

ISTANBUL TECHNICAL UNIVERSITY ★ GRADUATE SCHOOL OF SCIENCE
ENGINEERING AND TECHNOLOGY

**DESIGN AND FABRICATION OF LOW COST PASSIVE MICROFLUIDIC
SYSTEMS FOR PARTICLE SEPARATION**

M.Sc. THESIS

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Department of Advanced Technologies

Materials Science and Engineering Programme

JANUARY 2012

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**MİKRO PARTİKÜL AYRIŞTIRMALRI İÇİN DÜŞÜK MALİYETLİ PASİF
MİKROAKIŞKAN SİSTEMLERİ TASARIMI VE ÜRETİMİ**

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Date of Defense : **23 January 2012**

To my family & friends,

FOREWORD

This thesis was written for my Master degree in Advanced Technologies - Materials Science and Engineering program at Istanbul Technical University. The aim of the thesis is to produce a low cost, polymeric based microfluidic channel for particle separation processes. This research was executed with the support of TUBITAK at ITU MEMS Laboratories.

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ABBREVIATIONS

MEMS	: Micro Electro Mechanical Systems
PDMS	: Polydimethyl Siloxane
DI	: De -ionized
μTAS	: Micro Total Analysis Systems
CFD	: Computational Fluid Dynamics
DEP	: Dielectrophoresis
pDEP	: positive Dielectrophoresis
nDEP	: negative Dielectrophoresis
PFF	: Pinch Flow Fractionation
D_h	: Hydraulic Diameter
F_L	: Lift Force
Re	: Reynolds Number
Re_p	: Particle Reynolds Number
a_p	: Particle Diameter
U_L	: Lateral Migration Velocity
L_p	: Minimum Microchannel Length
De	: Dean Number
IPA	: Isoprophyl Alcohol

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DESIGN AND FABRICATION OF LOW COST PASSIVE MICROFLUIDIC SYSTEMS FOR PARTICLE SEPARATION

SUMMARY

Particle separation which is an important part for chemical and biological processes is one of the most studied technology in MEMS. In recent years, several research groups studied on this subject for understanding the particle focusing mechanism and defining the optimum microchannel design for the highest particle focusing yield. Particle separation in microchannels can rely on external forces like magnetic field or acoustic effects, but it can also rely on the effects of the flow of carrier fluid.

In passive microchannels, particle focusing mechanism only relies on the effects of the flow on the particle. Mainly, a particle is affected by two forces when flowing with a carrier fluid. These are drag forces and lift forces. Drag forces are parallel to the fluid flow direction and move the particle in that direction. Lift forces are applied to the particle as perpendicular to the fluid flow resulting in changing the particle position in lateral axis. In microchannels with curved geometry, particles are also affected by secondary forces inside the fluid flow which is not directly affecting the particles but rather changing fluid's flow properties thus affecting the particles. In this experimental study, passive microchannels has been both due to their low fabrication cost using single lithography mask, and the separation mechanism solely depends on the mechanical forces, which in turn, they do not adversely affect the cells, when they are used for biological cell separation applications.

In this study, Polydimethylsiloxane (PDMS) is used as low cost microchannel material. Particle focusing characterization has been done using DI water solution with spherical fluorescent particles of 9.9 and 3.0 μm in diameter. For microchannel design, evenly placed contraction and expansion parts isare used on one side of themicrochannel. 80 contraction /expansion partsis areused inside the whole microchannel and the width of contraction part is 40% lower that the width of the expansion part. In this design, two district and equally distributed focused particle streamlines have been obtained.

The distinctive part of this experimental study is to make an angular modification at the entrance of contraction part. Particle focusing mechanisms and changes in focused particle streamline positions have been studied at 30°, 45°, and 60° angles. We have observed single focused particle streamlines at low flow rates of 105 and 120 $\mu\text{l}/\text{min}$. Due to these angular parts added to the basic geometry of the microchannel system, particle-focusing mechanism has been altered. Because of these angular parts, lift forces have become more effective on the particles by having x and y components compare to design without angled entry where particles are affected only perpendicular to the fluid flow direction. Y component of the lift force affects the particle so as to change the particle's lateral position. X component of the lift force is parallel to the fluid flow and opposite of its direction. Because of this, x component of the lift force

acts like as reducing the drag force effect on the particle. Increasing the angle value of these ramps leads to single focused particle streamlines at higher flow rates (60° ramp yields single focused particle streamline at 120 $\mu\text{l}/\text{min}$).

