DESIGN AND DEVELOPMENT OF GROOVE MICROMIXER FOR LAMINAR BLOOD-REAGENT MIXING

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ABSTRACT

Mixing of two fluids is an essential process for most of microfluidic device for Biomedical Micro-Electro-Mechanical System (Bio-MEMS) application. Mixing also important in Lab-On-Chip (LOC) system because the chemical reaction carried out in this system requires on-chip mixing. Mixing performance in this system relies mainly on effective and rapid mixing of sample and reagent. Therefore, development of groove micromixer for application of blood and reagent mixing carried out in this project. In this study, two fluids involve in the mixing, which is the blood and reagent (two type of reagent with lower and higher viscosity compared to blood). Two pattern of the groove namely oblique groove and herringbone groove were designed and simulated using CoventorWare2010 software at low Reynolds number. The design of groove micromixer obtained by analyzing the geometries effect of groove pattern on mixing performance of blood and reagent with the visualization of simulation and evaluation of mixing performance for difference geometry parameter of groove micromixer. In this study, it has been demonstrated that the Y-Shape mixer with the groove structure located at the floor of the mixing channel increased the mixing performance. Thus, the simulation result in this study shows that mixing performance can be enhanced when depth and width of groove is 40% of the channel width with the angle of an oblique groove is 45º. Whereas for the herringbone mixer, enhancement of mixing performance occured when the depth and width of herringbone groove is 25% of the channel width with the approximation of asymmetric index is quarter of the width of mixing channel.

ABSTRAK

Pencampuran dua cecair adalah satu proses yang penting bagi kebanyakan peranti bendalir mikro untuk aplikasi Bio-MEMS. Pencampuran juga penting dalam sistem LOC kerana tindak balas kimia yang berlaku dalam sistem ini memerlukan pencampuran pada komponen cip. Prestasi pencampuran dalam sistem ini bergantung terutamanya pada keefektifan dan kecepatan pencampuran sampel dan reagen. Oleh itu, reka bentuk alur pencampur mikro bagi aplikasi darah dan reagen telah dijalankan dalam projek ini. Dalam kajian ini, dua cecair terlibat dalam proses percampuran iaitu darah dan reagen (dua jenis kelikatan iaitu yang lebih rendah dan lebih tinggi berbanding dengan darah). Dua corak alur iaitu serong dan alur tulang hering telah direka dan disimulasi menggunakan perisian CoventorWare2010 pada nombor Reynolds yang rendah. Reka bentuk alur pencampur dicipta dengan menganalisis kesan geometri corak alur dan prestasi pencampuran darah dan reagen dengan visualisasi simulasi dan penilaian prestasi pencampuran untuk geometri parameter yang berbeza. Dalam kajian ini, simulasi pencampuran di antara darah dan reagen telah berjaya menunjukkan bahawa bentuk Y pencampur dengan struktur alur terletak di bahagian saluran pencampuran dapat meningkatkan prestasi pencampuran. Oleh itu, hasil simulasi dalam kajian ini menunjukkan bahawa prestasi pencampuran boleh dipertingkatkan apabila kedalaman dan lebar alur adalah 40% daripada lebar saluran pencampur dengan sudut alur serong ialah 45 º. Manakala untuk pencampur tulang hering, peningkatan prestasi pencampuran berlaku apabila kedalaman dan lebar alur adalah 25% daripada lebar saluran pencampur dengan indeks simetri adalah menghampiri suku daripada lebar saluran pencampuran.

TABLE OF CONTENTS

CHAPTER	CONTENTS	PAGE
	TITLE	**i**
	ACKNOWLEDGEMENT	**iii**
	ABSTRACT	**iv**
	TABLE OF CONTENTS	**vi**
	LIST OF FIGURE	**ix**
	LIST OF TABLE	**xii**
	LIST OF ABBREVIATION	**xiii**
	LIST OF SYMBOL	**xiv**
	LIST OF APPENDICES	**xv**
CHAPTER I	**INTRODUCTION**	
	1.1 Introduction	1
	1.2 Background	1
	1.2.1 Biomedical Micro-Electro-Mechanical System (Bio-MEMS)	2
	1.2.2 Overview on Microfluidic Device	3
	1.2.3 Micro-Total Analysis Systems (µTAS) and Lab-On-Chip (LOC)	4
	1.3 Objective of Study	5
	1.4 Problem Statement	6
	1.5 Scope of Study	7

1.6 Summary 7

CHAPTER II LITERATURE REVIEW

2.1 Introduction 8

2.2 Laminar Mixing for Blood and Reagent 8

2.2.1 Length Scale Object in Biology 9

2.2.2 Fluid Properties 10

2.2.3 Reynolds Number 12

2.2.4 Mass transport 14

2.2.5 Diffusion 15

2.3 Micromixer 16

2.4 Conclusion 23

CHAPTER III METHODOLOGY

3.1 Introduction 24

3.2 Methodology 25

3.2.1 Flow Chart 25

3.2.2 Geometric Parameter 29

3.3 The Y-Shape Micromixer 31

3.3.1 Difference of Width Mixing Channel 31

3.3.2 Length of Mixing Channel 32

3.4 The Y-Shape with Oblique Groove Mixer 32

3.4.1 Difference Aspect Ratio for Oblique Groove 33

3.4.2 Difference Depth for Oblique Groove 34

3.4.3 Difference Width for Oblique Groove 35

3.4.4 Difference of Angle for Oblique Groove 35

3.5 The Y-Shape with Herringbone Groove Mixer 37

3.5.1 Difference Width for Herringbone Groove 38

3.5.2 Difference Asymmetry Index for Herringbone Groove 39

3.6 Difference of Reagent Viscosity 40

3.7 Conclusion 42

CHAPTER IV RESULT AND DISCUSSION

4.1 Introduction 43

4.1.1 Evaluation Criterion of Mixing Performance 43

4.2 The Y-Shape Micromixer 45

4.2.1 Effect of Mixing Channel Width 45

4.2.2 Length of Mixing Channel 46

4.3 The Y-Shape Oblique Groove Mixer 49

4.3.1 Effect of Groove Aspect Ratio 49

4.3.2 Effect of Oblique Groove Depth 51

4.3.3 Effect of Oblique Groove Width 53

4.3.4 Effect of Oblique Groove Angle 54

4.4 Y-Shape Herringbone Groove Mixer 56

4.4.1 Effect of Herringbone Groove Depth 56

4.4.2 Effect of Asymmetry Index of Herringbone Groove 57

4.5 Effect of Reagent Viscosity 59

4.6 Conclusion 62

CHAPTER V CONCLUSION AND RECOMMENDATION

5.1 Conclusion 63

5.2 Recommendation 64

REFERENCES **66**

APPENDICES **71**

LIST OF FIGURE

FIGURE **PAGE**

2.1 A block model of solid material and a fluid contained between two plates. 10

2.2 Pressure driven flow in a parallel plate channel. 13

2.3 The schematic diagram of oblique ridges mixer. 19

2.4 The schematic diagram for SHM. 20

2.5 The schematic diagram of connected groove mixer. 23

3.1 Flow chart for modelling and simulation of blood reagent mixing. 26

3.2 Parameter geometry for (a) Y-Shape oblique groove and (b) Y-Shape herringbone groove. 30

3.3 The 3D model of oblique groove for different aspect ratio compare to channel height (a) aspect ratio is 0.125, (b) aspect ratio is 0.25, (c) aspect ratio is 0.375, and (d) aspect ratio is 0.5. 33

