell stress tensor, \( \vec{n} \) is a surface normal, and \( A \) is an arbitrary surface. The equation indicates that the optical force equals to the surface integral of the momentum flow, which is described by Maxwell stress tensor. The time-independent Maxwell stress tensor is expressed as

\[
T_{ij} = \varepsilon_0 E_i E_j + \mu_0 H_i H_j - \frac{1}{2} \left( \varepsilon_0 E^2 + \mu_0 H^2 \right) \delta_{ij}
\]  

(2.2)


Where $\varepsilon_0$ is the electric constant, $\mu_0$ is the magnetic constant, $E_i$ and $E_j$ are the two components of the electric field, $H_i$ and $H_j$ are the two components of the magnetic field, and $\delta_{ij}$ is the Kronecker's delta. Eq.(2.1) and (2.2) are the universal equation to calculate optical force on an object, but the calculation could be computationally intensive. Theoretical approximation is made to simplify the equations.

The regimes of optical manipulation can be divided into Mie regime, Rayleigh regime and intermediate regime based on the relationship between the particle radius and wavelength [141]. In the Mie regime, the particle radius is much larger than the wavelength and optical force can be calculated with ray optics approximation [142]. In the Rayleigh regime where particle radius is $<1/6$ of the wavelength, a particle could be treated as an electric dipole [143]. Optical force in the regime is the result of light absorption and re-emission by the dipole. In the intermediate regime, the particle size is comparable with the wavelength, and the optical force can be calculated based on Lorentz-Mie theory [144].

Since near-field optical manipulation focuses on nano-sized objects, Rayleigh approximation can be used in the optical force calculation. Based on rigorous quantitative derivation, the optical force is decomposed into optical gradient force and scattering force as [37]

\[
\vec{F}_{\text{grad}} = -\frac{2\pi n_r r^3}{c} \left( \frac{m^2 - 1}{m^2 + 2} \right) dI(\vec{r}) \quad (2.3)
\]

\[
\vec{F}_{\text{scat}} = \frac{128 n_0 \pi^5 r^6}{3c\lambda^4} \left( \frac{m^2 - 1}{m^2 + 2} \right)^2 I(\vec{r}) \quad (2.4)
\]

Where $m$ is the refractive index ratio of the particle to the surrounding medium, $n_0$ is the refractive index of the media, $r$ is the particle radius, $c$ is the velocity of light in
vacuum, $dI(\vec{r})$ is the intensity gradient as a function of position, $\lambda$ is the light wavelength, and $I(\vec{r})$ is the time-averaged energy intensity as a function of position. If the particle index is larger than the medium index, i.e. $m > 1$, the gradient force is attracting the particle to the intensity maximum. While if the particle index is smaller than the medium index, i.e. $m < 1$, the gradient force is pushing the particle away to the intensity maximum.

Another two forces in optical manipulation are the fluidic drag force and Brownian force. The drag force is calculated by \[ F_{\text{drag}} = 6\pi\mu r \cdot (v_f - v_p) \] (2.5)

where $\mu$ is the liquid viscosity, $v_f$ and $v_p$ are the flow velocity of the flow and particle, respectively. Brownian force is calculated by \[ F_{\text{Brown}} = \zeta \sqrt{\frac{12\pi\mu r \cdot k_B T}{\Delta t}} \] (2.6)

Where $\zeta$ is a normally distributed random number with a mean of zero and unit standard variation, $k_B$ is the Boltzmann constant, $T$ is temperature, and $\Delta t$ is the calculation time step. The equation indicates that Brownian force is a random force with the amplitude determined by liquid viscosity, particle size, and thermal energy.

Based on the above equations, the typical force levels for different-sized particles are summarized in Table 2.1. Here the optical energy intensity is $10^{10}$ W/m², the fluidic flow velocity is 20 $\mu$m/s, and the amplitude of Brownian force is calculated. It indicates that the optical force of 200-nm particle is comparable with the Brownian noise, i.e. the optical force is negligible. Whereas the optical force of 500-nm and 1000-nm particles, the optical force is much larger than the fluidic drag force and Brownian force. It also suggests that the light energy intensity is adequate...
to manipulate 500-nm and 1000-nm particles. However, to manipulate 200-nm particle, the energy intensity should be increased at least one order of magnitude.

Table 2.1: Typical value of difference forces on particles.

<table>
<thead>
<tr>
<th>Particle size</th>
<th>Optical force ($I_0: \sim 10^{10}$ W/m$^2$)</th>
<th>Drag force (Velocity: 20 μm/s)</th>
<th>Brownian force (Frame rate: 10 fps)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 nm</td>
<td>$\sim 0.001$ pN</td>
<td>0.005 pN</td>
<td>0.005 pN</td>
</tr>
<tr>
<td>200 nm</td>
<td>$\sim 0.01$ pN</td>
<td>0.04 pN</td>
<td>0.01 pN</td>
</tr>
<tr>
<td>500 nm</td>
<td>$\sim 1$ pN</td>
<td>0.1 pN</td>
<td>0.02 pN</td>
</tr>
<tr>
<td>1000 nm</td>
<td>$\sim 50$ pN</td>
<td>0.2 pN</td>
<td>0.03 pN</td>
</tr>
<tr>
<td>HIV virus</td>
<td>$\sim 0.008$ pN</td>
<td>0.02 pN</td>
<td>0.008 pN</td>
</tr>
<tr>
<td><em>E. Coli</em></td>
<td>$\sim 20$ pN</td>
<td>0.5 pN</td>
<td>0.05 pN</td>
</tr>
</tbody>
</table>

The particle motion in an optical field is governed by Langevin equation as expressed [146]:

$$m \frac{d^2x}{dt^2} = F_{\text{Brow}} + 6 \pi \mu r (v_f - \frac{dx}{dt}) + F_{\text{Opt}}(r)$$  \hspace{1cm} (2.7)

Where $m$ is particle mass, the left term corresponds to the overall force, the terms on the right are the Brownian force, fluidic drag force and optical force, respectively. The particle’s motion can be calculated based on the above equation using finite element simulation.
2.4.2 Near-field implementation

Optical force can be divided into far-field and near-field approaches based on the optical configurations. Far-field manipulation exploits the optical force from the propagating wave in free spaces, while near-field manipulation exploits the force from the evanescent wave in guided modes. The near-field approach is more effective dealing with nanoscale biomolecules. Eq.(2.3) and (2.4) suggest that the optical gradient force and scattering force are proportional to the third and sixth power of the particle radius, i.e. the optical scattering force is decreasing much faster than the gradient force when the particle size is decreased. Therefore, the optical gradient force is the dominant force in dealing with nanoscale objects. In far-field approach, the gradient force is induced by diffraction-limited optical spots; while in near-field approach, it is induced by the exponentially decaying evanescent field. Since the gradient force is directly proportional to the intensity gradient, the gradient force in near-field is much larger than that in far-field. Various implementations of near-field manipulation have been demonstrated in recent decades. They are classified into different types based on the configuration: prism-based, planar waveguide-based, resonator-based and plasmonic-based.

A straightforward way to obtain a near-field light field is to project a free-space light on a prism above the critical angle. The configuration origins from the surface plasmon resonance-based biosensor [147, 148] and is adapted to optical manipulation [149-152]. A near-field optical conveyor belt is demonstrated based on a motional standing wave on a prism surface [149]. An individual particle with size from 350 nm to 800 nm is moved over a distance of 36 μm. 520-nm and 750-nm particles are separated selectively from particle mixtures. An enhanced transporting speed is achieved in a similar configuration [150]. The apparent merit of the prism-
based optical manipulation lies in the simple chip fabrication which is usually complicated in near-field manipulation. The configuration exploits the mature light shaping technique to modulate light fields, and avoids the fabrication-intensive on-chip light shaping. Meanwhile, the experimental setup can be adapted from a far-field setup with minor modifications. These features are potentially attractive for researchers who have limited access to device fabrication. However, the configuration brings in issues such as incompatibility with microfluidic systems, bulky system size, etc.

The advancement in integrated optical systems, such as silicon photonics, metamaterials, etc. benefits the development of near-field manipulation. The integrated near-field manipulation is compatible with microfluidic systems, which facilitates its use in vast Lab-on-a-chip applications [153, 154]. Solid-core waveguide is utilized as the component to trap and transport particles [153]. The earliest work uses a channel waveguide to trap 1 - 5 μm polystyrene particles and transports them at a speed up to 14 μm/s. The propulsion of 10 - 40 nm gold nanoparticles is demonstrated in an extended work [155]. The maximum velocity is 8 μm/s with a guided power of 500 mW. Flowing liquid is then added to the later works. A near-field manipulation platform is presented based on a planar SU-8 waveguide integrated with PDMS microfluidic channel. Trapping and transport of 3-μm particle are experimentally demonstrated with the light field perpendicular or opposite to the flow direction. The particle velocity along the waveguide reaches 28 μm/s with a guided power of 53.5 mW. Similar works are demonstrated with various waveguide designs such as ARROW waveguide [156], photonic crystal waveguide [157], etc. Although near-field manipulation has inherent advantage in dealing with nanoscale biomolecules, tremendous efforts are still needed for nano-sized biomolecules
manipulation [129, 158]. Slot waveguides, made of two closely-placed single mode waveguide, are utilized to trap and transport 75-nm dielectric particles [42]. The optical energy is confined in the slot region which is 50 nm and 120 nm in width. The highly condensed optical field greatly increases the optical force and makes it manageable for nanoparticle and DNA manipulation.

To increase the trapping force, optical resonators are used to enhance the local light field. A simple way is to use optical ring resonators [159-162]. The light field in the resonator is greatly enhanced when the applied laser source is on the resonance wavelength. A ring resonator with micrometer radii is used to trap 0.5-μm and 1.1-μm particles [161]. The field intensity enhancements are 1.50 and 1.76 for 5-μm and 10-μm ring resonators, respectively. In another work, the resonance wavelength is found to be influenced by the presence of a trapped particle. An optofluidic ring resonator switch is demonstrated using the phenomenon [162]. The field intensity is enhanced by 2.5 times and 80% particles are diverted onto the ring at an on-resonance state. Quality factor (Q-factor) is the parameter which determines the intensity amplification of a resonator. Resonators with higher Q-factor are developed to further enhance the light intensity. A whispering gallery mode (WGM) resonator is demonstrated to trap 280-nm nanoparticles [163]. The Q-factor is as high as $10^6$ and the excitation power is only 32 μW. A drawback of the WGM or ring resonator-based manipulation is that the particle rotates along the microsphere or ring rather than resides at a specific location, which is opposite to the precise location requirement in biological manipulation. A photonic crystal resonator-based manipulation is reported to trap nanoparticles [41]. The photonic crystal resonator consists of 16 holes and a defect at the center. When the applied laser is on the resonance wavelength, the light intensity is tightly localized in an extremely small volume. The Q-factor of the
resonator reaches \( \sim 2500 \) in water. The trapping of 48-nm and 62-nm are demonstrated in the system.

Another method to enhance the light field is based on surface plasmon resonance (SPR). SPR describes the field enhancement or absorption caused by the coherent oscillation of valence electrons in noble metals [164]. Either the incident light or the metal surface is patterned in SPR-based optical manipulation. In an early demonstration, the optical force on a particle is measured using a photonic force microscope. The result shows that the force is enhanced 40 times compared to non-resonant illumination [165]. The localized SPR (LSPR) in metal structure or nanoparticles is also utilized in many works. The trapping and sensing of 10 nm metal particle are demonstrated in a dipole antenna structure [166]. The trapping is achieved by the optical trap induced by the LSPR between two closely places antennas. The event of a single trapping is resolved by monitoring the scattering spectra. The SPR-based manipulation traps particles tightly at the specific location, and therefore no particle transport is allowed in the classical configuration. An optical manipulation platform integrating waveguide and LSPR is demonstrated to transport particle to the pre-designed location. Gold bowtie structure is used to generate the highly localized optical field and the trapping force reaches 652 pN/W on 20-nm polystyrene particles. Other SPR-based phenomena are also exploited to trap nanoparticles [167-169]. Self-induced back-action (SIBA) effect is demonstrated to trap and sense 50-nm nanoparticles [170]. SIBA effect is proven to reduce the required light intensity by an order of magnitude compared to the prior art.
2.4.3 Applications in biomedical science

Optical manipulation technique has grown enormously in recent decades. It provides a non-invasive tool for handling biomolecule samples. Many research works have demonstrated the various implementation and functionality for practical biological study. Biomolecule is the biological matter in living organisms which include nucleic acids, virus, microvesicle, cell, etc. The size of biomolecule generally ranges from several tens of nanometers to several micrometers. The refractive index is generally close to the index of water, ranging from 1.355 -1.42 [39]. The small molecular size and low index contrast significantly reduce the optical force and poses a challenge to optical manipulation. Near-field optical manipulation minimizes the issue by enhancing the optical field, and has been used in broad applications such as biophysical research, Raman spectroscopy, force measurement and so forth.

The fundamental functionalities of an optical manipulation are trapping and transport. Their combination evolves into new functionalities such as patterning, sorting, binding, etc. Parallel trapping of yeast cells is demonstrated in a microfluidic environment based on plasmonic structures [171]. The light field is patterned by gold disks with a diameter of 2 - 3 μm. The illumination intensity is $10^2$ mW/μm². The pattern of the trapped bacteria is configurable by designing the landscape of gold disk [172]. In another work, *Escherichia coli* (*E. coli*) bacteria is trapped and aligned in dipole antennas [173]. Metallic dipole antennas are patterned on a glass substrate to produce an LSPR-induced trapping force. Incident light from an 800-nm laser is used to minimize the photodamage to *E. coli* [43]. The energy intensity is $10^3$ mW/μm², which is at least an order of magnitude smaller than other works [171, 174]. Bacterial growing and dividing of the trapped *E. coli* are observed in a period of two hours. Several later works demonstrate the manipulation of nanoscale biomolecules [175,
The trapping and release of \(\lambda\)-DNA are demonstrated in a 60-nm-wide slot waveguide [42]. The DNA is YOYO-1 labeled and 48 kbp in length. The laser wavelength is 1550 nm and the optical power is 250 - 300 mW at the fiber tip. A common concern on the DNA trapping is the photodamage issue in the work. The slot waveguide confines the optical power, which is as high as 300 mW, tightly in a small volume. Meanwhile, water has high absorption in 1550 nm. Substantial amount of heat is expected to generate in the configuration, and is possible to damage the DNA molecules.

Near-field optical manipulation provides an unprecedented platform for biophysical research. The biophysical properties of biomolecules are studied under an external stretch force [81, 177-180]. A near-field optical stretcher is proposed based on an add/drop ring resonator system [180]. The biological material is stretched by the additive surface force in the optical field. Trapping and stretching event are monitored by the output spectrum in real-time. In another work, individual double-stranded DNA is trapped and stretched in a silicon photonic circuit [81]. The photonic circuit manipulates the trapped molecule with a nanometer precision based on the phase control of standing waves. Each end of the DNA is bonded to a 490-nm particle to form a DNA dumbbell. DNA is stretched by controlling the position of particles in the DNA dumbbell. The system greatly facilitates DNA research in two aspects. First, the configuration facilitates microscopic observation by trapping the DNA on the imaging plane. It avoids the troublesome adjustment of each particle position in the traditional dual-beam optical trap. Second, the configuration allows the parallel manipulation of multiple DNAs, which has an apparent advantage over the traditional method.
Near-field optical manipulation has been integrated into various biomedical instruments such as Raman spectroscopy [181-183], force measurement [184-186], and many others [187]. A double nanohole structure in a metal film is reported for Raman spectrum analysis [182]. 20-nm particle is trapped in the optical field and the Raman spectrum is recorded simultaneously. Although nanoscale biomolecule is measured in the system, the work still has high foreseeable potential in single molecule spectroscopy, which is challenging in traditional optical tweezers [188, 189]. The optical force on a trapped microsphere is measured by combining a calibrated total internal reflection microscopy and a lock-in detection method [184]. The measurement resolution is as low as 1 fN in 100 seconds, which is close to the thermal limit in liquids.

Near-field optical manipulation greatly facilitates the biological research, but there are several issues or concerns in practical biological applications. The major concern is the potential photodamage to the biomolecules [43, 190, 191]. The photodamage to *E. coli* is studied in an optical trap. The rotation rates of cells are quantitatively measured to analyze the cell viability. The result suggests that the photodamage shows minima at 830 nm and 970 nm, and maxima at 870 and 930 nm. The maximum photodamage is ~5 times larger than the minimum value. Another issue is the potential molecule absorption on the trapping structure [192]. For example, the surface tethering disrupts the molecular structure in protein folding studies [40]. The buffer solution and surface condition need to be prepared carefully in the experiment.
2.5 Summary

Based on the literature survey presented, there are still some unexplored fields in the optofluidic studies. First, optofluidic waveguide is a fundamental component in optofluidic systems. The light in it shows a distinct behavior, but few efforts are made on its biomedical applications. Second, the optical performance of current optofluidic lenses is usually poor due to severe optical aberrations. Reducing the optical aberrations can greatly enhance the focusing power and broadens its application in sample illumination, and multiplexed detection. Third, the current near-field manipulation technique mainly focuses on trapping, which can only handle a limited number of biomolecules at a time. An optical sorting system is greatly useful in biomolecule purification and enrichment.
CHAPTER 3

LIGHT PROPAGATION IN OPTOFLUIDIC WAVEGUIDES

This chapter studies the light propagation manner in optofluidic waveguides and utilizes it as a signal for chemical sensing. The index profile of optofluidic waveguides is investigated, including the comparison with solid gradient index waveguide, an analytical model, and the index profile measurement. Subsequently, the light propagation pattern in optofluidic waveguides is studied, including an analytical model and the light pattern as a function of the Péclet number and interface positions. Finally, the optofluidic waveguide is used as a sensor for chemical reaction monitoring and diffusion coefficient measurement.
3.1 Diffusion-induced index profile

3.1.1 Index profile comparison

Optofluidic waveguide is formed by a core flow stream and two cladding flow streams as illustrated in Figure 3.1. The refractive index of the core flow stream is higher than that of the cladding streams to confine the lightwave in the waveguide. Isotropic diffusion will happen at the interface of the cladding and core flow streams due to their miscible nature, which leads to the gradient index (GRIN) profile of optofluidic waveguides.