At last, the effect of aspect ratio of the microchannel was studied. For this reason, depth of the microchannel was decreased. This caused the particle focusing mechanisms so that the particles tend to obtain a single focused particle streamline at different locations of the microchannel at different flow rates (105 and 120 $\mu\text{l}/\text{min}$ yields single focused particle streamline at bottom of the microchannel. 180 and 200 $\mu\text{l}/\text{min}$ yields single focused particle streamline at top of the microchannel)

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ÖZET

Bir çok kimyasal ve biyolojik prosesin önemli bir parçası olan filtrasyon işlemleri, üzerine en çok çalışılan MEMS teknolojilerinden birisidir. Son yıllarda, bir çok araştırma grubu, parçacık fokuslanma mekanizmasını kavrayabilmek ve en yüksek parçacık fokuslama verimine sahip optimum kanalı tasarlamak için çalışmaktadır. Mikrokanallar vasıtasıyla sıvı içerisinde parçacık ayırıştırma işlemleri, manyetik alan veya akustik etkiler gibi dış etmenler ile gerçekleştirilebildiği gibi taşıyıcı sıvının akışından dolayı oluşa etkilerden yararlanılarak da gerçekleştirilmektedir.

Bu tez kapsamında, taşıyıcı akışkana dışarıdan herhangi bir kuvvetin etki etmemesi prensibine uygun pasif bir mikrokanal tasarlanılmıştır. Dış kuvvetler altında çalışan mikro ayırıştırma sistemlerinin bir çok avantajı bulunsa da, yüksek üretim maliyetleri ve enerji kaynağına ihtiyaçlarından dolayı kapladıkları alanın büyük olması gibi dezavantajları bulunmaktadır. Pasif kanal teknolojisi temel olarak taşıyıcı sıvının hareketi sırasında, sıvı içerisinde bulunan parçacıklara etki eden kuvvetlerle gerçekleşmektedir. Parçacıkların ayrışmasında, bu kuvvetlerin yanısıra kullanılan geometrinde etkisi olduğu düşünülse bile, sisteme etki eden kuvveti belirleyen en önemli etkenin sistemin geometrisinin olduğu bilinmelidir. Doğrusal geometriye sahip bir tasarıma sahip mikrokanallarda parçacıklar, etki eden eylemsizlik kuvvetlerinden dolayı birbirlerinden ayrıştırılırken, eğrisel geometrideki kanallarda ise parçacıklara eylemsizlik kuvvetlerinin yanısıra etki eden ikincil kuvvetlerde bulunmaktadır. Dean sürüklenme kuvveti bu anlamda eğrisel kanallarda gerçekleşen oldukça önemli bir mekanizmadır.

Doğrusal veya eğrisel bir mikrokanal içerisinde parçacıklara temel olarak 2 kuvvet etki etmektedir, bunlar sürüklenme ve kaldırma kuvvetleridir. Sürüklenme kuvvetleri, parçacıklara akış yönünde etki ettiğinden dolayı parçacıkların hızlanmasına neden olmaktadır. Kaldırma kuvvetleri ise, akışa dik bir eksenle parçacıklara etki ettiğinden dolayı ayırıştırmada etkili olan kuvvetlerdir. Bir parçacığa etki eden kaldırma kuvvetlerinin bazıları birincil dereceden yani direk olarak parçacığa etki etmektedir. Bunlar kayma gradyanı kaynaklı kaldırma kuvveti ve duvar etkisi kaynaklı kaldırma kuvvetleridir. Bu iki kuvvetin yanısıra, eğrisel kanal geometrilerinde etkisi görülmekte olan ikincil kuvvetler bulunmaktadır. İkincil kuvvetler parçacıklara direk olarak etkide bulunmamakta ama bu kuvvetlerin akışkanda gerçekleştirdikleri değişikliklerden dolayı parçacıkların ayrışmasında rol oynamaktadırlar.