3.4 Parameter related to the geometry of the oblique groove depth and width. 34

3.5 Schematic diagram of Y-Shape oblique groove with different inlet angl, (a) $\theta_{inlet} = 26°$, (b) $\theta_{inlet} = 45°$, and (c) $\theta_{inlet} = 56°$. 36

3.6 Schematic diagram of Y-Shape oblique groove with different groove angle, (a) $\theta_g = 26°$, (b) $\theta_g = 45°$, and (c) $\theta_g = 56°$. 36

3.7 The Y-Shape mixer with the herringbone groove, (a) The 3D model of symmetry herringbone structure in mixing channel, (b) 2D layout of symmetry index of herringbone pattern. 38

3.8 The 2D layout for different asymmetry index of herringbone structure, (a) 5μm distance at x-axis and (b) 10μm distance at x-axis. 40

4.1 Cross section mixing visualization of Y-Shape micromixer for blood and toluene. 44

4.2 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for Y-Shape micromixer with different width of mixing channel. 46

4.3 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for Y-Shape micromixer without groove and Y-Shape micromixer with groove. 47

4.4 Model contour for Y-Shape micromixer (a) without groove, and (b) with groove. 48

4.5 Model contour and slice image for (a) 5μm groove width, (b) 10μm groove width, (c) 15μm groove width, and (d) 20μm groove width. 50

4.6 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for Y-Shape mixer with different size of oblique groove. 51

4.7 Image cross section along x plane located at the bottom and middle of groove structure for (a) 5μm groove depth, (b) 10μm groove depth, and (c) 15μm groove depth. 52

4.8 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for Y-Shape oblique groove with different depth of groove. 52

4.9 Image cross section along x plane located at the bottom and middle of groove structure for (a) 10μm groove width, (b) 15μm groove width, and (c) 20μm groove width. 53

4.10 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for Y-Shape oblique groove mixer for different groove width. 54

4.11 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for oblique groove with 45°

angle mixer with different groove angle. 55

4.12 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for Y-Shape oblique groove mixer with different inlet angle. 56

4.13 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for Y-Shape herringbone groove mixer with different depth. 57

4.14 Graph of standard deviation of viscosity distribution for mixing of blood and toluene for Y-Shape herringbone groove mixer for difference asymmetry index. 58

4.15 Graph of standard deviation of viscosity distribution for laminar mixing of blood with low viscosity of reagent (toluene). 60

4.16 Graph of standard deviation of viscosity distribution for laminar mixing of blood with low viscosity of reagent (benzyl). 60

4.17 The 3D translucency contour model for (a) Y-Shape without groove mixer, (b) Y-Shape with oblique groove and (c) Y-Shape with herringbone groove. 61

LIST OF TABLE

TABLE		PAGE
2.1	Length scale of typical objects in biology.	10
3.1	Geometries parameters for different width of mixing channel.	32
3.2	Geometries parameters for micromixer without groove and with groove.	32
3.3	Geometries parameter for different aspect ratio of oblique groove.	33
3.4	Geometries parameter for the different depth of oblique groove.	34
3.5	Specification dimension for various width of oblique groove.	35
3.6	Geometries parameter for different oblique angle when $\theta_{inlet1, 2} = 26^{o}$.	37
3.7	Geometries parameter for different oblique angle when $\theta_{inlet1, 2} = 45^{o}$.	37
3.8	Geometries parameter for different oblique angle when $\theta_{inlet1, 2} = 56^{o}$.	37
3.9	Geometries parameter for different depth of herringbone groove.	38
3.10	Geometries parameter for different asymmetrical index of herringbone groove.	39
3.11	The boundary condition of the blood and reagent.	41
3.12	Geometries parameter for three design of Y-Shape micromixer.	42

LIST OF ABBREVIATION

Bio-MEMS	-	Biomedical Micro-Electro-Mechanical System
CFD	-	Computational Fluid Dynamics
FVM	-	Finite Volume Method
LOC	-	Lab-On-Chip
MEMS	-	Micro-Electro-Mechanical System
μTAS	-	Micro-Total Analysis Systems
SHM	-	Staggered Herringbone Mixer
SGM	-	Slanted Groove Mixer

LIST OF SYMBOL

A	-	Cross sectional area
D_{hyd}	-	Hydraulic diameter
D	-	Diffusion coefficient
D_g	-	Depth of groove
D_h	-	Depth of herringbone
H	-	Height of channel
H_{inlet}	-	Height of inlet
L	-	Length of channel
L_{inlet}	-	Length of inlet
μ	-	Dynamic viscosity
p	-	Asymmetry index
P_{wett}	-	Wetted perimeter
ρ	-	Density of fluids
Q	-	Volume flow rate
Re	-	Reynolds number
t	-	Time
θ_g	-	Angle of oblique groove
θ_h	-	Angle of herringbone groove
θ_{inlet}	-	Angle of inlet
u	-	Velocity of fluids
v	-	Kinematic viscosity
W	-	Width of channel
W_g	-	Width of groove
W_h	-	Width of herringbone
W_{inlet}	-	Width of inlet
x	-	Distance of particle

LIST OF APPENDICES

APPENDIX	PAGE
Paper submitted for review for 6th Biomedical Engineering International Conference (BMEiCON2013).	72

CHAPTER I

INTRODUCTION

1.1 Introduction

This chapter consists of two sections. The first section describes the background of Biomedical Micro-Electro-Mechanical System (Bio-MEMS) field and it contribution to biological application. Overview on microfluidic device and development of Micro-Total-Analysis System (μTAS) and Lab-on-Chip (LOC) device for Bio-MEMS application also given in this chapter. The second part of this chapter provides an introduction of this project given by the objectives of this study together with the scope and problem statement of this project.

1.2 Background

Bio-MEMS have emerged as a subset of Micro-Electro-Mechanical System (MEMS) device for application in biomedical research and medical microdevices. These systems encompass all interfaces of the life sciences and biomedical disciplines with micro and nano scale systems. Bio-MEMS represent an exciting and growing field with opportunities of improving the human condition and reducing the cost of health care delivery.