Figure 3.2(a-b) shows the 2D index profile of solid GRIN waveguides and optofluidic waveguides. In the transverse direction as shown in Figure 3.2(c), the index profile of optofluidic waveguides clearly shows a step profile at $x = 0$ (solid blue) when the core liquid and the cladding liquids begin to come into contact. At $x = L/2$ (solid red), the sharp core/cladding flow stream interface disappears and the index profile becomes smoother. At $x = L$ (solid green), the index profile is further relaxed. The continuously varying profile is distinctively different with the profile of traditional solid GRIN waveguide (dashed black) which follows an invariant Gaussian profile across the light propagation direction. In the longitudinal direction as shown in Figure 3.2(d), the refractive index of optofluidic waveguides at $y = 0$ (solid blue) is decreased from upstream to downstream. Whereas the profile is homogenous for the traditional solid GRIN waveguide (dashed black).
Figure 3.1: Schematic illustration of optofluidic waveguides.

Figure 3.2: Index profile comparison. 2D index profile of (a) optofluidic waveguide and (b) solid GRIN waveguide. (c) Transverse refractive index profile of solid GRIN waveguide (dashed black) and optofluidic waveguide at $x = 0$ (solid blue), $x = 0.5$ (solid red) and $x = 1$ (solid green). (d) Longitudinal refractive index of solid GRIN waveguide (dashed black) and optofluidic waveguide (solid blue) at $y = 0$. 
3.1.2 Analytical model of the index profile

The index profile of optofluidic waveguide is induced by the diffusion and convection processes between the core and cladding flow streams. Navier–Stokes equation describes the diffusion-convection transport which can be expressed as [193]

$$\frac{\partial C}{\partial t} = D \cdot \nabla^2 C - U \cdot \nabla C$$  \hspace{1cm} (3.1)

where, $C$ is the concentration, $D$ is the diffusion coefficient, $U$ is the velocity and $t$ is the time. The first term on the right side corresponds to diffusion and the second term describes convection. For a steady-state flow, the concentration does not vary with time and therefore the term on the left side equal to zero, i.e. $\partial C/\partial t = 0$.

In the laminar flow regime, the transverse mass transport is dominated by diffusion and the convection is negligible. Figure 3.3 shows the dimensionless model of the diffusion-induced index profile. Assuming $y' = y/W$ and $x' = x/W$ are the normalized coordinates and $C' = C/C_0$ is the normalized concentration, the core flow stream has a concentration of 1 and the cladding flow streams have a concentration of 0. The core-cladding interface locates at $y' = r$. When they flow through the microchannel, the three flow streams are mixed gradually and form a homogenous solution at the outlet ($x' = \infty$). The boundary conditions are expressed as

$$\begin{align*}
C' |_{x'\leq0} &= 1; \quad C' |_{x'\leq0, r} = r; \quad C' |_{x'\leq0, r} = 0 \\
\frac{\partial C'}{\partial y'} |_{y'\geq0} &= 0; \quad \frac{\partial C'}{\partial y'} |_{y'\geq0} = 0
\end{align*}$$  \hspace{1cm} (3.2)
The analytical solution to the concentration distribution is derived by solving Eq.(3.1) with the above boundary conditions [194], which is expressed as

\[
C'(x', y') = r + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{\sin(n\pi r)}{n} \cos(n\pi y') \exp\left[\frac{1}{2} (Pe - \sqrt{Pe^2 + 4n^2\pi^2}) x' \right]
\] (3.3)

where, \( Pe = \frac{UW}{D} \) is the Péclet number which describes the ratio of convection and diffusion between different flow streams, \( U \) is the velocity field, and \( r \) is the normalized initial interface position between the core and cladding flow streams. The interface position \( r \) is expressed as [195]

\[
\lambda \alpha (2r - 1)^3 + 6\alpha(1 - 2r)r(1 - r) - r^2 (3 - 2r) = 0
\] (3.4)

where \( \lambda \) is the viscosity ratio, and \( \alpha \) is the flow rate ratio between the cladding and core streams.

For most chemical solutions, the refractive indices are linearly proportional to their concentrations. Hence, the index profile is expressed as

\[
n(x', y') = k \cdot C(x, y) + b
\] (3.5)

where \( k \) and \( b \) are two constants related to liquid properties.
Equation (3.3) indicates that the index profile is related to two parameters, the Péclet number $Pe$ and the initial interface position $r$. The Péclet number describes the contribution of diffusion and convection on the concentration profile. Figure 3.4 shows the index profiles when the interface position $r$ is 0.3 and the Péclet number increases from 100 to 2000. It shows that the index profile follows a step-index profile at $x' = 0$ for all the cases. Whereas at $x' = 1$, the index contrast is decreased with smaller $Pe$. To better visualize the index change, the transverse profile at the outlet ($x' = 1$) and the longitudinal profile along the central line of the microchannel ($y' = 0$) are plotted in Figure 3.5. The results are reasonable considering smaller $Pe$ stands for more intensive diffusion.
Figure 3.5: (a) Transverse index profile at \( x' = 1 \) and (b) longitudinal index profile at \( y' = 0 \) when \( r = 0.3 \), \( Pe = 100 \) (blue), 500 (red) and 1000 (green).

Figure 3.6: Index profiles when \( Pe = 1000 \) and \( r = 0.2, 0.25, 0.3 \) and 0.5.
Similarly, the initial interface position, \( r \), describes the position where the diffusion begins. Figure 3.6 shows the index profiles when Péctel number is 1000 and the interface position \( r \) increases from 0.2 to 0.5. The transverse index profile at the outlet \((x' = 1)\) and the longitudinal profile along the central line of the microchannel \((y' = 0)\) are plotted in Figures 3.7(a) and (b), respectively. We can see that the maximum index is decreased when \( r \) becomes smaller, while the minimum index is unchanged. The index profile has a “flat-roof” at the centre when \( r = 0.5 \) and follows a Gaussian profile when \( r = 0.2 \) and 0.3. The results indicate that the diffusion is more significant when the core flow stream is narrower, i.e. \( r \) is smaller.

3.1.3 Index profile measurement

The index profile is measured to verify the analytical model. In the experiment, deionized (DI) water (RI: 1.332 @ 25°C) and ethylene glycol (RI: 1.432 @ 25°C) are used as the cladding and core flow streams, respectively. A 10× objective lens (Nikon, numerical aperture (NA) = 0.3) and a digital CCD camera (Nikon, DS-
Ri1) are used to capture the light propagation pattern. In the measurement of the index profile, the relationship between the fluorescence intensity and refractive index is correlated. Rhodamine 6G (concentration: ~10^{-6} g/mL) is added into pure ethylene glycol. The ethylene glycol is mixed with deionized water to obtain 20%, 40%, 60% and 80% ethylene glycol solutions. Then, the solutions are pumped into the microchannel for pixel intensity quantification. The pixel intensity is linearly proportional to the mass fraction of ethylene glycol as shown in Figure 3.8. The percentage of nonlinearity can be expressed as [196]

\[
\text{nonlinearity} \% = \left( \frac{\text{MaxPositiveDerivation} + \text{MaxNegativeDerivation}}{\text{MaxSignal}} \right) \times 100 \quad (3.6)
\]

The nonlinearity is measured to be 6%, which is mainly induced by the nonlinearity of the CCD camera and experimental errors during solution preparation. Like the majority of chemicals, the refractive index of ethylene glycol is also linearly proportional to the mass fraction of ethylene glycol as shown in Figure 3.8. Normalized pixel intensity as a function of the mass fraction of ethylene glycol.

Figure 3.8: Normalized pixel intensity as a function of the mass fraction of ethylene glycol.
proportional to its mass fraction. Therefore, we can infer that the refractive index is in a linear relationship with the captured pixel intensity.

Figure 3.9: (a) Fluorescent image of the ethylene glycol distribution in the optofluidic waveguide. (Scale bar: 30 μm) (b) The measured refractive index at \(x_1\) (blue), \(x_2\) (red) and \(x_3\) (green).

The fluorescent image of the optofluidic waveguide is shown in Figure 3.9(a). Both the cladding and core flow rates are set to 4.0 μL/min in this case. The refractive index profiles along dashed-line \(x_1\), \(x_2\) and \(x_3\) are plotted in Figure 3.9(b). The results
show that the flow streams start to mix near to the interface at $x_1$, and show a gradient index profile at $x_2$ and $x_3$. The index contrast at $x_3$ is smaller than that at $x_2$ due to the longer diffusion time. The experimental result confirms that the analytical model in Paragraph 3.1.2 well describes the index profile in optofluidic waveguides and can be used for the theoretical derivation of light trajectories.
3.2 Light propagation patterns

3.2.1 Analytical model of light propagation

The index profile of optofluidic waveguides is described by Eq.(3.3) and (3.5). When the collimated laser source is injected to the waveguide, the light will focus periodically with increased focal length. Assuming the light ray propagations close to the optical axis, when \( y' = 0 \), Eq.(3.3) can be expanded in Taylor series as

\[
C'(x', y') = r + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{\sin(nr\pi)}{n} (1 - \frac{1}{2} n^2 \pi^2 y'^2) \exp\left[\frac{1}{2} (Pe - \sqrt{Pe^2 + 4n^2 \pi^2})x'\right] \tag{3.7}
\]

Substitute Eq.(3.7) into Eq.(3.5), the index profile is given by

\[
n(x', y') = k \cdot C + b = n_0(x')[1 - \frac{g^2(x')}{2} y'^2] \tag{3.8}
\]

where \( k \) and \( b \) are two constant, \( n_0(x') \) and \( g^2(x') \) are defined as

\[
\begin{align*}
n_0(x') &= kr + \frac{2k}{\pi} \sum_{n=1}^{\infty} \frac{\sin(nr\pi)}{n} \exp\left[\frac{1}{2} (Pe - \sqrt{Pe^2 + 4n^2 \pi^2})x'\right] + b \\
g^2(x') &= \frac{2k}{n_0(z')} \sum_{n=1}^{\infty} n \pi \sin(nr\pi) \exp\left[\frac{1}{2} (Pe - \sqrt{Pe^2 + 4n^2 \pi^2})x'\right]
\end{align*}
\tag{3.9}
\]

Equation (3.8) indicates that the index profile near to the optical axis (x-axis) is parabolic. It has been rigorously derived that the ray trajectory in media with the parabolic profile is expressed as [197]

\[
\frac{\partial^2 y}{\partial x^2} + \frac{1}{n_0(x)} \frac{\partial n_0(x)}{\partial x} \frac{\partial y}{\partial x} + g^2(x) y = 0 \tag{3.10}
\]

The solution to Eq.(3.10) is expressed as

\[
y(x') = \left[\frac{g_0}{g(x')}\right]^{1/2} \cos\left[\int_0^{x'} g(x)dx\right] \tag{3.11}
\]
Equation (3.11) indicates that for the traditional gradient index waveguide in which \( g(x) \) is constant, the trajectory function is reduced to \( y(x') = \cos(g_0 x') \). In other words, the ray will focus periodically with a constant period \( 2\pi/g_0 \). In contrast, for the optofluidic waveguide, the amplitude and period will change with the \( x \) position along the microchannel.

Figure 3.10 shows the theoretical calculation results of the light trajectory when \( Pe \) is 500, and \( r \) increases from 1/3 to 3/5. The results show that as the light rays propagate from left to right, the ray amplitudes and focal lengths increase considerably at \( r = 1/3 \), slowly at \( r = 1/2 \) and insignificantly at \( r = 3/5 \). We can also observe that at a large \( r \), the ray amplitude is nearly constant and the focal length increases slightly. The results indicate that the longitudinal diffusion has a greater

![Figure 3.10: Light trajectories along the microchannel with interface position of (a) \( r = 1/3 \), (b) \( r = 1/2 \) and (c) \( r = 3/5 \) when \( Pe = 500 \).](image)
impact on focal lengths at a small $r$. Such light behavior is due to the more severe diffusion when the core flow stream is narrower ($r$ is smaller).

Similarly, Figure 3.11 shows the light trajectories when $r$ is 1/3 and $Pe$ increases from 1000 to 20000. The results show that the ray amplitudes and focal lengths increase gradually with significant diffusion (small $Pe$), whereas the change is negligible with insignificant diffusion (large $Pe$). It suggests that the amplitude and focal length are determined by both the transverse and longitudinal diffusion.
3.2.2 Light pattern vs interface position

Based on the analytical model in the last section, the focal length is related to the interface position $r$. Here the relationship between the 1st focal length and the interface position is experimentally investigated. In the experiment, DI water (RI: 1.332 @ 25°C) and ethylene glycol (RI: 1.432 @ 25°C) are used as the cladding and core flow streams, respectively. Rhodamine 6G (concentration: $\sim 10^{-6}$ g/mL) is added to visualize the light propagation pattern. Unpolarized green laser source ($\lambda = 514.5$ nm) from an argon laser (Modu-Laser, Stellar-Pro Select) is coupled into the optofluidic waveguide through a single-mode fiber with a numerical aperture of 0.12. A 5× objective lens (Nikon, NA = 0.15) and a digital CCD camera (Nikon, DS-Ri1) are used to capture the light propagation image. The Péclet number is 500 and 1000 by maintaining the overall flow rate to 3 $\mu$L/min and 6 $\mu$L/min, respectively. The flow rates of core and cladding flow streams are calculated based on Eq.(3.4) to tune the interface position $r$ changing from 0.1 to 0.4. All the experiments are done in triplicate.

The light propagation patterns are shown in Figure 3.12. We can clearly see that the widths of the light patterns become wider when $r$ increases from 0.1 to 0.4. It is because, with larger $r$ (wider core stream), the light beams need larger transverse distance to reach the interface position. Meanwhile, as shown in Figure 3.13(a), the 1st focal length decreases slowly with $r$ and reaches a minimum value at $r = 0.2$. When $r$ is further increased, the 1st focal length increases again. The reason is that the liquids generally have stronger ability to focus light beams when the index contrast is higher, i.e. the focal length is shorter when the index difference is larger. When $r$ is small, the liquids are over-mixed due to the strong diffusion and therefore the index contrast is reduced. When $r$ is large, the liquids are under-mixed due to insignificant diffusion.
The paraxial region where the light beam travels is still filled with the core liquids and therefore the index contrast is small. Figure 3.13(b) shows the 1st focal length as a function of the interface position $r$ when $Pe$ is 1000. The results show that the 1st focal length increases monotonically with $r$ increasing from 0.1 to 0.4. It is because the liquid is under-mixed even when $r$ is small due to the high overall flow rates. The interface position $r$ is determined by the flow rate ratios. In order to reduce the focal length shift caused by flow fluctuation, i.e. $r$ fluctuation, the optimized interface position $r$ is $\sim0.2$ when $Pe = 500$ and to $\sim0.1$ when $Pe = 1000$. 

Figure 3.12: Light propagation patterns when $Pe = 500$ and interface position (a) $r = 0.1$, (b) $r = 0.2$, (c) $r = 0.3$ and (d) $r = 0.4$. (Scale bar: 100 μm)
3.2.3 Light pattern vs Péclet number

Based on the analytical model in Paragraph 3.2.1, the focal length is also related to the Péclet number $Pe$. Here the relationship between the 1st focal length and the Péclet number is experimentally investigated. In the experiment, the flow rate ratio of the core and cladding flow streams is 1:1 or 1:2, which corresponds to the

Figure 3.13: The relationship between the 1st focal length and the interface position $r$ when (a) $Pe = 500$ and (b) $Pe = 1000$. 
interface position \( r \) of 0.23 and 0.14, respectively. The Péclet number increases from 250 to 1500 by controlling the overall flow rates.

Figure 3.14 shows the light propagation patterns when \( r = 0.23 \) and Péclet number (a) \( Pe = 375 \), (b) \( Pe = 500 \), (c) \( Pe = 750 \), and (d) \( Pe = 1000 \) (Scale bar: 100 \( \mu \)m)

Figure 3.14 shows the light propagation patterns when \( r = 0.23 \) and \( Pe \) increases from 375 to 1000. The white arrow denotes the 1st focal position. The relationship between the 1st focal length and the Péclet number \( Pe \) is summarized in Figure 3.15(a). The results show that the 1st focal length decreases to a minimum value when \( Pe \) increases from 250 to 750 and increases slowly when \( Pe \) is further increased. The reason for the focal length shift is based on the fact that the liquids generally have stronger ability to focus light beams with higher index contrast. When \( Pe \) is small, the liquids are over-mixed due to the significant diffusion and therefore
the index contrast is reduced. When $Pe$ is larger than 750, the liquids are under-mixed due to the limited diffusion. The paraxial region where the light beam travels is mainly filled with the core liquids and therefore the index contrast is small.

Figure 3.15: The relationship between the 1st focal length and the Péclet number $Pe$ when (a) $r = 0.23$ and (b) $r = 0.14$. 
Figure 3.15(b) shows the 1st focal length as a function of $Pe$ when $r = 0.14$. The focal length declines rapidly when $Pe$ increases from 250 to 625, which is similar to the case when $r = 0.23$. The sharp decline is due to the reduced diffusion and increased index contrast when $Pe$ is increased. However, when $Pe$ is further increased to 1500, the focal length is approximately invariant, which is different when $r = 0.23$. That is because when $Pe$ is large and $r = 0.14$, the diffusion is dominantly determined by the interface position $r$. Since $r$ is fixed, the focal length is approximately unvaried in the case. Péclet number is a parameter related to the diffusion coefficient of liquids, i.e. the $Pe$ change is an indicator of the diffusion coefficient change. To obtain a larger focal length shift caused by $Pe$ change, the Péclet number should be smaller than 750 and 625 when $r = 0.23$ and 0.14, respectively.
3.3 Chemical sensing in optofluidic waveguides

3.3.1 Principle and design

Based on the study in Paragraph 3.1 and 3.2, the focal length in an optofluidic waveguide is related to the interface position and the Péclet number. The interface position is determined by the ratio of flow rates. The Péclet number is proportional to the overall flow velocity and channel width, and is inversely proportional to the diffusion coefficient. Once the flow rates and channel width are known, the focal length is solely related to solution diffusion coefficients. Therefore, focal length can be used as a signal to detect chemical solutions with different diffusion coefficients.