Yapılan deneysel çalışmalarda doğrusal geometriye sahip mikrokanallarda parçacık fokuslanma mekanizmaları ve kanal geometrisinin fokuslanma mekanizmasına olan etkisi incelenmiştir. Bu alanda detaylı literatür taraması gerçekleştirilmiştir. Doğrusal

kanal geometrisine ait yapılan ilk çalışmada, kanalın yarıçapının yaklaşık 0.60 'ında sistemde bulunan parçacıkların dengeye ulaştığı gözlemlenmiştir. Bu çalışmaların devam ettirilmesiyle, kanal kesit geometrisine bağlı olarak parçacıkların belirli bölgelerde odaklandıkları tespit edilmiştir. Eğrisel kesiti olan bir kanalda parçacıklar merkezden eşit uzaklıkta bulunan bir hat üzerinde odaklanırken, karesel kesiti olan bir kanalda parçacıklar merkezden eşit uzaklıkta olacak şekilde kanal kenar merkezlerinde 4 katlama simetrisinde odaklanırlar. Sistemin dikdörtgen bir kesite sahip olması durumunda ise parçacıklar, merkezden eşit uzaklıkta olacak şekilde sadece uzun kenarların merkezlerinde 2 katlama simetrisinde odaklanmaktadır.

Deneyisel çalışmada, düşük maliyetinden dolayı polidimetilsiloksan (PDMS) mikrokanal üretim malzemesi olarak kullanılmıştır. Litografi yöntemiyle üretilen PDMS mikrokanal yapıları, cam ile birleştirilerek nihai ürün elde edilmiştir. Parçacık odaklanma deneyleri de-iyonize su içerisinde çözölmüş olan 9.9 ve 3.0 μm çaplı floresan parçacıklar ile gerçekleştirilmiştir. Mikrokanal geometrisi olarak, kanalın tek tarafına eşit boyutlarda ve birbirini tekrar edecek şekilde dar ve geniş bölgeler yapılmıştır. Dar ve geniş bölgelerden oluşan bu sistem kendini 80 defa tekrar etmektedir. Dar bölgelerin genişlikleri geniş bölgelerin 0.40 'ı kadardır. Bu sistemde, daha önceden literatürde benzer bir tasarım olan çift taraflı daralma ve genişleme geometrisiyle belirlenen mekanizmaya uygun bir mekanizma gözlemlenmiştir. Bu geometri ile yapılan ilk çalışmada, birbirinden ayrık ve neredeyse eşit yoğunlukta 2 farklı odaklanmış parçacık hattı gözlemlenmiştir. Bu odaklanmış parçacık hatları kanalın engebeli ve düz olan bölümlerinde odaklanmışlardır.

Özgün olarak tasarlanan ve mekanizması incelenen geometri ise, tek taraflı daralma ve genişleme geometrisine sahip kanallarda dar bölge girişlerine farklı açılara sahip eğik rampalar eklenmiştir. Sisteme eklenen bu rampaların taban ile yaptığı açının 30° , 45° veya 60° olmasına göre odaklanma mekanizmasının ve odaklanma bölgelerinin değiştikleri gözlemlenmiştir. Kanaldaki temel geometriye dahil edilen rampaların etkisiyle, literatürde bahsedilen odaklanma bölgeleri sayısı düşürülerek, parçacıkların kanalın tek bir bölgesinde odaklanması sağlanmıştır. Geometriye dahil edilen rampaların, odaklanma mekanizmasına olan etkisi bir teori ile yorumlanmıştır. Öngörülen teoriye göre, parçacıklara rampanın etkisiyle normalden daha erken bir duvar etkili kaldırma kuvveti etki etmektedir. Burada önemli olan durum ise bu kaldırma kuvvetinin rampadan dik bir şekilde olması ve akış yönüne dik olmamasıdır. Parçacık üzerinde, rampanın etkisiyle oluşan bu kuvvetin y bileşeni akış yönüne dik olduğundan parçacığın eksenel yer değiştirmesini yönetmektedir ve normalden daha uzun süre etki ettiğinden dolayı parçacıkların tek bir bölgede yani kanalın üst ve engelsiz kısmında birikmesini sağlamaktadır.

Rampa yapısının etkisiyle, sistemde oluşan ve normal olarak bir kaldırma kuvveti olan duvar kaynaklı kaldırma kuvvetinin x bileşeni ise akışa dik bir yönelmeye sahip değildir, bunun aksine bu kuvvet akışa paralel ve ters yönlüdür. Sistemde oluşan bu sıradışılık sayesinde parçacıklara etki eden sürüklenme kuvveti azalmakta ve parçacıkların rölatif hızları düşmektedir. Daha yüksek açılı rampalarda etki eden kaldırma kuvvetinin x bileşeni daha büyük olduğundan dolayı bu sistemlerde daha yüksek hızlarda tek olarak odaklanmış parçacık hatları gözlemlenebilmektedir. Örneğin; 60° 'lik rampaya sahip mikrokanal tasarımında, diğerlerinden farklı olarak 120 $\mu\text{l}/\text{dak}$ debide kararlı ve tek adet odaklanmış parçacık hattı bulunmaktadır.