1.2.1 Biomedical Micro-Electro-Mechanical System (Bio-MEMS)

Bio-MEMS can be defined as ‘‘a devices or systems constructed using techniques inspired from micro or nano-scale fabrication, that are used for processing, delivery, manipulation, analysis, or construction of biological and chemical entities’’ (Bashir, 2004). Bio-MEMS device structure are typically considered that having at least one feature's dimension in the submicron to micron range from 100nm up to 200μm and other dimension of up to several milimeter (Saliterman, 2005).

The integration of Bio-MEMS technology with microscale sensors, actuators, microfluidics, micro-optics, and structural elements with computation, communications, and controls for medicine application could contribute to the improvement of human health (Polla, 2001). For example, microactuators are useful in biomedical applications when biological objects or their environment needed to controlled on the microscopic scale. Therefore, the ability to integrate many microactuators in single chip makes it feasible to produce complex microsystem capable of controlling many parameters (Judy, 2000).

Biological application is one of the most promising and challenging application fields for MEMS and microsystem technology. The review of MEMS technology in physiological aspect by Grayson, *et al.* (2004) emphasize that MEMS have many characteristics that make it interesting for biological applications. For example, the ability of MEMS device to control physical and chemical characteristics for biological material on the micrometer and nanometer scale. They also drawn attention to the fact that MEMS for biological applications is growing rapidly with opportunity in certain areas such as biosensors, pacemakers, immunoisolation capsules, and drug delivery. In addition, the significant of these applications are due to the unique features of MEMS for it maximum impact (Grayson *et al*., 2004).

The biological applications of MEMS and microfluidics are closely related because the majority of devices for biological and medical analysis work with samples in liquid form (Maluf, 2002). Moreover, microfluidic has emerged as a new approach for improving performance and functionality of biochemistry and medical analysis through miniaturization and integration system into single chip (Saliterman, 2005). The several advantage of miniaturized biochips are lower manufacturing costs, reproducibility, small sample size and reagent used, improved signal-to-noise ratio, improved response time, precise control of mixing, reacting and discarding of waste products, in line embedded detection methods, and high throughput.

1.2.2 Overview on Microfluidic Device

Microfluidic is the outgrowth of fluidic and commonly related with the technical field of working with fluids, mainly controlling their flows in a system of channels. Microfluidics characterized by the small size of the channels and emerged together with general area of MEMS, which become possible by applying the microfabrication technique originally developed by microelectronic. Microfluidic can be defined as a technology of handling small fluid flows in small device and microfluidic device can be simply characterized by dominant (smallest) channel width smaller than 1mm. Common present-day microfluidic device commonly use channel widths in the region from 0.1 to 1mm (Tesar, 2007).

Microfluidic system consists of device usually connected by interconnection channel and designed with objective to fulfil a particular task. The common passive fluidic device consist of two terminal, passive flow through fluidic device with the upstream input inlet and the output outlet terminal as a downstream exit (Tesar, 2007). For example, mixer used as separate device upstream from premixed-reaction reactor and usually needed in microchemistry field. As well, many biological processes such as antibody-antigen binding that required rapid and effective mixing.

Microfluidic device consist of channel and feature with precision approximately 1µm that enable the manipulation of small volume of fluid. Such controls bring several advantages. The advantage of small-scale device may be different for particular application, but smaller device generally cheaper, need only tiny amount of material. The several advantages of small scale device for microchemistry application are better control of process due to high surface volume ratio, less sample needed for analysis, more analysis simultaneously, portability, safely handled of dangerous substance and approaching cellular size (Tesar, 2007).

1.2.3 Micro-Total Analysis Systems (µTAS) and Lab-On-Chip (LOC)

The development of the µTAS and LOC device actually from the application of "hard" and "soft" fabrication technique for manufacturing the miniaturized devices that will perform all or part of a biochemical analysis. The µTAS can be describe as hybrid of multiple chips, integrated electronic, and external support whereas LOC refer more specifically to a microfluidic chip or device that perform a well-defined analytical task (Guber *et al*., 2004). The LOC device can be define as an integrated and scale down laboratory function and processes to miniaturized single-chip format task. The µTAS or LOC device is usually used to describe sensors and devices with some level of integration of different functions and functionality (Bhansali & Vaudev, 2012). These devices offer the several advantages such as integrating sample handling, preparation, mixing, separation, lysing of cells, and detection (Saliterman, 2005).

Microfluidics and sensing capabilities is a common feature that could make LOC device closely related to Bio-MEMS and µTAS. Microfluidic device are the primary component of most µTA and LOC device. Microfluidic can simply describe as a study of transport in microchannel. Microfluidic device such as LOC device may consist of channels, valves, mixers, pumps, filters, and heat exchanges. These component can perform the operation such as metering, dilution, flow switching, particle separation, mixing, pumping, incubation of reaction material and reagent, sample dispensing or injection, and also may incorporate various detect schemes (Saliterman, 2005).

The LOC device have been develop and used in wide range of biomedical and other analytical application. This micro device can be categorized into two main categories based on their final application which is hand-held LOC system and table-top LOC system (Bhansali & Vaudev, 2012). The hand-held LOC system are generally used to screen small sample for point-of-care testing while the table-top LOC system are typically used to analysed many sample for high-throughput application with interfaced with external detection system and pressure source. Many area of biological interest desired microfabrication system for rapid, high throughput and other requirement to achieve the specific goal. In most Bio-MEMs field, it is commonly required to prepared, deliver, or manipulate microscopic amount of bio-samples or reagent in microchannel. In µTAS and LOC device, the manipulation of the fluid and it sample may be including biological material. The primary of liquid transport in this microsystem may including whole blood, serum (containing protein, and other chemistries), bacteria suspension, and various reagent and buffer (Tian & Finehout, 2008).

Mixing is significant important in LOC system and bio-analysis system because the reaction carried out on microscale required on-chip mixing of sample and reagent. In this microsystem, fluid needed to be mixed with another fluid to dilute a sample or to perform a controlled chemical reaction (W. Wang & Soper, 2007). Mixing in microfluidic system can be perform by incorporate a specific mixing mechanism known as micromixer. Therefore, most of LOC device need to include micromixer in the flow path.

1.3 Objective of Study

The objectives for this project are:

1. To design the groove micromixer for laminar blood-reagent mixing using CoventorWare2010 software.
2. To observe the different geometry parameter of groove micromixer by analyzing the geometric effect of groove pattern on mixing performance for blood and reagent.
3. To evaluate the blood mixing performance with different viscosity of reagent.