To achieve chemical sensing using the light pattern in optofluidic waveguides, an optofluidic chip is designed as shown in Figure 3.16(a). The chip includes two central inlets, two cladding inlets, a microchannel and two outlets. The target solution is injected into the microchannel through the central inlets. Low refractive index liquid, which is usually DI water, is injected through the cladding inlets. Such a configuration forms an optofluidic waveguide in the microchannel. As analyzed in Paragraph 3.1, the liquids show a step-index profile at the entrance of the microchannel. The liquids then gradually mix and show a gradient-index profile at the midstream. As the liquids flow in the microchannel, the index profile is further relaxed at the downstream. When a light source is coupled into the optofluidic waveguide, the light will focus periodically with a focal length related to liquid diffusion coefficient. Figure 3.16(b) illustrates the light patterns of two solutions with different diffusion coefficients. The intensity profiles along the central line of the light patterns clearly show that different solutions have distinct focal lengths. The focal length shift is related to the different diffusion properties of the solutions.
Figure 3.16: Illumination of chemical sensing using the light propagation pattern in optofluidic waveguides. (a) Schematic of the chip design. (b) Simulated concentration profile. Simulated (c) light propagation patterns and (d) the intensity profiles of two chemical solutions with different diffusion coefficients. (Δx: focal length shift)
In order to verify the method in chemical sensing, the light propagation patterns in several chemical compositions are experimentally tested. Here ethylene glycol, glycerol and isopropanol (IPA) are used as a demonstration. The focal length is usually shorter with higher refractive index contrast. The refractive indices of them are adjusted to 1.378 by tuning their mass fractions to 45%, 35% and 100%, respectively. The refractive index is measured by a handheld refractometer (ATAGO, PAL-RI). As shown in Figure 3.17, the diffusion coefficient of ethylene glycol-water solution is inversely proportional to the mass fraction, i.e. a high mass fraction of ethylene glycol has a small diffusion coefficient. The diffusion coefficient of 45% ethylene glycol in water is $6.9 \times 10^{-10}$ m$^2$/s based on the black curve [198]. Similarly, the diffusion coefficient of glycerol-water solution decreases with the mass fraction of glycerol. The diffusion coefficient of 35% glycerol in water is $6.6 \times 10^{-10}$ m$^2$/s based on the red curve [198]. In contrast, the diffusion coefficient of IPA decreases to the minimum value of $1.68 \times 10^{-10}$ m$^2$/s when the mass fraction increases from 0 to 50%,
and then increase to $6.3 \times 10^{-10}$ m²/s when the mass fraction further increases to 100% [199]. Table 3.1 summarizes the properties of the three solutions.

Table 3.1: Chemical properties of ethylene glycol, glycerol and IPA.

<table>
<thead>
<tr>
<th>Liquids</th>
<th>Mass Fraction</th>
<th>Refractive index</th>
<th>Diffusion coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylene glycol</td>
<td>45%</td>
<td>1.378</td>
<td>$6.9 \times 10^{-10}$ m²/s [198]</td>
</tr>
<tr>
<td>Glycerol</td>
<td>35%</td>
<td>1.378</td>
<td>$6.6 \times 10^{-10}$ m²/s [198]</td>
</tr>
<tr>
<td>IPA</td>
<td>100%</td>
<td>1.378</td>
<td>$6.3 \times 10^{-9}$ m²/s [199]</td>
</tr>
</tbody>
</table>

Figure 3.18: Light propagation pattern and light intensity in the under-mixed region with the core solution of (a) ethylene glycol, (b) glycerol, (c) IPA and (d) the equal mixture of the three chemical solutions. (Scale bar: 100 μm)
In the experiment, 45% ethylene glycol, 35% glycerol, 100% IPA, the equal mixture of the three solutions, and the equal mixture of two of the solutions are pumped into the microchannel. The light propagation pattern in the optofluidic waveguide is captured by an inverted microscope (Nikon Eclipse Ti, 5× objective lens) and a digital CCD camera (Nikon, DS-Ri1). Firstly, the liquid diffusion is set to the under-mixed region by applying the core and cladding flow rates at 2 μL/min (Pe > 1000). Figure 3.18 shows the light propagation pattern and light intensity profile for ethylene glycol, glycerol, IPA and the equal mixture of the three chemicals. The red arrows denote the positions of the 1st focal point. The results show that the ethylene glycol and glycerol solutions yield a sharp light intensity profile, while the IPA solution and the equal mixture of the three chemicals yield a more diffuse light intensity profile.

Figure 3.19: Light propagation pattern and light intensity in the over-mixed region with the core solution of (a) ethylene glycol, (b) glycerol, (c) IPA and (d) the mixture of the three chemical solutions. (Scale bar: 100 μm)
glycol-water waveguide has the smallest 1st focal length, and the glycerol-water waveguide has a slightly longer one. The IPA-water waveguide has the longest focal length, while that of the solution mixture is in between glycerol and IPA. The reason for the focal length shift is as discussed in Figure 3.15, the 1st focal length is inversely proportional to the diffusion coefficient in the under-mixed region ($Pe > 1000$), i.e. the focal length is longer for the chemical with smaller diffusion coefficient.

![Figure 3.20: The focal length shift for different chemical compositions when the overall flow rates are 2.25 \(\mu\)L/min (blue) and 6 \(\mu\)L/min (red).](image)

Subsequently, the liquid diffusion is set to the over-mixed region by controlling the core and cladding flow rates at 0.75 \(\mu\)L/min ($Pe < 500$). Figure 3.19 shows the light propagation pattern and light intensity profile for ethylene glycol, glycerol, IPA and the equal mixture of the three chemicals. The result shows that the 1st focal length of ethylene glycol-water waveguide is the longest, while that of the IPA-water waveguide is the shortest. The reason is that in the over-mixed region, the focal length is directly proportional to diffusion coefficient, i.e. the focal length is longer for the chemical solution with larger diffusion coefficient.
The focal length shift relative to the minimum focal length is summarized in Figure 3.20. The sequence in the $x$-axis is arranged based on their diffusion coefficients from small to large. The results show that the focal lengths of IPA and IPA - glycerol mixture are considerably larger than the other solutions, which means the overall diffusion coefficient is much smaller when the initial IPA mass fraction is larger than 50%. Such observation is consistent with the fact that the diffusion coefficient of IPA is small when the mass fraction is between 40% - 60%. The results also show that for the same diffusion coefficient change, the focal length shift in the over-mixed region is larger than that in the under-mixed region. Based on the linear fitting, the sensitivity in the over-mixed region is 1.54 $\mu$m/(µm$^2$/s), which is 7.74 times better than that of 0.198 $\mu$m/(µm$^2$/s) in the under-mixed region. The limit of detection (LOD) is expressed as

$$LOD = \frac{3\delta}{S}$$

(3.12)

where $\delta$ is the standard deviation and $S$ is the system sensitivity. Therefore, the LODs in the over-mixed region and under-mixed region are determined to be $0.15 \times 10^{-10}$ m$^2$/s and $1.17 \times 10^{-10}$ m$^2$/s, respectively. The optofluidic waveguide sensor should work in the over-mixed region to achieve higher sensitivity in chemical sensing.

### 3.3.2 Chemical reaction monitoring

Microreactor technology is an efficient tool for chemical reactions such as synthesis and hydrolysis and has great potential applications in chemical and pharmaceutical industries [200, 201]. An integrated analytical tool is necessary and useful for fast and reliable reaction monitoring. The conventional methods for
chemical reaction monitoring include spectroscopy, photochemistry, electrochemistry and so forth [202-204]. The spectroscopy approach analyzes the chemical composition at different positions and hence determines the reaction rate. This approach is universal, but it requires expensive and complicated detection setup, which is difficult to be integrated into on-chip systems. The photochemistry and electrochemistry approaches are microchip compatible, but they are injected specifically to certain chemical reactions.

The Stokes-Einstein equation is used to estimate molecular diffusion coefficients, which is expressed as [45]

\[ D = \frac{kT}{6\pi\eta R} \]  

(3.13)

Where \( k \) is the Boltzmann constant, \( T \) is the absolute temperature, \( \eta \) is the liquid viscosity, and \( R \) is the effective molecular radius. The equation manifests that the diffusion coefficient is inversely proportional to the molecular size. In chemical reactions such as hydrolysis or synthesis, the molecular size will change considerably after the reaction, and therefore the diffusion coefficient will change accordingly. In this section, the light pattern in optofluidic waveguides is applicable to the chemical reactions accompanied by molecular size change. The molecular size change will induce a diffusion coefficient change, which will change the concentration profile and eventually lead to a focal shift. Here the sucrose hydrolysis reaction is used as a demonstration for two reasons. First, the molecular size is reduced by half during the reaction. The significant molecular size change will reduce the complexity in the experimental analysis. Second, the reaction is simple and safe. The reaction occurs easily by controlling the pH and temperature. The chemicals are easily accessible and do not raise safety concerns.
In the reaction, one mole of sucrose is hydrolyzed to one mole of $D$-glucose and one mole of $D$-fructose as represented by

$$C_{12}H_{22}O_{11} + H_2O \xrightarrow{\text{Invertase}} C_6H_{12}O_6 + C_6H_{12}O_6$$  \hspace{1cm} (3.14)

The diffusion coefficient of sucrose, $D$-glucose and $D$-fructose are $5.23 \times 10^{-10}$ m$^2$/s, $6.79 \times 10^{-10}$ m$^2$/s and $6.86 \times 10^{-10}$ m$^2$/s at 25°C, respectively [205]. It indicates that the overall diffusion coefficient of the solution will increase as the reaction occurs.

In the experiment, 40% w/w sucrose substrate (Sigma-Aldrich, S7903) is prepared and the molar concentration is calculated to be 1.375 M. The pH value of the sucrose substrate is measured by a pH meter (SevenExcellence Multiparameter) and adjusted to 4.5 with 1 M hydrochloric acid (Sigma-Aldrich, H1758). Then the substrate solution is divided into seven 1-mL portions and placed in 2 mL tubes. Invertase (Sigma-Aldrich, I4504) dissolved in DI water is added to each tube to achieve a 0.1 mg/mL enzyme concentration. The tubes are incubated in a 55°C oven (Memmert 100-800) for 6 intervals of 20 min each from 0 min to 120 min. Afterwards, the tubes are immediately immersed in boiled water for 10 min to stop the reaction. The refractive indices of the seven reaction products are measured to be 1.403 ± 0.0003 at 25°C by a handheld refractometer (ATAGO, PAL-RI). The reaction products and DI water are pumped into the microchannel as the core and cladding flow streams to form the optofluidic waveguide. Green laser source ($\lambda = 514.5$ nm) from an argon laser (Modu-Laser, Stellar-Pro Select) is coupled into the optofluidic waveguide through a single-mode fiber with a numerical aperture of 0.12. A 5× objective lens (Nikon, NA = 0.15) and a digital CCD camera (Nikon, DS-Ri1) are used to capture the light propagation image. The light intensity images are analyzed by intensity profiling using ImageJ. The experiment is done in triplicate.
Figure 3.21 shows the light propagation pattern and light intensity along the central line of the optofluidic waveguide for the reaction products after (a) 0, (b) 40 min, (c) 80 min and (d) 120 min. (Scale bar: 100 μm)

Figure 3.21 shows the light propagation pattern and light intensity along the central line of the optofluidic waveguide for the reaction products after 0, 40 min, 80 min and 120 min. Both the central and cladding flow rates are set to 1 μL/min and hence the liquids are in the over-mixed region ($Pe < 500$). The results clearly show that the 1st focal length increases gradually when the reaction time increases from 0 to 80 min and the focal length is invariant when reaction time further increases to 120 min. The reason for the focal length shift is that as the hydrolysis reaction takes place, the sucrose molecule decomposes into glucose and fructose which have small
molecular size and therefore the overall diffusion coefficient increases. Since the liquids are in the over-mixed region, the focal length becomes larger as the diffusion coefficient increases. When the hydrolysis reaction completes, the focal length is invariant as it is at $t = 80$ min and $t = 120$ min.

Figure 3.22: The 1st focal length shift as a function of (a) reaction time and (b) the concentration of hydrolyzed sucrose.
Figure 3.22(a) shows the relative focal length shift as a function of the reaction time. It shows that the focal length increases linearly when the reaction time is smaller than 60 min and then increases slowly to the maximum value. To obtain the relationship between the hydrolyzed sucrose and the reaction time, another experiment is conducted to obtain the 1st focal length shift as a function of the hydrolyzed sucrose concentration. In the experiment, deliberately prepared solutions are used to replace the reaction products. For example, 1.375 M sucrose solution are used to simulate the initial solution, while 0.825 M sucrose, 0.55 M fructose and 0.55 M glucose are used to simulate the reaction product with 0.55 M hydrolyzed sucrose. The same amounts of inactivated enzyme and buffer solution are also added to precisely simulate the reaction products. Afterwards, the prepared solutions are pumped to the optofluidic waveguide to observe the propagation patterns. The experiment is done in triplicate. Figure 3.22(b) shows that the focal length shift is linearly proportional to the hydrolyzed sucrose concentration. The sensitivity and LOD are determined to be 16.63 μm/M and 22.2 mM. The LOD is comparable with other integrated reaction monitoring methods. For example, the integrated luminescent sensor has a LOD of 11.5 mM in monitoring the redox reaction [202].

Based on Figures 3.22(a) and (b), the hydrolyzed sucrose concentration as a function of the reaction time is calculated and shown in Figure 3.23. The results indicate that the hydrolysis of sucrose catalyzed by invertase follows the kinetics of zero-order reaction [206]. It is consistent with the fact that the sucrose concentration is much larger than 25 mM, the reported Michaelis constant ($K_M$) [207]. The results also show that 50% of the sucrose is hydrolyzed in 35 min and the initial hydrolysis rate is 19.62 mM/min, which agrees well with the literature result of 22.0 ± 0.1 mM/min [207].
3.3.3 Diffusion coefficient measurement

Diffusion is a phenomenon which describes the molecules, ions, or other small particles spontaneously move from high concentration region to low concentration region [45]. The flow Reynolds number in microfluidics is usually below 100 and the flow is therefore laminar without turbulence. In this laminar flow regime, diffusion is fundamentally important because it is the primary, if not the only, process for liquid mixing [208]. Diffusion coefficient is the basic parameter to indicate the rate of molecular diffusion. Traditionally, diffusion coefficient is determined by the point-by-point measurement of liquid concentrations at different positions or at different times through micro-ring resonator [209], spectroscopy [210] and interferometry [211], etc. However, these methods generally require complicated experimental setup or time-consuming procedures, which hinder the integration in Lab-on-a-chip applications. In this section, the light pattern in optofluidic waveguides

Figure 3.23: The concentration of hydrolyzed sucrose as a function of the reaction time.
is used to determine the diffusion coefficient in binary solutions. Here the diffusion coefficient of ethylene glycol - DI water solution is measured as a demonstration.

To determine diffusion coefficient, simulation models are built up in COMSOL 5.2 and RSoft BeamPROP. Firstly, the concentration profile is simulated two-dimensionally in COMSOL 5.2. The concentration profile is then converted to refractive index profile for light pattern simulation in RSoft BeamPROP. In the simulation, both the central and cladding flow rates are set to 1 μL/min ($Pe: \sim 500$, over-mixed region). Figure 3.24(a) shows the concentration profiles when the diffusion coefficient is $3.0 \times 10^{-10}$, $5.0 \times 10^{-10}$, $8.0 \times 10^{-10}$, $12.0 \times 10^{-10}$ m$^2$/s, respectively. It illustrates that liquids mix much faster with higher diffusion coefficient. Figure 3.24(b) shows the light propagation patterns at the diffusion

Figure 3.24: Simulated concentration profile where the diffusion coefficient is set to be (a) 2.0, (b) 5.0, (c) 8.0 and (d) $10.0 \times 10^{-10}$ m$^2$/s and (e-h) the corresponding focal length difference ($\Delta$).
coefficients. Generally, the focal length increases with diffusion coefficient, which is consistent with the trend of the focal length shift in the over-mixed region. The difference between the 2\textsuperscript{nd} and 3\textsuperscript{rd} focal length (\(\Delta\)) is used as the indicator for diffusion coefficient.

![Graph](image)

Figure 3.25: Simulated focal length difference as a function of diffusion coefficient.

The focal length difference as a function of the diffusion coefficient is summarized in Figure 3.25. It shows that the focal length difference is roughly linear with the diffusion coefficient and increases from 2.6 \(\mu\)m to 101.4 \(\mu\)m when the diffusion coefficient increases from \(2.0 \times 10^{-10} \text{ m}^2/\text{s}\) to \(12.0 \times 10^{-10} \text{ m}^2/\text{s}\). Figure 3.25 will work as a ‘look-up graph’ to compare with the measured focal length difference.

In the experiment, pure ethylene glycol and DI water are injected into the microchannel as the core and cladding streams. The experiment setup is the same with the experiment in Paragraph 3.3.2. Here both the core and cladding flow rates
are pumped at 1 μL/min. The experiment is done in triplicate. Figure 3.26(a) shows the
capture light propagation pattern and Figure 3.26(b) shows the normalized light
intensity along the central line of the microchannel. It clearly illustrates that the 2nd
and 3rd focal lengths are measured to be 272.3 μm and 307.6 μm, respectively. The
focal length difference is therefore 35.3 μm in the case. The average focal length
difference of the three measurements is 34.6 ± 1.1 μm. Based on the ‘look-up graph’,
Figure 3.25, the diffusion coefficient of ethylene glycol and DI water solution is
determined to be 5.56 ± 0.12 × 10^{-10} m^2/s. The result is comparable yet slightly larger
than the literature results, which is generally between $2.43 \times 10^{-10}$ m$^2$/s [212, 213]. It is because diffusion coefficient is inversely proportional to the liquid concentration. The average diffusion coefficient is increased as ethylene glycol mixing with DI water in the optofluidic waveguide. The measurement result can be improved by using more sophisticated methods to reduce the concentration change along the microchannel.
3.4 Summary

This chapter focuses on the analysis of diffusion-induced light focusing in optofluidic waveguides and the applications in chemical reaction monitoring and diffusion coefficient measurement. The theoretical analysis of the diffusion-induced index profile studies the unique properties of optofluidic waveguides. It indicates the interface position and Péclet number are the contributing factors to the light propagation pattern. The theoretical and experimental analysis of the light propagation pattern investigates the influence of interface position and Péclet number on the focal positions. It demonstrates that the focal length shows a different behavior in the over-mixed and under-mixed region, which guides the experimental design in the following chemical sensing studies. Subsequently, an optofluidic chip is designed for chemical sensing applications. Three liquids with different diffusion coefficient are tested to verify the methods. In chemical reaction monitoring, the hydrolysis of sucrose is studied and the initial hydrolysis rate is determined to 19.81 $\mu$mol/min. In diffusion coefficient measurement, simulation models are built up to quantify the focal length different as a function of the diffusion coefficient. Then the diffusion coefficient of ethylene glycol - DI water solution is measured experimentally. The diffusion coefficient is determined to be $5.56 \pm 0.12$ m$^2$/s.

The study on the light propagation in optofluidic waveguides is innovative in the aspects as follows:

(a) This is the first comprehensive study on the contributing factors to the light propagation pattern in optofluidic waveguides. The study provides a useful guidance on the experimental design of the subsequent chemical sensing
studies. The limit-of-detection can be $0.15 \times 10^{-10}$ m$^2$/s under the optimized conditions.

(b) This is the first effort demonstrated to monitor chemical reactions through the diffusion coefficient change. The proposed optofluidic method overcomes the integration problem of the traditional spectroscopy method and can be easily integrated in Lab-on-a-Chip systems. The sensitivity of the method is 16.63 $\mu$m/M and the initial hydrolysis rate is 19.81 $\mu$mol/min, which is in line with the literature results.

(c) This study proposes an optofluidic method to measure diffusion coefficient with a single optical image. It is simple and rapid compared with the conventional point-to-point measurements using interferometers. The diffusion coefficient of ethylene glycol - DI water solution is determined to be $5.56 \pm 0.12$ m$^2$/s, which is comparable with the literature results. The measurement result can be further improved by reducing the concentration change along the microchannel.
CHAPTER 4

OPTOFLUIDIC HYPERBOLIC SECANT LENS

This chapter designs an optofluidic hyperbolic secant (HS) lens to improve the focusing power. The optical aberrations which deteriorate the optical performance are investigated, including the spherical and field curvature aberrations. Then the optimized index profile is derived based on coordinate transformation and a microfluidic gradient generator is designed to generate the index profile. Subsequently, simulations are conducted to verify the performance of the optofluidic HS lens. In the experiment, the performance of the lens is evaluated, including the focal length and beam waist at different divergence angles and off-center positions. The focusing experiment with multiple light sources is also demonstrated.
4.1 Design of the optofluidic hyperbolic secant lens

4.1.1 Optical aberrations in optofluidic lenses

Optofluidic lens is an important component for on-chip optical systems. It has many advantages over a solid lens in terms of reconfigurable geometry and tunable refractive index. Optofluidic lenses can change the focal length two-dimensionally, which have been used in integrated sample illumination and optical detections [28, 29]. However, the optical performance of optofluidic lenses is subject to optical aberrations such as spherical and field curvature aberrations [22, 24], which hinders its use in many applications.

Spherical aberration describes the optical engineering problem where the incident light beams are focused at multiple points by a lens [30]. Figure 4.1(a) shows that in the conventional optofluidic GRIN lens, light with incident angles of $\theta_1$ and $\theta_2$ is focused at two positions with a spherical aberration of $\delta$. While in the optofluidic lens with an optimized profile, the spherical aberration is reduced to zero as shown in Figure 4.1(b). A reduced spherical aberration in optofluidic lenses can greatly improve the optical performance in on-chip flow cytometry and integrated optical detection. For example, in fluorescent spectroscopy, the limit-of-detection is increased 3-fold with a reduced beam waist of 80 µm [28]. In on-chip flow cytometry, a small beam waist ensures a single sample is excited at a time in the detection region, which allows for higher sample concentration, and better performance in signal-to-noise ratio, the coefficient of variance (CV) and throughput [29, 31].
On the other hand, field curvature aberration describes that multiple light sources are focused on different focal planes when they are placed at different off-axis positions. It will cause unwanted signal variation in the detection. Traditionally, multiple light sources are generated by using integrated beam splitter or lens array, which increases the footprint and configuration complexity [32]. As shown in Figure 4.1(c), in the conventional optofluidic GRIN lens, the field curvature aberration will make the off-axis light focus on a focal plane nearer to the lens ($\Delta x' \neq 0, \Delta y' \neq \Delta y$). As a result, the focal points are not identically sharp when the light source is placed at different off-axis positions. In comparison, the optofluidic lens with optimized index profile can focus light on the same focal plane ($\Delta x' = 0$) and at the opposite position ($\Delta y' = \Delta y$) as shown in Figure 4.1(d). With suppressed field curvature,
multiple light sources can be focused on the same focal plane by using a single optofluidic lens. The single optofluidic lens can be exploited in applications such as barcoded particle scanning [33], particle velocity measurement [32], flow cytometry [34], photobleaching quantification [35, 36], etc.

4.1.2 Index profile derivation

Maxwell’s fisheye lens is a spherically symmetric gradient-index lens which is first invented by Maxwell in 1854 [214]. The index profile is expressed as

\[ n(r) = \frac{n_0}{1 + (r/R)^2} \quad (4.1) \]

Where \( n_0 \) is the index at the center point, \( R \) is the lens radius and \( r \) is the distance to the lens center. Maxwell’s fisheye lens is famous for its aberration-free nature and excellent optical performance [215]. However, in microfluidics, it is challenging to precisely generate the two-dimensionally (2D) symmetric gradient index in a circular geometry. In this section, the circular Maxwell’s fisheye lens with 2D gradient is transformed into the rectangular lens with a 1D gradient using coordinate transformations.

In the field of conformal mappings, the complex coordinate system is generally used as a customary practice. Two steps are required to transform a rectangle to a unit circle. In the first step, the complex number \( z = x + iy \) are used in \( z \)-plane (physical space) and the complex number \( q = q_1 + iq_2 \) are used in \( q \)-plane (temporary virtual space). Assume the target rectangle has a width of \( 2K \) and a height of \( iK' \), the rectangle can be transformed into the upper half plane based on Schwarz-Christoffel transformation [216], which can be expressed as
Chapter 4 Optofluidic Hyperbolic Secant Lens

\[ z(q) = A \int_0^q \frac{d\xi}{\sqrt{(1-\xi^2)(1-k^2\xi^2)}} = A \cdot F(q,k) \]  \hspace{1cm} (4.2)

where, \( F(q,k) = \int_0^q \frac{d\xi}{\sqrt{(1-\xi^2)(1-k^2\xi^2)}} \) is the elliptic integral of the first kind,

\[ K(k) = F(1,k) = \int_0^1 \frac{d\xi}{\sqrt{(1-\xi^2)(1-k^2\xi^2)}} \] is the complete elliptic integral of the first kind, and \( K'(k) = K(\sqrt{1-k^2}) \).

By solving with the boundary conditions, Eq.(4.2) can be solved as

\[ q(z) = sn(z \cdot K, k) \]  \hspace{1cm} (4.3)

Where ‘sn function’ is a sub-function of Jacobi’s elliptic function set.

In the second step, the Möbius transformation is conducted to transform the upper half-plane \( (q = q_1 + iq_2) \) in the temporary virtual space into a unit circle \( (w = w_1 + iw_2) \) in the virtual space [216]. The transform function between the two spaces is expressed as

\[ q = \frac{i(1-w)}{1+w} \]  \hspace{1cm} (4.4)

By solving Eq.(4.3) and Eq.(4.4) together, the transform function between the physical space \( (z\text{-plane}) \), and the virtual space \( (w\text{-plane}) \) can be expressed as

\[ w(z) = \frac{\sqrt{1-cn(z,k)}}{\sqrt{1+cn(z,k)}} \]  \hspace{1cm} (4.5)

Where ‘cn function’ is a sub-function of Jacobi's elliptic function set.
Suppose the refractive index profile in the \(w\)-plane and \(z\)-plane are \(n_{\text{circle}}\) and \(n(z)\), respectively. The index profile of the flattened Maxwell’s fisheye lens is expressed as

\[
 n(z) = \left| \frac{dw}{dz} \right| \cdot n_{\text{circle}} = \frac{dn(z, k)}{1 + cn(z, k)} \cdot n_{\text{circle}} \quad (4.6)
\]

Where ‘\(dn\) function’ and ‘\(cn\) function’ are two sub-functions of Jacobi’s elliptic function set. Assume the height of the rectangle is much larger than the width, it can be numerically proven that \(k\) is approaching zero. Therefore, Eq.(4.6) is further simplified into a hyperbolic secant (HS) profile as

\[
 n(z) = \frac{n_{\circ}}{2} \cdot \text{sech} y \quad (4.7)
\]

Here the flattened Maxwell’s fisheye lens is called optofluidic hyperbolic secant (HS) lens. Figures 4.2(a) and (b) show the light propagation in Maxwell’s fisheye lens and optofluidic HS lens. The grey coordinate lines indicate the spatial
relationship of the index profiles between the two lenses. The black lines show the spatial relationship when a light source is focused by the lenses. The two lenses are theoretically equivalent and should have the same optical functionalities.

4.1.3 Microfluidic gradient generator

The ideal index profile of the optofluidic lens is a hyperbolic secant profile ranging from 0 to $n_0/2$ based on Eq.(4.7). However, the indices of liquid mediums generally range from 1.3 to 1.7 [94]. As a result, the top and bottom regions of the rectangular lens (white region) have to be discarded as shown in Figure 4.3(a). Based on the spatial relationship of the two coordinate systems, the discarded region corresponds to the pole regions in Maxwell’s fisheye lens as shown in Figure 4.3(b). When the incident angle of light beams is sufficiently large to make the light beam reach the discarded regions, the light cannot be focused anymore as illustrated in Figures 4.3(c-d). Therefore, the index approximation reduces the maximum divergence angle. The spatial relationship indicates that higher index contrast is favored to reduce the discarded regions and hence to achieve a larger maximum divergence angle.

The optofluidic HS lens has a parabolic profile in the index range of liquid mediums. The parabolic profile can be easily realized using microfluidic gradient generators [217]. Figure 4.4(a) illustrates the configuration of the gradient generator. Three flow streams with different concentrations are injected into the microfluidic network. The flows are repeatedly split, mixed and recombined. After six stages of micromixers, each of the nine branch flows contains different concentration values. Then the different branch flows are brought into a single channel to form the target
profile. The splitting ratio is determined by the pressure above and below each branching point. Figure 4.4(b) shows the analysis of the splitting ratio in the highlighted microchannel. Since the channel resistance is the vertical channel is negligible compared with that of horizontal mixers, the splitting ratio can be simplified to the quantitative proportion of mixers above and below the branching point. To generate a parabolic profile, the middle inlet will be applied with high index liquid, and the top and bottom inlets will be applied with DI water.

Figure 4.3: The spatial relationship of the discarded region between (a) Maxwell’s fisheye lens and (b) the optofluidic HS lens. (c-d) Illustration of the light propagation in the two lenses with index approximation.
4.1.4 Theoretical analysis and simulation

Figure 4.5 illustrates the simulated refractive index profile of the optofluidic lens using COMSOL Multiphysics 5.0. It shows that the flow streams have discrete refractive index values in the branch channels and mix gradually in the mixing chamber to form a smooth profile.

Figure 4.4: (a) Gradient generator using complex microfluidic network. (b) Analysis of the splitting ratio in the highlighted microchannel.
Figure 4.6: (a) Index profile of the optofluidic lens under different core/cladding flow rates (Solid lines: simulated profiles, dashed-lines: fitted ideal profiles). (b) Maximum (Solid lines) and minimum (Dashed lines) refractive index at $x_1$ as a function of flow rate ratio when the cladding flow rate is 1.0 μL/min (red) and 10 μL/min (blue), respectively.

Figure 4.6(a) plots the refractive index profiles under different cladding and core flow rates at the position of $x_1$. It shows that the index profiles fit well with the refractive index formula given by Eq. (4.7). The mismatch at the edge is caused by the slower flow rate and longer diffusion time near the microchannel sidewall. To
Chapter 4 Optofluidic Hyperbolic Secant Lens

study the relationship between the ratio of flow rates and the range of index profiles, the maximum and minimum indices are summarized in Figure 4.6(b) when the cladding flow is 1.0 μL/min (red) and 10 μL/min (blue), and the ratio of the core and cladding flow rates changes from 0.2 to 4.0. The result shows that the index profile has the largest index difference when the ratio of flow rates and the cladding flow rate are 2.25 and 10 μL/min, respectively.

The spherical and field curvature aberrations of the optofluidic lens are investigated using ray tracing simulation. The concentration profile is simulated by using the ‘Laminar Flow’ and ‘Transport of Diluted Species’ modules in COMSOL 5.0. Then the ‘Geometrical Optics’ module is used to simulate the trajectories of light rays. Figures 4.7(a) and (b) illustrate the ray-tracing simulation when the light source is placed at the center and 30 μm above the center. Figure 4.7(c) shows that the focal length and maximum divergence angles as a function of the flow rate ratio when the cladding flow rate is 10 μL/min. The maximum divergence angle is defined as the angle at which light is focused with spherical aberration δ smaller than 15 μm. The result shows that the focal length decreases sharply to a minimum value when the ratio of flow rates is smaller than 1.5 and then increases gradually when the flow rate ratio is increased further. On the other hand, when the flow rate ratio is 2.25, the divergence angle reaches a maximum value of 35° and the light focusing is maximized. By referring to Figure 4.6(b), we can infer that the focal length decreases and the divergence angle increases when the refractive index contrast is increased. Therefore, large index contrast is favored to better suppress the optical aberrations. The maximum divergence angle can be further increased by using more sophisticated and precise methods to reduce the refractive index mismatch at the edge of the microchannel.
Figure 4.7(c) also indicates that the focal length and divergence angle are correlated at a given ratio of flow rates, which means that it is impossible to change the maximum divergence angle and focal length independently. However, it is still possible to achieve this goal by changing the channel width. Figure 4.8 shows the
simulated focal length as a function of the channel width when the flow rate ratio is 2.25. It clearly shows that the focal length is linearly proportional to channel widths.

Figure 4.8: Ray tracing simulation of light beams with channel width of (a) 80 μm, (b) 120 μm, and (c) 150 μm. (d) Simulated focal length as a function of channel widths with the core/cladding ratio of 2.25.
Figure 4.9 shows the ray tracing simulation of light beams with different divergence angles $(\theta)$ in the (a) optofluidic GRIN lens and (b) optofluidic HS lens.

Figure 4.9 shows the ray tracing simulation of light beams with divergence angle increasing from $12^\circ$ to $35^\circ$. It shows that the focal length of the outer rays is longer than that of the inner rays in the optofluidic GRIN lens, while in the optofluidic HS lens, they are focused at the same position on the optical axis. Similarly, Figure 4.10 shows the ray tracing simulation of light beams with different off-axis positions. It shows that when the light beams are placed above the center, the outer and inner rays are focused at multiple points in the optofluidic GRIN lens, while they are focused to a single point in the optofluidic HS lens.

Based on the ray tracing results as shown in Figure 4.9, the spherical aberration of the optofluidic GRIN lens and the optofluidic HS lens are compared as a function of the divergence angle as shown in Figure 4.11(a). It indicates that the spherical aberration $\delta$ of both lenses is smaller than $15 \mu m$ when the divergence angle is smaller than $20^\circ$. However, with the divergence angle further increased, the
spherical aberration of the optofluidic GRIN lens increases nearly exponentially, while that of the optofluidic HS lens only increases slowly. The results show that the optofluidic HS lens increases the maximum divergence angle to $35^\circ$ for the same $\delta$ of 15 $\mu$m, which is 1.75-fold better than that of the optofluidic GRIN lens. Similarly, Figure 4.11(b) compares the field curvature aberration of the two lenses based on the ray tracing results in Figure 4.10. It shows that in the longitudinal direction, the focal positions of the optofluidic GRIN lens (Square, Red) are relative to the off-axis position of the source light, while those of the optofluidic HS lens (Square, Blue) are on the same focal plane of 612.0 $\mu$m. In the transverse direction, the focal positions of the optofluidic GRIN lens (Circle, Red) are generally closer to the optical axis, while those of the optofluidic HS lens (Circle, Blue) are equal to the off-axis positions.

Figure 4.10: Ray tracing simulation of light beams with different off-axis positions ($\Delta y$) in the (a) optofluidic GRIN lens and (b) optofluidic HS lens.
Figure 4.11: (a) Simulated spherical aberration as a function of divergence angle.
(b) Focal position as a function of light source positions. (Red: optofluidic GRIN lens, Blue: optofluidic HS lens)
4.2 Fabrication processes and experimental setups

4.2.1 Fabrication processes

The optofluidic chip is fabricated with Polydimethylsiloxane (PDMS) using soft lithography technique. The soft lithography technique is a common technique in fabricating microfluidic devices [218]. It provides faster and less expensive routes than silicon or glass etching-based techniques.

Two materials are involved in the fabrication: the SU-8 photoresist for master patterning and PDMS for microchip casting. SU-8 is a commonly used negative photoresist [219]. It is a very viscous polymer that can be spread over a thickness of several micrometers up to 300 μm. When exposed to UV light, the SU-8 molecular chains cross-link with together and make a solid layer. PDMS belongs to a group of polymeric organosilicon compounds which are commonly referred to as silicones [220]. It is widely used in microfluidics due to its features such as biocompatible, optically transparent, electrically insulating, chemically inert, etc.