1.4 Problem Statement

Mixing in microfluidic device generally slow that make mixing in this microchannel is difficult to achieve. In macroscale, mixing can be more effective through turbulent transport, but in microscale, mixing driven by laminar flow. In the laminar flow, the only mixing mechanism is diffusion, which is very slow due to low Reynolds number. Since diffusion is relatively slow, specific mixing geometries are required so that can shorten the diffusion length and decrease the mixing time. Designing micromixer generally require fast mixing time, small device area, and ability to integrate in a more complex system. Rapid mixing in micromixer achieved by increasing the contact surface and decreasing the mixing path. All micromixers are design to increase the interfacial area where the diffusion of two dissimilar fluids can occur.

In the project, the design and development of groove micromixer are carried out based on the concept chaotic advection through modification of microchannel surface by groove pattern on microchannel floor where it can enhance laminar blood-reagent mixing performance at low Reynolds number. The objective of this project is to design and develop groove micromixer by observing the effect of geometric parameter and analyzing the mixing performance of laminar blood and reagent mixing. In this study, two fluids involve in the laminar mixing that the blood is the centers point of fluid material and reagent fluid with lower and higher viscosity compared to blood. The laminar mixing of the two fluids inside these micromixers are simulated at Reynolds number less than 1. In this project, two design of groove micromixer taken into consideration namely oblique groove mixer and herringbone groove mixer. The design parameter of each groove mixer are developed based on the evaluation of mixing performance in the numerical simulation result. Design and development of groove micromixer for laminar blood-reagent mixing are carried out by numerical simulation approach using CoventorWare2010 software.

1.5 Scope of Study

The scopes of this project are:

i. Design Y-Shape groove micromixer by using CoventorWare2010 software.
ii. Simulate mixer for laminar blood reagent mixing and observe the geometries effect for the development of groove micromixer.
iii. Design and development of groove micromixer up to 500µm length.

1.6 Summary

Mixing of two fluids is an essential process for most of microfluidic device such as Lab-On-Chip (LOC) device. Mixing performance in this microsystem relies mainly on effective and rapid mixing of sample and reagent. Therefore, the objective of this project is to design and develop groove micromixer for application of blood and reagent mixing. In this study, numerical simulation of the fluid flow and mixing are perform by using CoventorWare2010 software. The fundamental theory related to laminar mixing and design concept of micromixer will be discus in the next chapter.

CHAPTER II

LITERATURE REVIEW

2.1 Introduction

This chapter overview the basic and fundamental theory involved in this project. In this chapter, the fundamental theory related to laminar mixing for blood-reagent and the design concept for micromixer in previous study are review. The first section in this chapter discussed the properties of the fluid and characteristic of fluid flow such as Reynolds number, mass transport and diffusion concept. The second part of this chapter will discussed the basic concept design used for designing micromixer and overview of previous study that focused on the concept design for groove structure.

2.2 Laminar Mixing for Blood and Reagent

Fluid mechanics encompasses the study of all types of fluids under static, kinematic and dynamic conditions. The study of properties of fluids is basic for the understanding of flow or static condition of fluids. Generally, the manipulation of microscopic amount of bio-samples or reagent occurs in microchannel. For that reason, the overview of the fluid mechanics such as viscosity of fluid, principle of fluid flow, and Reynolds number give the information of the fundamental related to fluid and compartment of fluid flow in parallel microchannel. Fluid behaviour at the microscale is often different from those at macroscale. Thus, the principle of mass transport effect in microchannel mixing also be studied, which provide the knowledge of molecular diffusion concept to enhanced the mixing performance in micromixer design.

2.2.1 Length Scale Object in Biology

An integrated LOC device can incorporate many of the necessary components and functionality of a typical room-sized laboratory into a small chip that performs a specific biological or chemical analysis, including sample treatment, transport, reaction, and detection (Saliterman, 2005). The fundamental properties of fluid in micro or nano scale may differ significantly from those in larger devices. Therefore, fluid and sample transport is a crucial issue in these LOC devices because many biological and chemical processes and experiments take place in aqueous environments (Hu & Li, 2007).

In order to design LOC device or microfluidic device for biological application, length scales of the biological objects are necessary to considered. According to Merriam Webster Dictionary, size can define as ‘physical magnitude, extent, or bulk: relative or proportionate dimensions’. The typical length scales or size of some of the biological objects show in Table 2.1. From this table, it can be seen that the diameter of the blood cell approximate 8µm, and the diameter for average cell in human body around 10µm. Therefore, the minimum length scale for designinig micromixer should not less than the diameter of an average cell in human body.

Table 2.1: Length scale of typical objects in biology (Hu & Li, 2007).

Typical objects in biology	Length scale
Diameter of glucose molecule	1 nm
Diameter of DNA helix	2nm
Diameter of insulin molecule	5nm
Thickness of cell wall (gram negative bacteria)	10nm
Size of typical virus	75nm
Diameter of the smallest bacterium	200nm
Diameter of red blood cell	8.4µm
Diameter of average cell in human body	10µm
Diameter of the largest bacterium	750µm

2.2.2 Fluid Properties

Fluid can be defined as a substances that deform continuously under the application of shear (tangential) stress of any magnitude (Saliterman, 2005). Figure 2.1 illustrate a shear streass applied to the block of solid model and to the fluids film contained between two plates. The right side model in this figure show the shearing force applied to the solid object. The solid object was deforms but it will return to original shape as long as the elastic limit is not exceeded. In contrast, a liquid or fluid film in the left side model in this figure that located between two plate was deforms after applying shearing force and stays deform after the shearing force is removed.

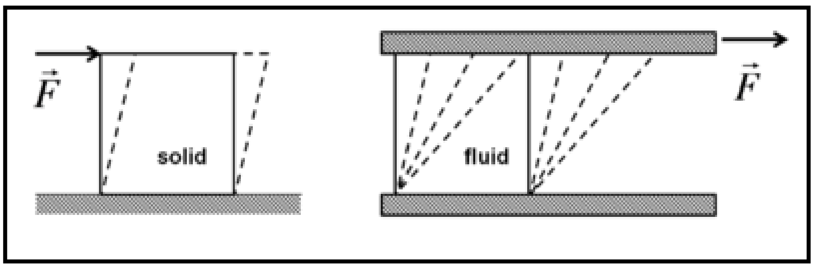

Figure 2.1: A block model of solid material and a fluid contained between two plates.

Fluid can be in form of gasses (i.e. air) or liquid (i.e. water). Liquid can be characterized based on three important parameter which is it density, pressure and viscosity. The density defined as the mass per unit volume. Pressure in the liquid only depends on the depth that makes pressure increase when going from the surface to the bottom and not affected by the shape of the vessel containing liquid. Microchannel is not a closed system due to the inlet and outlet opening, the pressure different induced externally at these opening is transmitted to the liquid and consequently inducing the liquid flow (Ong, Zhang, Du, & Fu, 2008).