Figure 4.12 shows the flow of PDMS fabrication processes. As shown in Figures 4.12(a) and (b), a layer of SU-8 (SU-8 100, MicroChem) is spin-coated on the acid-pretreated silicon substrate at 500 rpm for 5 s. Then the wafer is ramped to 3000 rpm at an acceleration of 300 rpm/s and held for a total of 30 s to obtain a thickness of 100 μm. Next, the wafer is put on a hotplate for soft baking at 65°C for 6 mins and at 95°C for 20 mins. At the exposure step, the wafer is exposed to UV light by a mask aligner machine at 11 mW/cm² for 35 s. The exposed wafer is then baked again at 65°C for 1 min and 95°C for 5 mins. The solidification of SU-8 occurs at the post exposure bake step and hence it is vital to carefully control the process conditions. Finally, the wafer is immersed into MicroChem’s SU-8 developer for 6
mins as shown in Figure 4.12(c). The developed SU-8 structures are attached to the wafer and the master is ready to use in PDMS molding. The recipe for the SU-8 process is provided by the manufacturer and optimized during the fabrication process. Sylgard 184 Silicone Elastomer Kit (Dow Corning) is used for the PDMS molding. The kit contains two-part liquid components: the base agent and curing agent. The base and curing agents are well mixed in a ratio of 10:1 in weight. The mixture is poured onto the mold master and then degassed in a vacuum chamber for 1 hour. After that, the mixture is cured at 75°C for 1 hour. The curing temperature and the ratio of the curing agent influence the stiffness and optical properties of the PDMS. Finally, the PDMS sheet is sliced and peeled off from the master as shown in Figure 4.12(d).

![Figure 4.12: Fabrication flow of PDMS chips.](image)

(a) Silicon wafer cleaning, (b) photoresist coating, (c) photoresist develop, (d) PDMS molding and (e) chip bonding.
For the PDMS chip bonding, the PDMS slab and the glass cover are carefully cleaned with ultrasonic cleaner and isopropanol (IPA) and dried under a gentle stream of nitrogen. After cleaning, both surfaces are treated with a handheld corona treater (Rotaloc, PB33-341). That is because the cured PDMS has a very low surface energy and is hydrophobic. It is difficult for chemical species to interact with the PDMS surface and therefore the adhesion is generally very poor. Increasing the surface energy will enhance the adhesion characteristics of the PDMS. The corona discharge electrically breaks down the chemicals comprising the air. After the surface treatment, both surfaces are brought into conformal contact and put in a 75°C oven overnight as shown in Figure 4.12(e). Figure 4.13 shows the fabricated PDMS microchip.

Figure 4.13: Photograph of the fabricated PDMS microchip.
4.2.2 Preparation of fluids

As discussed in Paragraphs 4.13 and 4.14, higher index contrast is favored to better suppress the optical aberrations. The refractive indices of common liquid mediums generally range from 1.3 to 1.7. In the experiment, 100% ethylene glycol (RI: 1.432 at 25°C) and 100% DI water (RI: 1.333 at 25°C) are used due to their relatively high index contrast and easy accessibility in our laboratory. Rhodamine 6G (−10⁻⁶ g/mL) is added into both ethylene glycol and DI water to visualize the light propagation in the optofluidic HS lens.

4.2.3 Experimental setup

Figure 4.14 shows the experimental setup of the optofluidic HS lens. The optofluidic chip is placed on an inverted microscope (Nikon, Eclipse Ti). The light propagation image is captured by using a 10× objective lens (Nikon, numerical aperture (NA) = 0.3) and a digital CCD camera (Nikon, DS-Ri1). Liquids are pumped into the chip with a high precision syringe pumps (Cetoni, neMESYS 290N). Green laser source (λ = 514.5 nm) from an argon laser (Modu-Laser, Stellar-Pro Select) is used in the experiments to measure the spherical and field curvature aberrations of the optofluidic lens. A single-mode fiber (NA: 0.12) is used to couple the laser light into the optofluidic chip. The light beam profile emitted from a single mode fiber is measured using a beam profiler (SP503U, Ophir-Spiricon). Figure 4.15 shows that the light beam (distance to fiber tip: 31.2 mm) follows a Gaussian beam profile and the beam divergence angle is measured as 12.13°. The light intensity images are analyzed by intensity profiling using ImageJ. Another green light (λ = 532 nm) from
a solid-state laser (Laser Quantum, Gem) is added in the multiple light manipulation experiment.

Figure 4.14: Experimental setup of the optofluidic HS lens.

Figure 4.15: Captured image of the beam profile from the single-mode fiber.
4.3 Experimental results and discussions

4.3.1 Index profile measurement

To validate the microfluidic gradient generator, the index profile at the mixing chamber and the optofluidic chamber is measured. In the measurement, fluorescent dye (Rhodamine 6G, Concentration: $\sim 10^{-6}$ g/mL) is added into pure ethylene glycol. Based on the analysis in Paragraph 3.1.3, the refractive index is in a linear relationship with the captured pixel intensity. Figure 4.16 shows the fluorescent image of the branch channels, the mixing chamber, and the optofluidic chamber. It shows that the flow streams have discrete refractive index values in the branch channels. The discrete refractive indices evolve into a continuous hyperbolic secant profile in the mixing chamber. Subsequently, the refractive index profile keeps invariant in the optofluidic chamber due to the high flow rate ($42.5 \mu\text{L/min}$).

The measured index profiles at $x_1$, $x_2$, and $x_3$ are plotted in Figure 4.17. As shown by the blue line, the index profile at $x_1$ shows nine distinct steps. It is caused by the insufficient mixing of the branch flows. The highest refractive index is 1.428, which is slightly lower than that of the pure ethylene glycol. The lowest refractive index locates near to the sidewalls and is close to that of DI water. Since the flow rate in the mixing chamber is relatively low, the liquids have sufficient diffusion time to evolve from the step-index profile to a smooth one. The red and green lines show the index profiles at $x_2$ and $x_3$. It clearly shows that the index profile is smoothened as expected. The highest refractive index is reduced to 1.407 and the lowest refractive index is increased to 1.343 caused by the diffusion in the mixing chamber. The results also show that the index profile at $x_1$ and $x_2$ are nearly identical. It is due to the high flow rate and the short diffusion time in the optofluidic chamber. The slight
asymmetry in the measured index profile is caused by the fabrication mismatch in the different stages of microfluidic mixers.

Figure 4.16: Fluorescent image of the branch channels, the mixing chamber and the optofluidic chamber (Scale bar: 100 μm).

Figure 4.17: Measured refractive index along the microchannel at the position of $x_1$, $x_2$ and $x_3$. 
4.3.2 Light propagation vs divergence angles

To evaluate the spherical aberration of the optofluidic HS lens, the light propagation images are investigated with different divergence angles. The divergence angle of the light beam from the single-mode fiber is 12°. The divergence angle of incident light is increased to 15°, 20°, 25°, 30°, 35°, 40° and 45° by using a series of PDMS diverging lenses. The PDMS lenses diverge lights through the air-PDMS interface at the end of fiber facet. They are center-aligned with the optofluidic chamber and placed 20 μm away from the chamber sidewall. These PDMS lenses are fabricated on the microchip through the soft-lithography processes.

Figure 4.18(a-d) shows the light propagation images with the divergence angle of 12°, 20°, 30° and 45° when the cladding and core flow rates are 10 μL/min and 22.5 μL/min, respectively. The red arrows denote the focal positions. The results show that the light beams are focused at the same position by the optofluidic HS lens when the divergence angle is smaller than 30°. However, when the divergence angle is further increased to 45°, a portion of the light beams escapes from the optofluidic HS lens and is scattered by the microchannel sidewall as shown in Figure 4.18(d). Meanwhile, the focal length is slightly longer than that when the divergence angles are 12°, 20° and 30°.

Figure 4.19 plots the light intensities along the central line of the microchannel. The results show that the focal length increases slightly from 571.6 to 582.8 μm when the divergence angle increases from 12° to 35°, and increases significantly to 618.5 μm when the divergence angle is 45°. It means that the spherical aberration increases considerably when the divergence angle is 45°. On the other hand, the beam waists are identical when the divergence angles are 12°, 20°, and 30°, while it is much wider when the divergence angle is increased to 45°.
Figure 4.18: Light propagation images with the divergence angle of (a) 12°, (b) 20°, (c) 30° and (d) 45°, respectively. (Scale bar: 50 μm)
The longitudinal focal position and spherical aberration as a function of the divergence angle is shown in Figure 4.20. Each data point is the average value of three measured focal positions. The spherical aberration of the optofluidic lens can
be estimated by measuring the paraxial focus (green dot) and the best focal point (black spot) as shown in Figure 4.21. The focal length of the paraxial rays is estimated as the $y$-intersection of the focal position curve as shown in Figure 4.20. The focal length of the best focal point is the measured by plotting the intensity profile along the optical axis and finding the position with maximum intensity. The distance between the paraxial focus and best focal points $\Delta l$ is three-quarters of the spherical aberration $\delta$ [221]. At $35^\circ$, the focal length of the paraxial rays and the best focal point are estimated to be 568.2 µm, and 582.8 µm, respectively. Therefore, the spherical aberration $\delta$ of the optofluidic HS lens is 19.5 µm at $35^\circ$. To measure the beam waist, the longitudinal intensity profile is plotted along the central line of the microchannel to find the best focal position. Then the transverse intensity at the focal position is fitted with the Gaussian function to determine the full width at half maximum (FWHM). The FWHMs with divergence angles of 12°, 20°, 30° and 45° are determined to be 6.4, 7.8, 6.3 and 10.6 µm, respectively. The results indicate that the optofluidic lens with HS profile has a superior focusing power than the conventional optofluidic lenses, which generally have a spot size larger than 20 µm [22, 24]. However, the beam waist is still limited by the current index generation method. Currently, the index profile is configured by changing the flow rates in the microfluidic gradient generator. We cannot achieve pixel-level control on the index profile to make it perfectly match the ideal index profile. The optical performance can be further increased by using more sophisticated index tuning methods, such as thermal or hydrogel-assisted diffusion [85].
4.3.3 Light propagation vs off-axis positions

To investigate the field curvature aberration of the optofluidic HS lens, the focal positions in the longitudinal and transverse directions are investigated when the light source is placed at different off-axis positions. A series of optofluidic chips with different fiber slot positions is fabricated using the soft-lithography. The incident light is applied from a single-mode fiber directly with a divergence angle of 12°.

The light propagation images with the off-axis positions of 0, 15 μm, 30 μm and 45 μm are shown in Figure 4.22(a-d). It shows that the light sources are focused on the same focal plane in the longitudinal direction. In the transverse direction, the transverse distance between the source and the focal point is 0, 29.8 μm, 58.4 μm and 84.3 μm at the four off-axis positions. The result indicates that the field curvature is smaller when the light source is placed closer to the optical axis and the largest variance (|Δy − Δy'|) is 5.7 μm at an off-axis position of 45 μm.
Figure 4.22: Light propagation images when the light source is placed with the off-axis position of (a) 0, (b) 15 μm, (c) 30 μm and (d) 45 μm, respectively. (Scale bar: 50 μm)

Figure 4.23 shows the normalized light intensity along the dashed lines in Figure 4.22(a-d). By fitting the intensity profiles with Gaussian functions, the FWHM
of the focal points is measured to 8.7 µm, 8.8 µm, 7.8 µm and 7.6 µm, respectively. It shows that the FWHM is nearly the same when the off-axis positions are 0 and 15 µm, while the FWHM is reduced slightly when the off-axis positions are further increased to 30 µm and 45 µm. The reason is that under a large off-axis position, a portion of the light beams escapes the optofluidic HS lens and therefore the beam waist is smaller at the focal position. The FWHW variance can be further reduced by using liquids with higher index contrast to better suppress the field curvature aberration.

The transverse and longitudinal focal position as a function of the off-axis position are summarized in Figure 4.24. Each data point is the average value of three measurements. The results clearly show that the light beams are focused on the focal plane of 572.3 ± 3.4 µm in the longitudinal direction, and are focused at the opposite positions with a variation of 5.7 µm in the transverse direction.

![Figure 4.23: Normalized light intensity on the focal plane when the light source is placed at different off-axis positions.](image-url)
4.3.4 Light focusing for multiple light sources

The optofluidic HS lens can focus multiple light sources because of the reduced optical aberrations. Figure 4.25 schematically illustrates the application in multiplexed detection. The optofluidic HS lens can focus a light source array uniformly and minimize the difference of illumination intensity at the detection region. In addition, due to the low dispersion of ethylene glycol and water [222], the lens can focus multi-color light beams with chromatic aberration < 5 μm based on simulation results. When the barcoded particle flows through the detection region, it will be excited by the focused laser beams of specified wavelength.

The light propagation image with two light sources is shown in Figure 4.26(a). An argon laser (λ = 514.5 nm, Modu-Laser, Stellar-Pro Select) and a solid-state laser (λ = 532 nm, Laser Quantum, Gem) are used in the experiment. The two light sources are coupled to the optofluidic chamber through two closely-placed bare fibers (fiber
diameter: 125 µm). The distance between the two fiber cores is 125 µm, and the width of the optofluidic chamber is 200 µm. It clearly shows that the two laser sources are coupled into the optofluidic HS lens at position A and position B from the left sidewall. Then the laser beams are bent gradually and focused at the opposite transverse positions. Since the two laser beams are incoherent, there is no interference between them in the optofluidic HS lens.

Figure 4.26(b) plots the normalized light intensity along the dashed line in Figure 4.26(a). The FWHMs of source A and B are measured to 10.9 and 12.4 µm, respectively. The slight FWHM difference is possibly caused by the beam profile mismatch between the two laser sources. Two lasers with similar beam profiles are expected to reduce the beam waist variation in real-world applications.

Figure 4.25: Schematic illustration of the potential application in multiplexed detection.
Figure 4.26: (a) Light propagation image with two sources. (Scale bar: 100 μm, vertical direction is magnified by 1.5-fold) (b) FWHM of the two focal points.
4.4 Summary

This chapter focuses on the optical aberrations, the index profile derivation, microfluidic design, chip fabrication and experiments of the optofluidic HS lens. The spherical and field curvature aberrations are two aberrations to deteriorate the optical performance in optofluidic lenses. The optimized index profile is derived from Maxwell’s fisheye lens through two-step coordinate transformation. A microfluidic gradient generator is designed to generate the index profile. The chip fabrication processes are developed for the fabrication of the optofluidic HS lens using polymer PDMS material. The experimental results show that low spherical aberration and field curvature is achieved when the ratio of the core and cladding flow rates is 2.25. The spherical aberration $\delta$ is smaller than 19.5 $\mu$m and the FWHM of the focal point is 7.8 $\mu$m with a divergence angle of 35°. The light source at different off-axis positions is focused on the focal plane with $\Delta x' < 6.8$ $\mu$m and at opposite transverse positions with $|\Delta y - \Delta y'| < 5.7$ $\mu$m. In addition, light focusing experiment for multiple light sources is conducted. The optofluidic lens significantly enhances the focusing power and is capable of manipulating multiple light sources for potential lab-on-a-chip applications such as sample illuminations, on-chip light manipulation and multiplexed detection, etc.

The innovation of the developed optofluidic HS lens is summarized as follows:

(a) This is the first effect to improve the optical performance of microfluidic lenses by optimizing the index profile. The previous optofluidic lenses mainly focus on the demonstration of tunable light focusing, but neglect the optical performance which is important in certain applications. This work
investigates the influence of spherical and field curvature aberrations in the optical performance and derives the ideal index profile based on the coordinate transformation of Maxwell’s fisheye lens. The beam waist of the designed optofluidic HS lens is smaller than 10 μm, which is twice better than the prior art [22, 24].

(b) This work shows an example of designing an optofluidic component from its solid counterpart. Previously, the optofluidic components are borrowed directly from the solid one, i.e. the geometry and index profile are preserved in the microfluidic realization. However, the geometry and index profile of many solid optical devices, especially those with fancy functionalities, are challenging to be realized in microfluidics. This work uses the coordinate transformation to make the configuration of the optical device easier for microfluidic realization. This design method is anticipated to inspire the emergence of more integrated optofluidic devices with complex functionalities.

(c) The work demonstrates the focusing of multiple light sources and illustrates its novel application in multiplexed detections. The conventional method generally uses a micro-lens array, beam splitter or cylinder lens to focus multiple light sources. Here thanks to the suppressed optical aberrations, this work can focus multiple light sources using a single optofluidic HS lens and in the meanwhile doesn’t compromise the focusing power.
CHAPTER 5
NANOPARTICLE MANIPULATION
IN NEAR-FIELD OPTICS

This chapter designs a photonic pillar array-based optofluidic manipulation system for nanoparticle sorting and bacteria manipulation. The design of the optofluidic system, including the microfluidic subsystem and the photonic subsystem, is discussed. Then the experimental preparation and setup are presented in detail, including the optimized buffer and surface conditions, the fabrication process, the experimental setup and the optical force calibration using a single nano-waveguide. In the experiment, the separation of 500-nm nanoparticle from particle mixtures is demonstrated, including the force analysis, the trajectory analysis, and the statistical analysis of the particle distribution. Finally, the trapping and alignment of *Shigella* are demonstrated in the optofluidic system.
5.1 Design of the optofluidic system

The photonic pillar array (PPA)-based optofluidic manipulation system is illustrated as shown in Figure 5.1. It is designed to be a versatile platform for various kinds of biomolecule manipulation, i.e. it can not only sort spherical biomolecules such as virus and microvesicles, but also massively align rod-shaped bacteria such as *Shigella*, and *E. coli*. The system consists of a microfluidic subsystem and a photonic subsystem. The function of the microfluidic subsystem is to direct the target sample to the optical field for particle separation. The function of the photonic subsystem is to engineer an optical interference pattern, which is called PPA, to exert distinct optical forces on different particles. Figure 5.1 illustrates that when particles flow through the PPA, they are separated based on the different properties such as size, refractive index, etc. The designs of the microfluidic and photonic subsystem are discussed in this section.

![Figure 5.1: Illustration of the optofluidic system for nanoparticle and bacteria manipulation.](image-url)
5.1.1 Design of the microfluidic subsystem

The task of the microfluidic subsystem is to direct the target samples to the optical field. There are three requirements to the subsystem. Firstly, the sample particle needs to be confined in the region of the optical evanescent field to achieve higher sorting/trapping efficiency. The optical evanescent field in silicon photonic devices is usually less than 400 nm [223], and therefore the microchannel height should be thinner than ~1 μm. Secondly, the flow carrying the sample particles needs be slow and stable. Since the optical force is generally a sub-piconewton force [132], the flow velocity needs to be on the order of ~10 μm/s to introduce a comparable fluidic drag force. Thirdly, the particles are required to flow into the optical field from nearly the same position to enable particle separation based on their lateral displacements, i.e. hydrodynamic focusing of the particles is needed.

In this work, a shallow microchannel with 1-μm height is used to confine particles in the field of the evanescent wave. It is challenging to fabricate such shallow channels using soft materials such as PDMS. Because the PDMS channel will collapse due to deformation when the ratio of channel width and height is higher than 10 [224]. To overcome this problem, a silicon channel and a glass top cover are used to form the microchannel. The dimension of the microchannel is 3000 μm (long) × 100 μm (width) × 1 μm (height). The average flow velocity of 10 μm/s corresponds to a flow rate of 0.06 nL/min, which is too small for most syringe pumps. Here branch channels are designed to reduce the flow rate in the shallow channel. Two flow streams, a particle flow stream and a sheath flow stream, are used to hydrodynamically focus the particles to the left side of the microchannel.
Figure 5.2 illustrates the design of the microfluidic subsystem. It includes a shallow main channel on the silicon chip, two branch channels on the glass cover, a connecting channel bridging the shallow main channel and the branch channels, two
inlet holes, and an outlet hole. The ratio between the liquids flowing into the branch channel and the main channel is determined by their hydraulic resistance ratio. Figure 5.3 shows the equivalent hydraulic circuit. \( R_b, R_s \) and \( R_c \) represent the hydraulic resistance of the branch channel, the shallow main channel and the connecting channel, respectively. The hydraulic resistances are determined by the channel dimension, which are given by

\[
R = \frac{12\lambda L}{1-0.63(h/w) h^3w} \tag{5.1}
\]

Where \( R \) is the hydraulic resistance, \( \lambda \) is the viscosity, \( L \) is the channel length, \( h \) is the channel height, and \( w \) is the channel width. Since the dimension of the main channel is restricted by the optical design, the hydraulic resistance ratio is therefore tuned by the dimension of the branch channels. To optimize the dimension, the flow velocity in the main channel as a function of the branch channel dimensions is investigated as shown in Figure 5.4. A pumping flow rate of 1 \( \mu \text{L/min} \) is used in the calculation.

Figure 5.4: The flow velocity in the main channel as a function of the branch channel dimensions.
Figure 5.4 indicates that multiple channel dimensions can be used to obtain a flow velocity of 10 μm/s. Here the branch channel is designed to 20 μm in height and 300 μm in width. Table 1 summarizes the dimension and hydraulic resistance of the channels in the microfluidic subsystem. It shows that the hydraulic resistance in the main channel is 11,162 times larger than that in the branch channel, which greatly reduces the liquids flowing into the main channel.

Table 5.1: Summary of the dimension and hydraulic resistance.

<table>
<thead>
<tr>
<th>Channel</th>
<th>Dimension (L × w × h)</th>
<th>Hydraulic Resistance Pa/(μL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Channel</td>
<td>3000 μm × 100 μm × 1 μm</td>
<td>6.05 × 10⁶</td>
</tr>
<tr>
<td>Connecting Chanel</td>
<td>1300 μm × 400 μm × 1 μm</td>
<td>5.79 × 10⁵</td>
</tr>
<tr>
<td>Branch Channel</td>
<td>7000 μm × 300 μm × 20 μm</td>
<td>5.42 × 10²</td>
</tr>
</tbody>
</table>

The particle flow stream is hydrodynamically focused by controlling the ratio of particle and sheath flow rates. The width of the focused particle stream is given by [195]

\[
\eta(a - 1)(a + 3)a^2 + Q_{\text{ratio}} \cdot \eta(a - 1)^2(a^2\eta - a^2 - 2a\eta + 4a + \eta) - a^4 = 0 \quad (5.2)
\]

Where \( \eta \) is the viscosity ratio between the particle and sheath flow streams, \( a \), which equals to \( w_{\text{particle}}/w_0 \), is the width of the particle stream normalized to the main channel, and \( Q_{\text{ratio}} \), which equals to \( Q_{1}/Q_{2} \) in Figure 5.3, is the ratio between the particle and sheath flow rates. By solving the equivalent hydraulic circuit and Eq.(5.2), the relationship between the normalized width of the particle stream, \( w_{\text{particle}}/w_0 \), and the inlet flow rate ratio, \( Q_1/Q_2 \), is calculated as shown in Figure 5.5. The result shows that the width of the particle stream increases sharply from 0 to 1
when the flow rate ratio changes from 0.91 to 1.10. For the sheath stream with different viscosities, the width is narrower with higher solution viscosity. Meanwhile, the curve slope is sharper with low viscosity near $w_{particle}/w_0 = 0$, and is sharper with high viscosity near $w_{particle}/w_0 = 1$. In this work, water buffer solution is selected as the sheath stream due to its compatibility to biological samples.

![Graph](image)

**Figure 5.5:** The relative width of the particle streams, $w_{particle}/w_0$, as a function of the inlet flow rate ratio, $Q_1/Q_2$.

### 5.1.2 Design of the photonic subsystem

The task of the photonic subsystem is to engineer the optical interference pattern (PPA) to exert distinct optical forces on different particles. In the optical field design, we need to compromise between adequate light-particle interaction regions, and strong enough optical intensity. The adequate light-particle interaction ensures enough work to separate particles. However, larger interaction area will result in a lower optical intensity. When the optical intensity is too small, the optical force,
which is directly proportional to the optical intensity, will be too weak to compete with other forces such as fluidic drag force and Brownian force.

Figure 5.6 illustrates the schematic of the photonic subsystem. The photonic subsystem mainly includes two parts: the beam splitter and the waveguide-pair array, as shown in Figure 5.6(a). The beam splitter divides the laser source equally into the waveguide-pair array. The waveguide-pair array consists of $N$ waveguide-pairs. Each waveguide-pair is formed by two geometrically identical waveguides. As shown in Figure 5.6(b), the width and height of the waveguide are defined as $w$ and $h$, respectively. The gap between two waveguides is defined as $g$. The gap between the adjacent waveguide-pairs is defined as $l$.

Beam splitter is a basic component in silicon photonic circuits. The function of beam splitting can be realized by many silicon photonic components such as
multimode interference (MMI) coupler [225, 226], directional coupler [227] and Y-branch coupler [228]. In this design, multiple stages of beam splitters are used to divide the laser source into $N$ waveguide-pairs. The Y-branch coupler is selected due to its compact footprint and the simple configuration. However, the standard Y-branch typically has an insertion loss of 1 dB (21% power loss) [229], which is too high to be used in series. Here an improved Y-branch is used to reduce the insertion loss to 0.28 dB (6.2% power loss) [230]. Figure 5.7(a) shows the design of the beam-splitter. The E-field distribution at 1550 nm is simulated as shown in Figure 5.7(b). The geometry is listed in Table 5.2. The result shows that the laser beam is split equally into two beams and there is no obvious light scattering and back-reflection at the bifurcation point.

![Figure 5.7: (a) Design of the improved beam splitter. (b) Simulation result of the E-field distribution at 1550 nm.](image)

**Table 5.2: Design parameter of the improved beam splitter.**

<table>
<thead>
<tr>
<th>$w_1$</th>
<th>$w_2$</th>
<th>$w_3$</th>
<th>$w_4$</th>
<th>$w_5$</th>
<th>$w_6$</th>
<th>$w_7$</th>
<th>$w_8$</th>
<th>$w_9$</th>
<th>$w_{10}$</th>
<th>$w_{11}$</th>
<th>$w_{12}$</th>
<th>$w_{13}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.5</td>
<td>0.6</td>
<td>0.7</td>
<td>0.9</td>
<td>1.26</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.31</td>
<td>1.2</td>
<td>1.2</td>
<td></td>
</tr>
</tbody>
</table>
In the design of the waveguide-pair array, the geometry of a single waveguide-pair and the number of the pairs are considered. The geometry of the waveguide-pair, which includes the waveguide height $h$, width $w$, and gap $g$, determines the coupling length $L_c$ to transfer the laser power entirely from one waveguide to the other [231]. The coupling length determines the width of each photonic pillar in the waveguide and therefore affects the trajectories of different particles. The waveguide height is determined by the structure layer thickness of the silicon-on-insulator (SOI) wafer, which is 220 nm in the case. The influence of the waveguide width and gap on the coupling length is calculated using Lumerical FDTD.

![Schematic illustration of coupling length ($L_c$).](image)

![Coupling length as a function of the waveguide width and gap.](image)

Figure 5.8: (a) Schematic illustration of coupling length ($L_c$). (b) Coupling length as a function of the waveguide width and gap.
Figure 5.8 shows the coupling length as a function of the waveguide width and gap. It shows that the coupling length is directly proportional to the waveguide width and gap. In particle manipulation, each photonic pillar in the PPA works as the basic unit to cause a small trajectory difference. Therefore, shorter couple length is favored to have more photonic pillars and to obtain distinct accumulated trajectories. Here the waveguide gap is designed to 200 nm limited by the minimum linewidth in lithography. The waveguide width is designed to 350 nm by compromising between the photonic pillar width and the propagation loss. The coupling length is 7.77 μm in the design.

Another design consideration in the waveguide-pair array is the number of the waveguide-pairs. It is a compromise between the area and intensity of the optical field. The optical intensity, which is the confined power per unit area, should be large enough to have sufficient optical force. The minimum guided power $P_{\text{min}}$ is usually larger than ~ 6 mW in a micro-waveguide [80, 232]. In this work, nano-waveguides are used and the minimum power can be reduced to ~ 2 mW based on the calibration experiment which will be discussed in Paragraph 5.2.4. The guided power in a single waveguide-pair can be expressed as

$$ P = P_0 \cdot (1 - \alpha)^{\log_2 N} / N \tag{5.3} $$

Where $P_0$ is the laser power coupled into the silicon photonic chip, $\alpha$ is the insertion loss of the beam splitter, and $N$ is the number of the waveguide-pair. Here the guided laser power $P_0$ is ~100 mW at the maximum, and the insertion loss is 6.2%. Based on Eq.(5.3), $N$ should be smaller than 36 to make the guided power $P$ larger than 2 mW. Therefore, 5 stages of beam splitters are designed to divide the laser source into 32 waveguide-pairs. The design parameters of the photonic subsystem are summarized in Table 5.3.
Table 5.3: Design parameters of the photonic subsystem.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$N$</td>
<td>30</td>
<td>Number of waveguide-pairs</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>-0.28 dB</td>
<td>Insertion loss of the beam splitter</td>
</tr>
<tr>
<td>$w$</td>
<td>350 nm</td>
<td>Waveguide width</td>
</tr>
<tr>
<td>$h$</td>
<td>220 nm</td>
<td>Waveguide height</td>
</tr>
<tr>
<td>$g$</td>
<td>200 nm</td>
<td>Waveguide gap</td>
</tr>
<tr>
<td>$l$</td>
<td>800 nm</td>
<td>Distance between waveguide-pairs</td>
</tr>
<tr>
<td>$L_c$</td>
<td>7.77 $\mu$m</td>
<td>Coupling length</td>
</tr>
</tbody>
</table>
5.2 Experimental preparation and setup

5.2.1 Fabrication processes

The process flow of the chip fabrication is shown in Figure 5.8. In general, the fabrication includes three parts: the fabrication of the silicon photonic chip, the fabrication of the glass chip, and the bonding of the silicon photonic chip and the glass chip. The silicon photonic chip is fabricated on 8-inch SOI wafers as shown in Figure 5.9(a). The thicknesses of the structure layer, SiO$_2$ insulating layer and substrate layer are 220 nm, 2 \( \mu \)m and 700 \( \mu \)m, respectively. The fabrication starts with patterning the waveguide structure using deep ultraviolet (UV) lithography and reactive ion etching (RIE) as shown in Figure 5.9(b). Then a SiO$_2$ layer with 1 \( \mu \)m thickness is deposited using high-density plasma chemical vapor deposition (HDPCVD) at low temperature in Figure 5.9(c). After that, the window is patterned and opened using lithography and HF vapor release process as in Figure 5.9(d). The SiO$_2$ window exposes the waveguide surface and works as the shallow channel in the microfluidic subsystem. Before chip dicing, a trench (94 \( \mu \)m) is etched using deep RIE to obtain a smooth edge for laser source coupling. The dimension of the fabricated silicon photonic chip is 16 mm (length) \( \times \) 6.1 mm (width) \( \times \) 0.92 mm (thickness). The scanning electron microscope (SEM) images of the beam splitter and waveguide-pair array are shown in Figure 5.10.

In the fabrication of the glass chip, a 6-inch glass wafer with 1 mm thickness is coated with a thin layer (100nm) of PDMS. To do it, the uncured PDMS is diluted with hexane with a ratio of 40:1 to reduce the viscosity. The diluted PDMS is spin-coated on a glass wafer using a spin coater at 3000 rpm. Then the PDMS is cured by placing the wafer in a 95°C oven for 5 min. Then the whole wafer is diced.
Figure 5.9: Fabrication process flow of the silicon-glass hybrid chip.
into small pieces as shown in Figure 5.9(f). After that, inlet and outlet holes are drilled on the diced glass chip using an ultrasonic driller as shown in Figure 5.9(g). Finally, microchannels are engraved on the glass chip using direct laser writing machine. The microchannel works as the branch channel in the microfluidic subsystems. The dimension of the glass top cover is 25 mm (length) × 5.8 mm (width) × 1 mm (thickness).

To bond the silicon photonic chip and the glass chip together, the surfaces of both parts are treated with oxygen plasma for 5 mins. Then the two parts are aligned manually and kept in contact carefully. The chip is ready for use after annealing for 5 mins. During the process, the Si-OH bond on each surface is broken by high energy O$_2$ plasma, and then forms the Si-O-Si bond when the two surfaces are brought in contact. The contact angle is measured to verify the surface treatment. The contact angles of the silicon photonic chip and PDMS-coated glass cover are 63° and 112° before the treatment, and reduced to smaller than 5° after the treatment.

![Figure 5.10: SEM image of the fabricated silicon photonic chip: (a) waveguide-pair array, and (b) beam splitter.](image)
5.2.2 Experimental setup

The size of the silicon-glass hybrid chip is only 16 mm in length and 5.8 mm in width, which makes it difficult to apply two flow streams into the chip. To solve the problem, a set of chip holder is designed deliberately as shown in Figure 5.11. The chip holder set includes a bottom holder, two gaskets, and a top metal clasp. The stage 1 and 2 on the metal bottom holder are used to hold the silicon photonic chip and the glass cover, respectively. The top surface of the glass cover will be on the same level with the stage 3 surface when the hybrid chip is placed properly. Two rubber gaskets are made using laser cutter machine to avoid liquid leakage during the experiment. The metal clasp is designed to fix the microfluidic tubing. The clasp’s position is confined by the positioners on the bottom holder. Figure 5.12 is the photograph of the assembled chip holder.

![Figure 5.11: Schematic illustration of the chip holder set.](image)
As shown in Figure 5.13, the experimental setup includes two parts: the laser coupling and flow pumping part on a stationary optical breadboard, and the sample observation part on an XY translation stage. Figure 5.14 illustrates the procedure of laser coupling. The 1550 nm laser source is emitted from a tunable laser (Santec TSL-510, continuous wave). The laser power from the tunable laser is 2 mW and is amplified to >100 mW through an Erbium-doped fiber amplifier (EDFA, Amonics). Then the laser polarization is tuned to the transverse magnetic (TM) mode using a polarization beam splitter (Newport, F-PBC-15-SM-FP) and a polarization controller (Newport, F-POL-PC). The laser source is coupled to the fabricated chip through a lensed fiber controlled by a piezo-actuated alignment stage (Newport, M-561D-XYZ). The light signal after the chip is connected to a power meter (Newport 1918-R). The liquid is pumped to the device using two syringe pumps (Cetoni, neMESYS 290N). On the other hand, the sample is observed by using a moveable fluorescent
microscope (Nikon FN1). The images are collected by a 40× objective (Nikon, NA = 0.6) and a CCD camera (Nikon DS-Ri1).

Figure 5.13: Illustration of the experimental setup.

Figure 5.14: Illustration of the laser coupling procedure.
5.2.3 Sample preparation and surface treatment

In near-field manipulation, the particle-surface interaction cannot be neglected because it could overwhelm the optical force and lead to particle adhesion or insignificant optical force [42]. The particle-surface interaction includes the hydrophobic interaction and electrostatic interaction [233]. The hydrophobic interaction describes the attractive force between hydrophobic surfaces. The electrostatic interaction describes the attractive or repulsive force between two charged surfaces. To prevent it from ruining optical manipulation, the particle-surface interaction is controlled carefully in two aspects: the buffer solution preparation and the channel surface treatment.

In the preparation of the sample buffer solution, the pH value, ionic strength and the surfactant type are considered. The pH value determines the electrostatic state of particles in solution. For example, a particle could be positively charged at low pH and gradually change to negatively charged when the pH value is increased. The ionic strength determines the thickness of the electric double layer (Debye length) and therefore determines the minimum distance to have electrostatic interaction. Surfactant is a commonly used reagent to reduce particle aggregate. It has many types and could have different effects in the optical manipulation application.

To begin with, the effect of pH value and ionic strength are investigated. High concentration of 0.5-μm particle (ThermoFisher, R500, ~10^6 particle/mL) is added to three common buffer solutions. The properties of the buffer solutions are summarized in Table 5.5. Then the solutions are divided equally to 1 mL and placed in 2 mL tubes. Small silicone pieces (5 mm × 5 mm) are immersed in each tube for 1 hour and then rinsed gently with DI water. The images of the sticked particles are captured using a microscope as shown in Figure 5.15. It shows the sodium chloride (NaCl) solution
has the fewest sticked particles, while the PBS buffer has the most particles. It indicates that the sticked particle is directly proportional to the solution conductivity. The 1× TAE buffer is selected as the buffer solution due to its modest conductivity and stable pH condition.