If the density of a fluid varies significantly due to moderate changes in pressure or temperature, then the fluid is knows as compressible fluid. Generally, gases and vapours under normal conditions classified as compressible fluids. In these phases, the distance between atoms or molecules is large and cohesive forces are small. Therefore, increase in pressure or temperature will change the density by a significant value. If the change in density of a fluid is small due to changes in temperature and or pressure, then the fluid is knows as incompressible fluid. All liquids are classified under this category (Kothandaraman & Rudramoorthy, 2007).

The viscosity defined as an internal friction or resistance during setting fluid into motion. The kinematic viscosities of fluid are another important parameter that relates the dynamic viscosity to density that is defines as:

$$v = \frac{\mu}{\rho} \tag{2.1}$$

Where v is the kinematic viscosity, ρ is the density or mass per unit volume and μ is the dynamic viscosity.

Fluid classified as a Newtonian if the shear stress (shear force/area fluid contact) is directly proportional to the rate of strain. Most of the gasses and fluid are categorize in this category. However, if the fluid viscosity changes with the shear stress, these fluids can be termed as Non-Newtonian fluid (i.e. blood). The use of Non-Newtonian fluids as compared to Newtonian fluids is more promising for the development of microfluidics devices. In non-Newtonian fluids, either the viscosity grows (shear thickening) or decreases (shear thinning) with increasing shear rate. There can be turbulent-like instabilities in flows of such fluids at low Reynolds number. These "elastic turbulence" could be generated in microfluidic channels to act as efficient mixers (Ong *et al*., 2008).

2.2.3 Reynolds Number

Fluid flow generally categorized into two flow regimes: laminar and turbulent. Laminar flow characterized by smooth and constant fluid motion, whereas turbulent flow characterized by vortices and flow fluctuations. Physically, the two regimes differ in terms of the relative importance of viscous and inertial forces. The flow of fluid can be considered as laminar, transition or turbulent is dependent on the fluid density and viscosity, characteristic velocity, geometry of the channel and whether the flow past an object.

The flow pattern typically classified based on the dimensionless number know as Reynolds number. The flowing fluid maybe influenced by the properties of fluid and flow which kinematic properties (velocity, viscosity, acceleration, vorticity), transport properties (viscosity, thermal conductivity, diffusivity), thermodynamic properties (pressure, thermal conductivity, density) and other properties (surface tension, vapour pressure, surface accommodation coefficient) (Nguyen & Wereley, 2002). Reynolds number can be describing as a ratio of measurement between inertial force and viscous force in particular flow. This dimensionless values can defines as:

$$Re = \frac{Inertial\,force}{Viscous\,force} = \frac{\rho u D_{hyd}}{\mu} = \frac{u D_{hyd}}{v} \tag{2.2}$$

Where u is the mean velocity of the fluid flow, D_{hyd} is the hydraulic diameter, v is the kinematic viscosity, ρ is the density or mass per unit volume and μ is the dynamic viscosity. The different regime of behavior in Reynolds number can be Re << 1 (viscous effect dominate inertial effect), Re ≈ 1 (viscous effect comparable to inertial effects), and Re >> 1 (inertial effect dominate viscous effect).

Many microdevices have long straight passages with constant cross section as illustrated in Figure 2.2. Flow through these channels is important flow phenomenon at small length scales. The flows in this system are control by pressure gradient, the pipe diameter or hydraulic mean diameter, the fluid properties like viscosity and density and the pipe roughness. If the density of the flowing fluid is the same all over the flow field at all times, then such flow called incompressible flow. Flow of liquids considered as incompressible even if the density varies a little due to temperature difference between locations.

Streamline defined as a trace of any point in a moving fluid. Usually, the directions of streamline are parallel with the motion direction of the moving fluid. Generally, a streamline can change its position and its shape in a steady state flow. A stream tube made up by a bundle of streamline through all point of a closed curve.

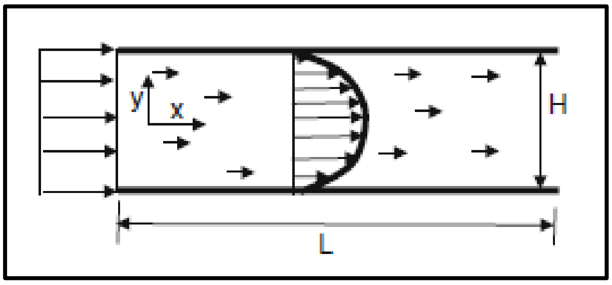

Figure 2.2: Pressure driven flow in a parallel plate channel (Chakraborty, 2010).

In addition, many of these long straight passages have cross sectional geometric that are different from circular pipe. The hydraulic diameter for different shape of cross-sectional for parallel flow can be defines as:

$$D_{hyd} = \frac{4\ x\ Cross\ sectional\ area}{Wetted\ perimeter} = \frac{4A}{P_{wett}} \tag{2.3}$$

Where A is the cross sectional area, and P_{wett} is the wetted perimeter. The concept of hydraulic diameter used to assess flows through both completely filled channel as well as those only partially filled. The term 'wetted perimeter' refers to the perimeter of the channel that is in direct contact with the flow while the 'area' refers to the area through which the flow is occurring. For the channel that are completely filled, the wetted perimeter is simply the perimeter of the channel and the area is the cross sectional area of the channel. The state parameter used to specify a state at a location in a fluidic flow could be either volume or mass flow rate. The volume flow rate of fluid flow defined as:

$$Q = A\ x\ v \tag{2.4}$$

Where Q is the volume flow rate, v is the fluid velocity and A is the cross section area. The relationship between flow rate and velocity as a state parameter are the main influence on the shape of the channel cross section.

2.2.4 Mass transport

Generally, in microfluidic systems the mass transport can be grouping into two type of transport based on the nature of the driving agent behind the transport which directed transport and statistical transport (Ong *et al.*, 2008). Directed transport controlled by exerting work on the fluid. These work results in a volume flow of the fluid, where the flow usually be characterized by a direction and flow profile. The work often generated mechanically by a pump or electrically by a voltage. Flow that driven mechanically are knows as pressure-driven flow and flow driven by a voltage called electro-osmotic flow. On the other hand, statistical transport typically deals with concentration of the molecule. A typical situation of the statistical transport is the transport of molecules from the side with high concentration to the side with zero concentration (i.e. by the presence of a concentration gradient).

Mass transport in microscale can also be categories based on transport effect mechanism such as diffusive transport, advective transport, taylor-aris dispersion or chaotic advection (Nguyen & Wereley, 2002). Diffusive transport are cause by the random motion of molecule and knows as Brownian motion. The mixing rate in these transports are determine by the flux of the diffusion. Moreover, the advection transport can caused the mass transport due to a mass flux while the distributed velocity profile across the microchannel due to a pressure-driven flow known as taylor-aris dispersion. Convection transport at the fluid layer with different velocities in the pressure-driven flow transportation mechanism causes as apparently higher axial dispersion produced pure molecular diffusion.