<table>
<thead>
<tr>
<th>Buffer Solution</th>
<th>pH</th>
<th>Conductivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mM NaCl</td>
<td>4.93 - 6.26</td>
<td>0.438 ms/cm</td>
</tr>
<tr>
<td>1× TAE buffer</td>
<td>7.90</td>
<td>1.585 ms/cm</td>
</tr>
<tr>
<td>1× PBS buffer</td>
<td>7.52</td>
<td>15.301 ms/cm</td>
</tr>
</tbody>
</table>

Subsequently, the effect of different surfactant on particle adhesion is studied. The tested surfactants include: Hyamine 1622 (1% v/v, cationic), sodium dodecyl sulfate (SDS) (0.1% v/v, anionic), Span 80 (1% v/v, non-ionic), Tween 20 (1% v/v, non-ionic), and Triton X-100 (1% v/v, non-ionic). Figure 5.16 shows the fluorescent image of the sticked particles for different surfactant solutions. It shows that the SDS solution has fewest sticked particles and the Hyamine 1622 solution has the most
sticked particles. It is caused by the different charge of the two surfactants. Meanwhile, the other surfactants have comparable performance to avoid particle adhesion. Here Tween 20 is selected as the surfactant due to its non-ionic nature and the availability.

![Images of the sticked particles for solutions (a) without surfactant and with surfactant of (b) Hyamine 1622, (c) SDS, (d) SPAN 80, (e) Tween 20 and (f) Triton X-100.](image)

In the treatment of the channel surface, a thin layer of molecules is deposited to change the property of the channel surface. Here 1% w/w bovine serum albumin (BSA), 5% w/w BSA, 1% w/w 1,2-Dioleoyl-sn-glycero-3-phosphocholine (DOPC), 1% w/w polyethylene glycol (PEG) and 1% w/w 3-Aminopropyltriethoxysilane (APTES) solutions are prepared in 1× TAE and 1% v/v Tween 20 buffer. The silicon pieces are immersed in the solutions immediately after oxygen plasma treatment. The fluorescent images of the sticked particles for different surface treatments are shown.
in Figure 5.17. It indicates that the 1% BSA, 5% BSA, 1% DOPC, and 1% PEG solutions have similar performance in resisting particle adhesion. Meanwhile, the treatment with the APTES solution significantly increases the particle adhesion. It is because the deposited APTES layer is positively charged, while the particle is negatively charged. The 1% BSA solution is used as the treatment solution in the following experiments due to its easy accessibility. The optimized conditions of the buffer solution and the surface treatment are summarized in Table 5.5.

![Figure 5.17: Images of the sticked particles (a) without surface treatment and with different surface treatments of (b) 1% BSA, (c) 5% BSA, (d) 1% DOPC, (e) 1% PEG, and (f) 1% APTES.](image-url)
Table 5.5: Summary of the buffer solutions and the surface treatment.

<table>
<thead>
<tr>
<th>Name</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buffer solution</td>
<td>1× TAE buffer</td>
</tr>
<tr>
<td>Surfactant</td>
<td>1% v/v Tween 20</td>
</tr>
<tr>
<td>pH value</td>
<td>7.90</td>
</tr>
<tr>
<td>Conductivity</td>
<td>1.585 ms/cm</td>
</tr>
<tr>
<td>Surface treatment</td>
<td>1% BSA</td>
</tr>
<tr>
<td>Zeta potential (500-nm, latex)</td>
<td>-36.3 mV</td>
</tr>
</tbody>
</table>

5.2.4 Force calibration

To estimate the optical force in waveguide-pair arrays, a calibration experiment is conducted in a single waveguide. Optical scattering force is equal to the fluidic drag force when the particle is moving with uniform velocity. The fluidic drag force can be easily determined based on the particle velocity, which is expressed as [80]

\[
F_{\text{Scattering}} = F_{\text{Drag}} = \beta \cdot 6\pi r \mu v
\]  

(5.4)

Where \( \beta \) is the correction term for near-wall particles, \( r \) is the particle radius, \( \mu \) is the viscosity, and \( v \) is the particle velocity. The correction term \( \beta \) is given by

\[
\beta = \frac{1}{1 - \frac{9}{16} \left( \frac{r}{h} \right) + \frac{1}{8} \left( \frac{r}{h} \right)^3 - \frac{45}{256} \left( \frac{r}{h} \right)^4 - \frac{1}{16} \left( \frac{r}{h} \right)^5}
\]  

(5.5)

Where \( h \) is the distance between the particle center and the surface. In the calibration experiment, the particles with 500 nm, 1.0 \( \mu \)m, and 2.0 \( \mu \)m diameter are trapped and pushed along the waveguide. Their movements are captured using video recording software (NIS-Elements BR).
Figure 5.18 shows the time-lapse images of particle movements on a single waveguide under a guided power of ~10 mW. It indicates that the 500-nm particle moves fastest, while the 2.0-μm particle moves slowest along the waveguide. It is because the effective region of particle-light interaction is limited to ~500 nm above...

Figure 5.19: Measured optical force as a function of guided power for particles of different diameters.
the surface. The optical force will not increase further when the particle size is larger than a critical diameter (~500 nm). The particle velocity will, therefore, decrease for large particles based on Eq.(5.4). The measured optical force as a function of the guided power is plotted in Figure 5.19. It indicates that the optical force is proportional to the square of the guided power. The optical force on the 500-nm particle is smallest although it moves fastest along the waveguide. The force on the 1.0-μm particle is slightly larger than that on the 2.0-μm particle. It suggests that the 1.0-μm particle has comparable optical force, yet smaller resistance forces when moving along the waveguide.
5.3 Nanoparticle separation

5.3.1 Sorting mechanism and force analysis

The PPA-based optofluidic manipulation system is used to separate nanoparticles based on their physical properties such as size, refractive index, shape, mass, etc. Figures 5.20(a) and (b) illustrate the separation of different sized particles in the optofluidic system. The PPA is formed by the back and forth coupling in each pair of the waveguide-pair array. Each localized optical field is called a photonic pillar. The different sized particles are hydrodynamically focused near to the left sidewall of the microchannel. When the nanoparticles flow through the PPA, they will have distinct trajectories: the large particle (red) has the most significant lateral displacement, the medium particle (blue) have the modest displacement, and the small particle (white) have the negligible displacement. They can be collected by different outlets in the downstream.

As illustrated in Figure 20(b), the PPA is basically the array of the optical field in a waveguide-pair. The optical field in a waveguide-pair is the back and forth repetition of photonic pillars coupling between the two waveguides. The optical force in the optical field can be divided into in-plane and out-of-plane forces. The out-of-plane force attracts the particle towards the waveguide surface and does not influence the particle trajectory directly. Therefore, only the in-plane optical force in the first three photonic pillars is calculated to reduce the computational complexity. The light intensity is simulated using commercial finite-difference time-domain (FDTD) tool. Figure 5.21 shows the simulated intensity distribution of the first three photonic pillars in the waveguide-pair. The white dashed line denotes the direction of the energy flow (Poynting vector).
Figure 5.20: Schematic illustration of (a) the chip design and (b) the separation of different-sized particles in the PPA.

Figure 5.21: Simulated light field in a waveguide-pair (Vertical direction is magnified by 5-fold).
Since the particle radius is smaller than 1/6 of the wavelength, the optical force can be calculated using Rayleigh approximation [234]. Based on the Rayleigh model, the optical force is divided into optical scattering force and optical gradient force which are expressed as

$$F_{\text{grad}} = \frac{2\pi n_r r^3}{c} \left( \frac{m^2 - 1}{m^2 + 2} \right) dl$$  \hspace{1cm} (5.6)

$$F_{\text{scat}} = I_0 \frac{128\pi^5 r^6}{3\lambda^4} \left( \frac{m^2 - 1}{m^2 + 2} \right)^2 n_2$$  \hspace{1cm} (5.7)

Figure 5.22: Calculated (a) $x$-component and (b) $y$-component of the resultant force distribution for 200-nm particle (Dashed box: trapping region, unit: pN).
where \( m \) is a constant related to the refractive index contrast of the particle and surrounding media, \( n_2 \) is the refractive index of the media, \( r \) is the particle radius, \( c \) is the velocity of light in vacuum, \( dI \) is the intensity gradient, \( I_0 \) is the energy intensity, and \( \lambda \) is the light wavelength. The fluidic drag force is calculated based on Eq. (5.4) and (5.5).

Figure 5.23: Calculated (a) \( x \)-component and (b) \( y \)-component of the resultant force distribution for 500-nm particle. (Dashed box: the trapping region, unit: pN)

In the force calculation, the light intensity is obtained from the FDTD simulation result in Figure 5.21. The particle is assumed to be 50 nm on the top of
the waveguide surface, the guided power in a waveguide-pair is 3 mW, and the particle velocity is 10 μm/s. Figure 5.22 and 5.23 show the x-component and y-component of the resultant force on 200-nm and 500-nm particles. The result shows that in the x-direction, the optical scattering force is dominant for the 500-nm particle, while the gradient force dominant for the 200-nm particle. The resultant force on a 500-nm particle is 0.2 pN, which is ~67 times larger than the 0.003 pN on the 200-nm particle. On the other hand, in the y-direction, the resultant force can be zero in the dashed-box, i.e. the particle is trapped in the y-direction. The trapping region (dashed-box) of the 500-nm particle is larger than that of the 200-nm particle as shown in Figures 5.22(b) and 5.23(b). When a particle flows outside the trapping region (position 1) as shown in Figure 5.24, it moves with the flow streams in the y-direction, and is only deflected slightly in the x-direction. However, when the particle flows into the trapping region (position 2), it is trapped in the y-direction, then deflected significantly along the waveguide, and eventually leaves the optical field at the edge of the trapping region.

The width of the trapping region \( D \) determines the lateral displacement of a particle in the photonic pillar. The left and right boundary are the positions where the particle is just larger or smaller than ten times the thermal energy \[80\]. Figure 5.25 shows the width of the trapping region \( D \) as a function of the particle diameter. It indicates that the particle diameter should be larger than a critical diameter to have the significant lateral displacements. The critical diameters are 193 μm, 135 μm and 104 μm when the guided power (the optical power guided in the waveguide-pair array) is 1 mW, 2.5 mW and 5 mW, respectively. Meanwhile, Figure 5.25 also suggests that the curve tends to saturate when the particle diameter is far away from the critical diameter.
To separate two particles of different sizes, the width difference of the trapping regions should be larger than the mean squared displacement (MSD) caused by Brownian motion. The MSD of a particle is expressed as:

\[
MSD = 2Dt = \frac{k_BTt}{3\pi\eta r}
\]  

(5.8)
where $D$ is the diffusion coefficient of particle, $t$ is the exposure time of a CCD frame, $k_B$ is the Boltzmann constant, $T$ is the absolute temperature, $\eta$ is the liquid viscosity, and $r$ is the particle radius. When the exposure time is 0.1 s, the MSD for 300-nm, 400-nm, and 500-nm particles are calculated to be 0.54 \( \mu m \), 0.47 \( \mu m \) and 0.42 \( \mu m \), respectively. Based on Figure 5.25, the MSD is corresponding to a size difference, which is defined as the sorting resolution. The calculated sorting resolution under different guided powers is summarized in Table 5.6. The results suggest that to obtain a high sorting resolution, the guided power and flow velocity need to be optimized to make the particle size near to the critical diameter.

<table>
<thead>
<tr>
<th>Power</th>
<th>Size</th>
<th>300 nm</th>
<th>400 nm</th>
<th>500 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 mW</td>
<td>-</td>
<td>5.6 nm</td>
<td>8.2 nm</td>
<td></td>
</tr>
<tr>
<td>2.5 mW</td>
<td>7.7 nm</td>
<td>23.5 nm</td>
<td>34.3 nm</td>
<td></td>
</tr>
<tr>
<td>5.0 mW</td>
<td>19.6 nm</td>
<td>41.1 nm</td>
<td>52.4 nm</td>
<td></td>
</tr>
</tbody>
</table>

### 5.3.2 Trajectory analysis of 200-nm and 500-nm particles

The trajectories of 200-nm and 500-nm polystyrene particles are studied experimentally. The particles are hydrodynamically focused near to the left sidewall. The laser power coupled into the chip is ~100 mW and the guided power in each waveguide-pair is ~3 mW. Figure 5.26 shows that the particles are separated after flowing through the optical field: the lateral displacement of the 200-nm particle is -1.415 \( \mu m \), while that of the 500-nm particle is 79.18 \( \mu m \). The particle displacement in the $y$-direction as a function of time is plotted in Figure 5.27. It clearly shows that the 200-nm particle (green line) has nearly constant velocity before and after entering
the optical field, i.e. the optical force has negligible influence on the 200-nm particle. In comparison, the 500-nm particle (orange line) slows down considerably at $t = 2.5$ s after entering the optical field. The particle is trapped and moves discontinuously in the $y$-direction. The 200-nm particle moves slightly slower than the 500-nm particle before entering the optical field because it is nearer to the sidewall.

Figure 5.26: Trajectories of 200-nm and 500-nm particles.

Figure 5.28 shows the particle displacement in the $x$-direction as a function of time. It shows that the motion of the 200-nm particle is dominated by Brownian fluctuation in the $x$-direction. The optical force is too small to deflect the 200-nm particle. Whereas the 500-nm particle moves gradually in the $x$-direction. The overall velocity is $2.45 \, \mu m/s$, and the peak velocity, which occurs in the trapping regions, is $4.61 \, \mu m/s$. 

Waveguide-pair Array
5.3.3 Separation of 500-nm particle

The PPA-based optofluidic manipulation system is used to sort nanoparticles massively. Here 500-nm polystyrene particles are separated out from 200-nm and 300-nm particles. The particle concentration is $\sim 1 \times 10^6$ particle/$\mu$L. The flow velocity is $\sim 20 \mu$m/s. Particles are hydrodynamically focused to the left sidewall and the
guided power in each waveguide-pair is ~3 mW. Figure 5.29 shows the superposition image of a single 200-nm (green), 300-nm (blue) or 500-nm (orange) particle when flowing through the waveguide-pair array. It shows clearly that different-sized particles have distinct lateral displacements: the lateral displacement of 200-nm particle is -1.3 μm, while that of the 300-nm and 500-nm particles are 41.6 μm and 96.7 μm, respectively. For 200-nm particle, the optical scattering force is negligible and the fluidic drag force and Brownian motion are dominant. For 300-nm and 500-nm particles, the scattering force and fluidic drag force co-affect the particle trajectories. The detailed force analyses are investigated in Paragraph 5.3.1.

Figure 5.29: Superposition image of the 200-nm, 300-nm and 500-nm particles when flowing through the waveguide-pair array. (Scale bar: 20 μm)
The particle distribution of massive particles before and after the optical field is analyzed statistically. Figure 5.30(a) shows the probability density at different lateral positions before entering the optical field. It indicates that 92.85% of 200-nm, 100% of 300-nm and 500-nm particles locate at the left side of the microchannel (0 - 40 μm). The result shows that a small number of 200-nm particles comes into the right side of the microchannel. They are the particles adhered to the sidewall when...
tuning the hydrodynamical focusing, and randomly released under the co-action of Brownian motion and fluidic drag force during the experiment. The particle distribution follows a Gaussian profile with the center position of 2.15 \( \mu m \), 8.52 \( \mu m \), and 2.24 \( \mu m \) for 200-nm, 300-nm, and 500-nm, respectively. When the particles flow through the optical field, the particle distribution changes dramatically as shown in Figure 30(b): 100% of the 200-nm and 300-nm particles stay in the left half side of the microchannel (0 - 40 \( \mu m \)), while 94.76% of the 500-nm particles move to the right side (81 - 100 \( \mu m \)). The particle distribution still follows a Gaussian profile, but the center position changes to 1.33 \( \mu m \), 29.31 \( \mu m \), and 96.6 \( \mu m \). The result demonstrates that 500-nm particles are separated out from the particle mixture with high accuracy. The applicable size in the sorting system ranges between 200 nm and 1000 nm in the current design. The minimum size is the smallest particle size that the optical force could influence its motion. In the current configuration, the minimum size is 200 nm. The maximum size is determined by the penetration length of the evanescent field. The particle size should match the evanescent field to have efficient light-matter interaction. The maximum size is 1000 nm, by considering the penetration length of \(~400 \) nm in the system and referring to the experimental results.
5.4 Bacteria trapping and alignment

5.4.1 Force analysis of bacteria trapping and alignment

The PPA-based optofluidic manipulation system can be used to trap and align rod-shaped bacteria in parallel. Figure 5.31(a) illustrates the trapping and alignment of multiple bacteria in the system. When a bacterium flows into the optical field, it will be trapped on the surface of waveguide-pair arrays, aligned to the waveguide-length direction (x-direction), and pushed along the waveguide. The bacterial motion can be decomposed into the out-of-plane rotation, in-plane rotation, and translation motion. The out-of-plane rotation occurs when a bacterium flows through the optical field, one end of the bacterium is first trapped on the surface, and then the bacterium is rotated by the out-of-plane gradient force until fully in contact with the surface as shown in Figure 5.31(b). Similarly, the in-plane rotation occurs when the axial direction of a bacterium is non-coincident with the waveguide-length direction, the bacterium is rotated by the in-plane gradient force and aligned to the waveguide-length direction as shown in Figure 5.31(c). The translation motion occurs when a bacterium is partially or fully trapped on the surface, it is pushed by the optical scattering force along the waveguide as shown in Figure 5.31(d). The three types of motions may occur simultaneously. For example, when a bacterium flows into the optical field, it may rotate in the in-plane and out-of-plane directions, and in the meanwhile, moves along the waveguide.