Advection known as a transport of a substance within a moving fluid and generally occur in the direction of the flow and it has no effect on the traversal transport of the substance. Chaotic advection can be describe as a stirring flow occur in other direction of advection whose generate the transverse component of the flow, thus cause an exponential growth of the interfacial area and decrease in the striation thickness can improve the mixing performance. The stirring flow can be generated by the channel shape that stretch, fold, break and split the laminar flow over the cross-section of the channel (Capretto, Cheng, Hill, & Zhang, 2011). These transverse flows caused by either actively by external disturbance or passively by spatially periodic structure. When the flow passes through each of the structure, also called as the advection cycle, the cross sectional concentration distribution transformed into the next distribution. Repeating these advection cycle stretches, folds, and breaks up the fluids and leads to complete mixing (Nguyen & Wereley, 2002).

2.2.5 Diffusion

Diffusion is a statistical transport phenomenon. Diffusion occurs when there is a concentration gradient of one kind of molecule within a fluid. In laminar flow, two or more stream flowing in contact with each other only mixes by the diffusion. This is not advantage when mixing is desirable; therefore, passive of active mixing mechanisms is required. Particle movement by Brownian motion cause particle to spread out over time to make the average concentration of particles throughout the volume is constant. These concepts describe as the mean square displacement of a particle from its origin is proportional to time:

$$x^2 = 2Dt \tag{2.5}$$

Where x is the distance a particle moves, t is the amount of time, and D is the diffusion coefficient.

2.3 Micromixer

Generally, micromixer categorized as an active micromixer or passive micromixer. Active micromixer use external energy for mixing process while passive micromixer do not required external energy for mixing process but rely entirely on diffusion or chaotic advection. The difference between these two types of micromixer system is active mixing produces excellent mixing; however, the means of achieving mixing could involve moving parts that are difficult to fabricate and integrate into the microfluidic systems. On the other hand, passive mixing uses no external energy input and depends mainly on the mechanism used to generate fluid flow through the microchannel; therefore, only limited mixing can be achieved (Bayraktar & Pidugu, 2006).

Active micromixer enhance the mixing performance by stirring or agitating the fluid flow using some form of external energy supply. Active mixers typically use acoustic/ultrasonic, electrophoretic, electrokinetic time-pulse, pressure perturbation, electro-hydrodynamic, magnetic or thermal techniques to enhance the mixing performance (Chia Yen Lee, 2011). In contrast, passive micromixer contain no moving parts and require no energy input other than the pressure head used to drive the fluid flows at a constant rate (Chia Yen Lee, 2011). In passive micromixer, a fluid flow usually in laminar flow. Due to the inherently laminar characteristics of micro-scaled flows, mixing in passive micromixer relies predominantly on chaotic advection effects realized by manipulating the laminar flow within the microchannel or by enhancing molecular diffusion by increasing the contact area and contact time between the different mixing species (Capretto et al., 2011).

Rapid mixing in passive micromixer can be obtained by increasing the contact surface between different fluid and decreasing the diffusion path between them to improve molecular diffusion (Nguyen & Wereley, 2002). Many review on mixing operation in micromixer done previously by Nguyen, *et al.* (2005), Hessel, *et al.* (2005), Lee, C. Y. *et al.* (2011), and Capretto, *et al.* (2011) usually categorized passive micromixer into several group based on mixed phase operation condition of the mixer. Passive micromixer can be categorize into several group based on mixing principle such as Y-Shape or T-Shape mixer (Hsieh, Lin, & Chen, 2013), (Ait Mouheb, Malsch, Montillet, Solliec, & Henkel, 2012) parallel lamination (Wong, Ward, & Wharton, 2004), injection (Miyake, Lammerink, Elwenspoek, & Fluitman, 1993), segmentation lamination (Sheu, Chen, & Chen, 2012), (Nimafar, Viktorov, & Martinelli, 2012), sequential lamination (Yun & Yoon, 2004), focusing mixer (Knight, Vishwanath, Brody, & Austin, 1998), chaotic advection (Stroock *et al*., 2002), (Aubin, Fletcher, & Xuereb, 2005), (Yang, Huang, & Lin, 2005), (Yang, Fang, & Tung, 2008), (Ansari & Kim, 2007), zig-zag mixer (Mengeaud, Josserand, & Girault, 2002), obstacle mixer (C. K. Chung, Shihl, Chen, & Wang, 2008), (Y.-C. Lin, Chung, & Wu, 2007), (Balbino, Azzoni, & de la Torre, 2013), split and recombine mixer (Sudarsan & Ugaz, 2006), recirculation mixer (Y.-C. Chung, Hsu, Jen, Lu, & Lin, 2004), (C. K. Chung, Shih, Tseng, Chen, & Wu, 2007), (Hamid, Kamaruzzaman, & Jamil, 2011), (Alam & Kim, 2013), (Daghighi & Li, 2013), groove or rib mixer (Yang et al., 2005), (D. Lin et al., 2013), (Kasiteropoulou, Karakasidis, & Liakopoulos, 2013), and droplet mixer (Matsuyama, Mine, Kubo, & Mae, 2011).

The final stage of all mixing concept in generally is molecular diffusion. The mixing of micromixer based on molecular diffusion relies only on diffusive transport and mixing only optimized by the geometrical design and different transport effect. The rhombic mixer was reported by Hamid, *et al.* (2011) claims that fluid mixing of the rhombic micromixer is closely related to the rhombic geometric and Reynolds number. In this study, they also emphasize that the mixing is better if the reagent is smaller in viscosity compared to blood based on the simulation result that show the difficulty of mixing of blood with the high viscosity reagent.

The different geometry structure of micromixer based on several design method could improve the mixing performance in microchannel. Mixing performance in micromixer based molecular diffusion usually can be increase through modification of geometry structure of mixer. Therefore, comparative analysis method commonly used to evaluate the mixing performance with different geometric shape micromixer. The comparative study reported by Hamid, *et al.* (2011) claims that mixing performance for laminar blood-reagent fluid closely related to the geometric of the micromixer and Reynolds number. Three type of passive micromixer with different geometry channel which Y-Shape, Z-Shape and Rhombic are use in this comparative analysis. Among three type of micromixer, Z-Shape is superior compared to other two mixers due to larger recirculation of this mixer that enhance mixing performance. They also draw intension to the fact that viscosity of the fluid mixing effect the mixing process inside the mixing channel (Hamid & Jamil, 2008), (Hamid et al., 2011). The numerical simulation result in this work show that mixing performance is better if the reagent viscosity is smaller compared to the blood.