Since the size of bacteria is comparable with the optical wavelength [235], the optical force on a bacterium cannot be calculated using Rayleigh model as in Paragraph 5.3.1. Here a commercial FDTD software (Lumerical FDTD) is used to calculate the optical force instead. The FDTD calculation is extremely resource-
intensive and time-consuming in dealing with large simulation region. Meanwhile, the optical force field is the array of the force in two sequential hotspots. Therefore, only the optical force in the first three hotspots is calculated to reduce the computational complexity.

![Diagram](image)

Figure 5.31: (a) Schematic illustration of bacteria trapping and alignment in the optofluidic system. The bacterial motion can be decomposed into: (b) out-of-plane rotation, (c) in-plane rotation, and (d) translation motion.

In the simulation, the bacterium is modeled as a cylinder with a dimension of 0.8 μm (diameter) × 2.0 μm (length). The cylinder is placed 50 nm above the surface and the axial direction is parallel to the waveguide length-direction. The refractive index of the bacteria is set to 1.422 [235]. The guided power in the waveguide-pair is set to 3 mW. The center position of the bacteria is swept in the x-y plane. Figure 5.32 shows the simulated x-component, y-component and z-component of the optical force distribution. The black dashed line denotes the direction of the energy flow. The force
Figure 5.32: Simulated (a) $x$-component, (b) $y$-component and (c) $z$-component of the optical force distribution for the bacteria. (Unit: pN)
distribution in the $x$-$y$ plane indicates the bacteria will follow the energy flow and move along the waveguide to the right direction. In the $z$-direction, the bacterium is subjected to an attractive force to the surface ranging from 0.15 - 1.0 pN.

Figure 5.33: Simulated torque as a function of the rotation angle in the (a) $x$-$y$ plane and (b) $x$-$z$ plane at different positions.
The torque on the bacteria is calculated as a function of the rotation angle as shown in Figure 5.33. The body center and the center of the base surface are assumed to be the rotation center for the torque calculation in the $x$-$y$ and $x$-$z$ plane, respectively. Figure 5.33(a) indicates that the bacteria is subjected to a clockwise torque at different positions along the waveguide. The maximum of the torque is 14.6 pN·nm locating near to the intensity maximum of the top hotspot. Meanwhile, the torque is approaching zero when the bacteria is aligned to the waveguide length-direction. Figure 5.33(b) shows that the bacterium is subjected to a torque making it fully contact with the waveguide surface. The torque is much larger than that in the $x$-$y$ plane due to the high intensity gradient of the evanescent wave.

5.4.2 Trapping and alignment of individual *Shigella*

The motion of a bacteria in the optical field is decomposed into the out-of-plane rotation, in-plane rotation, and translation motion. Here the motion of a single *Shigella* is studied experimentally. *Shigella* is selected because it is a rod-shaped bacterium with a relatively high refractive index (RI = 1.422), which makes it an ideal object for the demonstration. The laser power coupled into the device is $\sim$100 mW and the guided power in each waveguide-pair is $\sim$3 mW. The length and diameter of *Shigella* are reported to be $2.74 \pm 0.67\ \mu m$ and $0.77 \pm 0.10\ \mu m$, respectively [235]. The *Shigella* in the experiment is $3.1\ \mu m$ in length and $0.8\ \mu m$ in diameter. The flow velocity is set to $5\ \mu m/s$. Figure 5.34 shows the out-of-plane ($x$-$z$ plane) rotation of a single *Shigella*. The angle of the *Shigella* to the surface is calculated by measuring the projected length and the full length of the *Shigella*. The result indicates that the *Shigella* rotates from $40.3^\circ$ to fully contact with the surface in 2.3 seconds. Similarly,
Figure 5.35 shows the in-plane (x-y plane) rotation of the *Shigella*. The *Shigella* rotates from 56.8° to 2.6° in 5.7 seconds. The time consumed in the x-y plane is longer than that in the x-z plane. It is because the optical torque in the x-z plane is much larger than that in the x-y plane as detailed previously. Figure 5.36 shows the translation motion of the *Shigella*. The result indicates that the *Shigella* moves 22.8 μm along the waveguide in 9.1 seconds, and the average lateral speed is 2.51 μm/s. The *Shigella* will continue to move until it is stopped by the right sidewall or another *Shigella*. For the other *Shigella* in the optical field, they will undergo the similar motions, and eventually be trapped and aligned on the surface.

![Figure 5.34: Out-of-plane (x-z plane) rotation of a single *Shigella*.](image-url)
5.4.3 Parallel trapping and alignment of *Shigella*

Figure 5.35: In-plane \((x-y)\) plane rotation of a single *Shigella*.

Figure 5.36: Translation motion of a single *Shigella*.
The optofluidic system can be used to trap and align multiple rod-shaped bacteria in parallel. The parallel trapping and alignment of *Shigella* are used as a demonstration. The *Shigella* concentration is $\sim 1 \times 10^3$ CFU/$\mu$L. The flow velocity

Figure 5.37: Images of (a) parallel trapping and alignment of *Shigella*, and (b) release the trapped *Shigella*. 

(a)

(b)
changes from 3 μm/s to 20 μm/s, and the guided power in each waveguide-pair changes from 0 mW to 5 mW. Figure 5.37(a) shows around 120 Shigella is trapped and aligned on the surface when the laser source is switched on for 10 minutes. Here the flow velocity is 5 μm/s and the guided power is 3mW. It shows that Shigella is trapped and aligned one after another starting from the right sidewall. Meanwhile, there are more trapped Shigella in the lower waveguide-pairs than the upper ones. The trapped Shigella exhibits varied length and width, which indicates the different growth phase of individual Shigella. When the laser source is switched off, the trapped Shigella is released and flushed away by the buffer liquids as shown in Figure 5.37(b). It shows the Shigella shows random orientations immediately after the release. Figure 5.38 shows the number of trapped Shigella in 5 minutes as a function of flow velocity and guided power. The result clearly shows that the number of trapped Shigella increases with the guided power and decreases with the flow.

Figure 5.38: Number of trapped Shigella as a function of flow velocity and guided power.
velocity. The trapping speed can reach 8.4 bacteria/min when the flow velocity is 3 μm/s and the guided power is 5 mW.
5.5 Summary

This chapter presents the design, fabrication and experimental preparation of an optofluidic system, and demonstrates its application in nanoparticle separation and bacteria manipulation. The design considerations and parameters of the optofluidic system are discussed in detail. The process flow is presented to fabricate the silicon-glass hybrid chip. The buffer solution and surface treatment are optimized to minimize the particle adhesion problem. Subsequently, the optofluidic system is used to separate nanoparticles based on their different trajectories. The width of the trapping region, the critical parameter related to the particle trajectory, is studied as a function of particle diameter and guided power based on a simulation model. In the nanoparticle separation experiment, the distinct trajectory of individual 200-nm and 500-nm particles are compared first, and then 500-nm polystyrene particles are separated out from particle mixtures with a recovery rate of 94.76%. In the bacteria trapping and alignment, the principle and force analysis are studied based on FDTD simulation. The motions of a single *Shigella*, which includes the out-of-plane rotation, in-plane rotation, and translation motion, are investigated experimentally. Then parallel trapping and alignment of *Shigella* are conducted with a trapping speed up to 8.4 bacteria/min. The optofluidic system can manipulate biomolecules with size ranging from a few hundred nanometers to several microns and is anticipated to benefit the biomedical applications such as exosome purification, DNA optical mapping, cell-cell interaction, etc.

The innovation of the developed optofluidic system is summarized as follow,

(a) The proposed near-field approach can sort nano-sized biomolecules benefiting from the large light-particle interaction region. The previous near-field approaches cannot sort nanoparticles efficiently, because the light-
particle interaction region is either limited to a single point (photonic crystal [41], surface Plasmon resonator [232], etc.), or limited to a single line (waveguide [42], ring resonators [161], etc.). This work generates a large optical field based on the evanescent coupling in waveguide-pair array, and demonstrates the separation of 500-nm particles with a recovery rate of 94.76%.

(b) The proposed near-field method inherently reduces the photo-damage to the sample molecules. The conventional near-field approaches focus on the optical field enhancement to have sufficient optical force effect in the small light-particle interaction region. However, the highly localized energy will generate considerable heat and may damage the sample molecules during the manipulation. This work distributes the optical energy and obtains an accumulated optical force effects in a large area. The guided power in each waveguide pair is only ~3 mW.

(c) This work provides a versatile platform for broad biological applications. The platform can not only trap and align rod-shaped bacteria on the surface for biophysical characterization, cell-cell interaction, etc., but also stretch DNA for on-chip optical mapping. Meanwhile, the platform is ready to be integrated with other microfluidic components or silicon photonic sensors to achieve more complex functionalities.
CHAPTER 6

CONCLUSIONS

6.1 Conclusions

Different applications of optofluidic waveguides have been investigated theoretically and experimentally, including a biochemical sensor to measure diffusion coefficient and monitor chemical reactions, an optofluidic lens with improved focusing power, and near-field manipulation platform for nanoparticle sorting and bacteria manipulation. Various aspects, including theoretical studies, system designs, fabrication technologies and experimental characterizations have been presented. The major conclusions drawn are listed here.

An optofluidic waveguide sensor to monitor chemical reaction and measure diffusion coefficient is developed based on the light focusing pattern in optofluidic waveguides. The index profile is studied theoretically. The influence of the contributing factors on the focal position is investigated theoretically and experimentally. A characterization experiment is designed to validate the use of the focal position as a sensing signal. In chemical reaction monitoring, the hydrolysis of sucrose is studied and the initial hydrolysis rate is determined. In diffusion coefficient measurement, simulation models are built up to quantify the focal length different as a function of the diffusion coefficient. The diffusion coefficient of ethylene glycol-DI water solution is measured experimentally.
(i) This is the first comprehensive study on the contributing factors to the light propagation pattern in optofluidic waveguides. The study provides a meaningful guidance on the experimental design of the subsequent chemical sensing studies. The limit-of-detection can be $0.15 \times 10^{-10} \text{ m}^2/\text{s}$ under the optimized conditions.

(ii) This is the first effort demonstrated to monitor chemical reactions through the diffusion coefficient change. The proposed optofluidic method overcomes the integration problem of the traditional spectroscopy method and can be easily integrated in Lab-on-a-Chip systems. The sensitivity of the method is $16.63 \ \mu\text{m}/\text{M}$ and the initial hydrolysis rate is $19.81 \ \mu\text{mol}/\text{min}$, which is in line with the literature results.

(iii) This study proposes an optofluidic method to measure diffusion coefficient with a single optical image. It is simple and rapid compared with the conventional point-to-point measurements using interferometers. The diffusion coefficient of ethylene glycol - DI water solution is determined to be $5.56 \pm 0.12 \text{ m}^2/\text{s}$, which is comparable with the literature results. The measurement result can be further improved by reducing the concentration change along the microchannel.

An optofluidic hyperbolic secant (HS) lens is developed to improve the focusing power. The optical aberrations which deteriorate the optical performance are investigated. The optimized index profile is derived based on coordinate transformation and a microfluidic gradient generator is designed to generate the index profile. The chip fabrication processes are developed for the fabrication of the optofluidic HS lens. Subsequently, simulations are conducted to verify the performance of the optofluidic HS lens. In the experiment, the performance of the
lens is evaluated, including the focal length and beam waist at different divergence angles and off-center positions. The focusing experiment with multiple light sources is also demonstrated.

(i) This is the first effect to improve the optical performance of microfluidic lenses by optimizing the index profile. The previous optofluidic lenses mainly focus on the demonstration of tunable light focusing, but neglect the optical performance which is important in certain applications. This work investigates the influence of spherical and field curvature aberrations in the optical performance and derives the ideal index profile based on the coordinate transformation of Maxwell’s fisheye lens. The beam waist of the designed optofluidic HS lens is smaller than 10 μm, which is twice better than the prior art [22, 24].

(ii) This work shows an example of designing an optofluidic component from its solid counterpart. Previously, the optofluidic components are borrowed directly from the solid one, i.e. the geometry and index profile are preserved in the microfluidic realization. However, the geometry and index profile of many solid optical devices, especially those with fancy functionalities, are challenging to be realized in microfluidics. This work uses the coordinate transformation to make the configuration of the optical device easier for microfluidic realization. This design method is anticipated to inspire the emergence of more integrated optofluidic devices with complex functionalities.

(iii) The work demonstrates the focusing of multiple light sources and illustrates its novel application in multiplexed detections. The conventional method generally uses a micro-lens array, beam splitter or cylinder lens to focus
multiple light sources. Here thanks to the suppressed optical aberrations, this work can focus multiple light sources using a single optofluidic HS lens and in the meanwhile doesn’t compromise the focusing power.

An optofluidic system is developed for nanoparticle and bacteria manipulation. The design considerations and parameters of the optofluidic system are discussed in detail. The process flow is presented to fabricate the silicon-glass hybrid chip. The buffer solution and surface treatment are optimized to minimize the particle adhesion problem. In the nanoparticle separation experiment, the trajectory of individual 200-nm and 500-nm particiles are compared, followed by the separation of 500-nm polystyrene particles from particle mixtures. The statistical analysis of the particle distribution is also conducted. In the bacteria trapping and alignment, the principle and force analysis are studied based on FDTD simulation. The motions of a single *Shigella* are investigated experimentally. Then parallel trapping and alignment of *Shigella* are conducted and the trapping rate is analyzed.

(i) The proposed near-field approach can sort nano-sized biomolecules benefiting from the large light-particle interaction region. The previous near-field approaches cannot sort nanoparticles efficiently, because the light-particle interaction region is either limited to a single point (photonic crystal [41], surface Plasmon resonator [232], etc.), or limited to a single line (waveguide [42], ring resonators [161], etc.). This work generates a large optical field based on the evanescent coupling in waveguide-pair array, and demonstrates the separation of 500-nm particles with a recovery rate of 94.76%.

(ii) The proposed near-field method inherently reduces the photo-damage to the sample molecules. The conventional near-field approaches focus on the
optical field enhancement to have sufficient optical force effect in the small light-particle interaction region. However, the highly localized energy will generate considerable heat and may damage the sample molecules during the manipulation. This work distributes the optical energy and obtains an accumulated optical force effects in a large area. The guided power in each waveguide pair is only \( \sim 3 \) mW.

(iii) This work provides a versatile platform for broad biological applications. The platform can not only trap and align rod-shaped bacteria on the surface for biophysical characterization, cell-cell interaction, etc., but also stretch DNA for on-chip optical mapping. Meanwhile, the platform is ready to be integrated with other microfluidic components or silicon photonic sensors to achieve more complex functionalities.

Optofluidic technology exploits the light and fluids interaction to create versatile systems. Optofluidic waveguide, as an important optofluidic component, has unexplored potential in biochemical detection, integrated optical component and particle manipulation. This thesis thoroughly studies the Lab-on-a-chip application of optofluidic waveguides from the fundamental theory to experimental demonstrations, aiming to innovate and gain a new insight into the optofluidic technology.

To further improve the development of optofluidic components, several future works with relevant recommendations are described in the following section.
6.2 Recommendations

Recommendations for future research are summarized as follows:

(a) In the optofluidic waveguide-based chemical reaction monitoring, the reaction occurs in off-chip tubes and then the reaction product is applied to the optofluidic chip manually for detection. Real-time reaction monitoring can be realized by integrating more sophisticated components such as microreactor, temperature controller, valves for reaction time control, etc.

(b) In the optofluidic waveguide-based diffusion coefficient measurement, the measured diffusion coefficient is the average value of the solution across the microchannel. As a result, the measured result is a bit larger than the actual values. To increase the measurement accuracy, the concentration change within the focal length should be reduced. Two possible approaches can be done. First, the overall flow rates can be increased to reduce the diffusion time. Second, the flow rate ratio of the cladding and core flow streams can be set to 2:1 or 3:1, rather than 1:1 in the experiment. Because a higher flow rate ratio generally results in a shorter focal length, and the diffusion time within is reduced accordingly.

(c) In the development of the optofluidic HS lens, the index profile is optimized by tuning the core and cladding flow rates. However, such a tuning method cannot precisely control the index profile to fully match with the aberration-free profile. Other index tuning methods such as thermal gradient or hydrogel can be considered to further improve the optical performance.

(d) The liquid medium used in the optofluidic HS lens are ethylene glycol (RI: 1.432) and water (RI: 1.332). Since a higher index contrast is favored to improve the optical performance, it can be increased in two ways. First,
ethylene glycol can be replaced with higher index liquids, such as benzothiazole (RI: 1.64) or cinnamaldehyde (RI: 1.62). Second, the solution with colloidal nanoparticle can be used due to its high effective index.

(e) In the development of the near-field manipulation platform, the syringe pump is used due to its accessibility in our laboratory. However, the use of syringe pumps necessitates the branch channel design to reduce the flow rate in the manipulation channel. The configuration not only wastes majority of sample solutions, but also makes the hydrodynamic focusing extremely sensitive to flow fluctuations. The use of pressure pumps can avoid the branch channel and perfectly solve the issues.

(f) The near-field manipulation platform has demonstrated the efficient separation of 500-nm particles from particle mixtures. The separation of biomolecules such as microvesicles, DNA, etc. can be tested in system.

(g) The laser wavelength in the near-field manipulation platform is 1550 nm. Water has high light absorption at the wavelength, which could raise the photodamage concern in practical biological application. The platform can be scaled for a laser wavelength of 830 nm, which has a minimum photodamage to biomolecules.

(h) The evanescent wave in silicon waveguide arrays is utilized in the manipulation platform. To further enhance the optical force, plasmonic waveguide arrays can be considered [236].
AUTHOR’S PUBLICATIONS

Journal Papers

Conference Papers (Selected)


[107] H. Y. Huang, K. Wei, Y. Zhao, Adaptive optofluidic lens(es) for switchable 2D and 3D imaging, Microfluidics, Biomems, and Medical Microsystems XIV, 9705(2016).


[160] R. Siriroj, W. Techidheera, P. Phatharacom, S. Chiangga, P. Yupapin, Micropropulsion generation model and simulation by wgm acceleration within
a panda ring resonator system, Microwave and Optical Technology Letters, 59(2017) 377-80.