Micromixer based on chaotic advection method can enhance mixing in microchannel by introduces secondary flow in mixing channel known as chaotic advection. These methods used either in a continuous flow or in multiphase flow. According to Nguyen, *et al.* (2005), chaotic process used as a basic design concept in generation of advection transportation by the modification of the channel shape for stretching, folding, and breaking of the laminar flow. In chaos condition, the necessary conditions are need such as the streamline should cross each other at different times. These effects were occurring in a time-periodic flow or spatially periodic flow. Chaotic advection can be generated by stirring the flow which is very effective for small Reynolds number due to the concepts of splitting, stretching, folding, and breaking up in the laminar flow (Nguyen & Wu, 2005). Rips or grooves on the channel wall can produced chaotic advection. In one of the earlier works, Stroock *et al.* (2002) proposed chaotic mixer based on bas-relief structure design on the floor of the channel to generate transverse flow in microchannel by using steady axial pressure gradient. Two design of bas-relief method reported which is the oblique ridges mixer by placing ridges on the floor of the channel at an oblique angle, and patterns of grooves on the floor of the channel known as Staggered Herringbone Mixer (SHM).

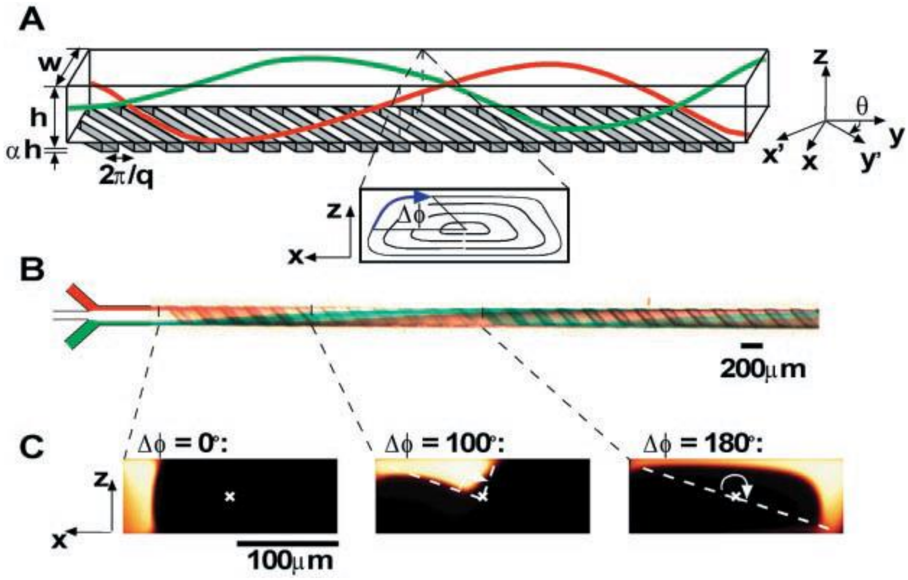

Figure 2.3: The schematic diagram of oblique ridges mixer (Stroock et al., 2002).

Oblique ridges mixers are fabricate by using soft lithography method. These ridges structure generate transverse flow in microchannel that used to induce chaotic stirring at low Reynolds number. These oblique ridges create anisotropic resistance to viscous flow, therefore produced less resistance to flow in the direction parallel to the peak and valley of the ridges than in the orthogonal direction. As the result of this anisotropy, an axial pressure gradient along channel generates a transverse component in the flow that originates at the structured surface. The fluid circulated back across the top of the channel produced the full flow helical streamlines as show in the Figure 2.3. These transverse component produced angular displacement of the fluid at vertical cross section (Stroock *et al*., 2002). In this mixer, the efficiency of mixing is depend on geometrical parameter which wave vector of the ridges, height of the channel, width of the channel and angle of the orientation of the ridges with respect to the channel.

Improved mixing has also been realized through the used of groove channel as generator of secondary flow. Staggered Herringbone Mixer (SHM) design based on subjected the fluid to a repeated sequence of rotational and extensional local flow that as result produces a chaotic flow. These sequences of local flows are achieved in the SHM by varying the shape of the grooves as a function of axial position in the channel. In the SHM, the efficiency of mixing is controlled by two parameters which asymmetry of the herringbones and the amplitude of the rotation of the fluid in each half cycle. The angular displacement in this design controlled by the geometry of the ridges and the number of herringbones per half cycle as illustrated in the Figure 2.4. In this design, they also claim that symmetric herringbones structure do not induced transverse flow, thus flow becomes non chaotic. Therefore, the change of asymmetrical index can induced chaotic flow and contributes in the controlling of the cross-sectional area will involved in the chaotic flow.

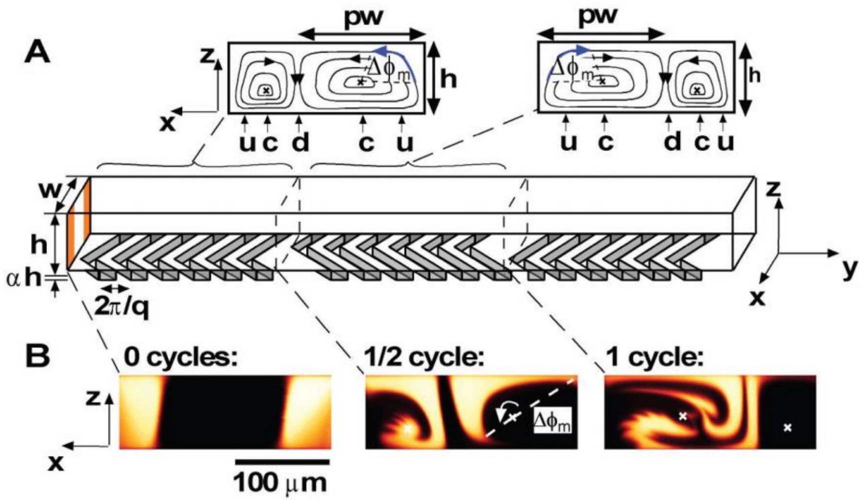

Figure 2.4: The schematic diagram for SHM (Stroock et al., 2002).

The effective designs of groove on wall attract many researchers to investigate the effect of geometric parameter of groove structure on the mixing performance in microchannel. The most common geometries of grooved micromixer are Slanted Groove Mixer (SGM) and SHM, both embedded on the floor of the microchannel. The SGM mixer designed with the angle respect to axial direction, whereas SHM groove have the shape of herringbone pattern. The advection of the fluid is enhance through the fluid transported along the oblique grooves to the downstream edges of the microchannel (outlet) while the herringbone pattern of the SHM generate two counter rotating helical flow with the asymmetry of the SHM groove generate the chaotic flow profile.

Two-step of design protocol suggested and discussed by Sabotin, *et al.* (2012) for designing groove pattern micromixer. The first step is by fixing the channel aspect ratio until the suitable groove depth achieved. Then the suitable groove depth stayed constant until other favourable geometry of the groove are obtain. The second step is the suitable groove geometry was further examined in various six-groove configurations. They also conclude that every groove in the groove design have its own mixing potential for enhance the mixing process in microchannel. They also show that rounding of inner groove's corner can improve mixing efficiency (Sabotin, Tristo, Junkar, & Valentinčič, 2013).

Numerical investigation carry out by Yang, J.-T., *et al.* (2005) to study the effect of geometric parameter of SHM with pattern groove by using the Taguchi method to observed the influence of geometric parameter on SHM performance. Numerical simulation result reveal that depth ratio and asymmetry index of the groove are the most geometric parameter that effect the mixing performance of a SHM follow by groove intersection angle and upstream to downstream channel width ratio. In this study, they also draw intention to the effect of flow rate inside the mixing channel that play one of the most significant roles in the mixing performance of the SHM design (Yang *et al*., 2005).

The effect of various geometrical parameter of a SHM on the mixing performance also performed by Aubin, J. *et al.* (2005) by using particle tracking method. In this study, the plotting of particles located at different axial position along channel mixer showing the distribution of the striation thickness corresponding to particle trace pattern due to mixing behavior. The results proved that the number of grooves per mixing cycle does not affect the mixing quality. On the other hand, a larger groove depth and width allow the maximum striation thickness to be rapidly reduced, without increasing the pressure drop across the mixer. They also highlighted that the wide grooves can create significant dead zones in the microchannel, whereas deep grooves improve the spatial mixing quality (Aubin *et al*., 2005).

Shape optimization of a SHM was also carry out by using numerical optimization technique by Ansari, M. A. *et al* (2007) to optimize the shape of the grooves on a single wall of the channel. Two design variables which is the ratio of the groove depth to channel height ratio and the angle of the groove are selected for optimization. In this study, the simulation performed with the mixing index is used as the objective function. The simulation results obtain by using the shape optimization technique show that the mixing is very sensitive to the shape of the groove which can be used in controlling the mixing in microdevices. Moreover, they also claim that the shape optimization of a SHM could increases the mixing near the inlet of the mixer. In this work, they conclude that the mixing is affected by the depth of the groove much more than the angle of the groove. In addition, pressure drop characteristic are also increases with an increasing in the angle of the groove, and also with a decreasing in the ratio of groove depth to channel height (Ansari & Kim, 2007).

In general, the patterned-groove micromixer mainly designs with the groove on a single side of a channel to generate transverse components and therefore enlarge the fluidic interface to enhance mixing. Through this design, the fluid is guide to transfer onto the bottom of the main channel only by anisotropy surface structure on the floor of the mixing channel. Therefore, the connected grooves channel introduced by Yang, *et al.* (2008) give a new concept of groove structure by employed groove on the bottom and side of the microchannel to promote the mixing. This mixer design composes of bottom groove along the sidewall groove to the top of the mail channel. This structure can cause the helical flow with a short pitch and generate the intense transverse field. The geometrical schematic of connected groove mixer illustrated in Figure 2.5.

The chaotic mixer reported by Stroock, *et al.* (2002) open the new way to develop the micromixer with 3D effect without going through the 3D complexities by embedding herringbone structure on the floor of the channel. This idea was extend by Wang, *et al.* (2012) by fabrication of cylindrical grooves design. In this work, three mixers are fabricate by embedding cylindrical grooves in to the main channel.

Their simulated and experimental results confirmed that the mixing enhancement occur in this mixer. They conclude that the effect of cylindrical grooves is more obvious at greater flow rates and this design are easily incorporated into a total microfluidic system (L. Wang, Liu, Wang, & Han, 2012).

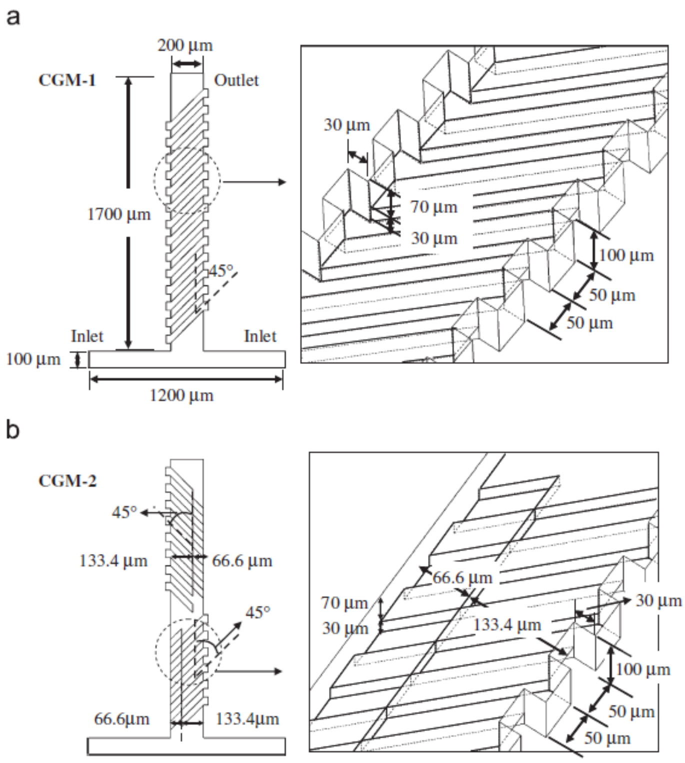

Figure 2.5: The schematic diagram of connected groove mixer (Yang *et al*., 2008).

2.4 Conclusion

As a conclusion, there are several method used to design the micromixer for laminar flow. Many groove structure previously reported by fabricate the groove structure inside the mixing channel. These structures are suitable method to enhance the mixing performance for laminar mixing especially at low Reynolds number. Groove pattern on the mixing channel floor are the basic design can be implement to enhance the laminar mixing for blood and reagent. Moreover, these designs are simple and easily fabricate inside the microchannel by using soft lithography method.

CHAPTER III

METHODOLOGY

3.1 Introduction

This chapter consists of two main sections that discuss the methodology used to conduct this project. In this chapter, the first section describes the process flow for modelling and simulation of laminar blood and reagent mixing. In this section, the design process of groove micromixer explained in detail to describe the process flow used in this study in order to design and develop the groove micromixer. Second section discussed the the geometries specification of each parameter design for Y-Shape micromixer model. In this section, the Y-Shape micromixer design are divided into three stage, the first stage is design the Y-Shape of micromixer without groove structure, and then the Y-Shape mixer with the oblique groove and lastly the Y-Shape mixer with herringbone groove structure. At the end of this chapter, all the model design structure are simulated with two different viscosity of reagent. The properties of two reagents with their boundary condition are given this chapter. All the modelling and simulation of the groove micromixer design are performed using CoventorWare2010 software.

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