Geometriye rampa sisteminin dahil edilmesi üzerine yapılan çalışmanın yanı sıra kanal geometrisine ait bir başka özellik daha incelenmiştir. Kanalin kesitine ait birimsiz bir faktör olan kesit oranı üzerine literatürde bazı çalışmalar bulunmaktadır. Yapılan deneysel çalışmada kanal derinliği $60\ \mu\text{m}$ 'dan $40\ \mu$ 'a indirilerek kanal kesit faktörünün azalması sağlanmıştır. Geri kalan tüm geometrik özellikler ise sabit tutulmuştur.

Yapılan deneysel çalışmalar sonucunda, kanalın kesit oranının azalmasıyla birlikte parçacık fokuslanma mekanizmasının değiştiği gözlemlenmiştir. Önceki çalışmalarda, düşük debilerde ($105 - 120\ \mu\text{l/dak}$) kanalın üst kısmında sadece tek fokuslar elde edilirken, bu sistemde düşük debilerde ($105 - 120\ \mu\text{l/dak}$) kanalın alt yani engelli kısmında tekli fokuslar elde edilmiştir. Önceki çalışmalarda, yüksek debilerde ($160 - 180\ \mu\text{l/dak}$) parçacıkların tekli fokusların dağıldığı veya iki ayrı fokuslanmış parçacık hattında dengelendiği gözlemlenmişken, kesit oranı azaltılmış sistemde yüksek debilerde ($160 - 180\ \mu\text{l/dak}$) parçacıkların kanalın üst kısmında tek ve oldukça dengeli bir şekilde fokuslandıkları gözlemlenmiştir.

1. INTRODUCTION

MEMS, Micro Electro Mechanical Systems, is the most rapid technology development in the world history [1]. MEMS devices are electromechanical systems within the size range of 1 – 300 micrometers. MEMS technologies have been used for making observations and determinations that are generally difficult with traditional methods [2]. With the introduction of fluidic and optical components in the MEMS technologies, the development of devices like microflow sensors, micropumps, and microvalves have been achieved in late 1980s and these developments gave birth to microfluidic technologies [1]. Then, Manz et al. introduced their research at the Fifth International Conference on Solid-State Sensors and Actuators in 1989; developments in the field of microfluidics are accelerated [1]. They indicated that life sciences and chemistry are the main application fields of microfluidics [3]. Microfluidic technologies are basically based on dealing with transport phenomena and fluid-based devices at micron scale [4]. In microfluidic devices, the advantages are obtained from the microscopic quantity of the fluid that is processed with the microfluidic device. In this type of devices, the important length scale is not the overall device size but rather the length scale that determines flow behavior.

Being able to transport, separate, mix or characterize particles all within one device is the ultimate goal of microfluidic technologies [2]. These integrated multifunctional analysis systems can work as a single device when needed. Today, microfluidic devices are commonly known as μ TAS (micro total analysis systems) or “Lab-on-a-chip” devices [2]. In 1994, the first integrated lab-on-a-chip device was produced for 3 different functions: mixing reactants, enzymatic reaction and separation [5].

1.1 Microfluidic Systems

Microfluidic systems are categorized according to their application fields such as external flow control, internal flow control, and microfluidics for life sciences and

chemistry [1]. Velocity sensors, microsynthetic jets, microvalves, micropumps, micromixers, microreactors and microseparators can be given as some general examples for microfluidic devices. Due to the fact that microfluidics is in an early development stage, new application fields and types of devices are invented with an exponential rate [1].

1.1.1 External flow control systems

External flow control systems are used for controlling macroscopic flow phenomena. Velocity sensors, shear stress sensors, microflaps, microsynthetic jets and micro air devices can be classified in this area. These types of devices are used for turbulence and point velocity measurements [1].

For example, tiny flow structures, named as eddies, are responsible for viscous drag increase of aerodynamics in turbulent regime. Eddy currents are generally several hundred microns in width and several millimeters in length [6]. Also the lifetime of eddy currents is on the order of milliseconds. Conventional instruments mostly cannot detect such a fast response because of their low response times. Microfluidic devices are suitable for controlling and measuring eddy currents in turbulent flow because of their small size [7].

1.1.2 Internal flow control systems

With the recent researches in life sciences, controlled transport of fluids at microscale became an important task [1]. Generally 3 different internal flow control systems are used for controlling the transport of fluids in these microsystems; Microvalves, Micropumps and Microflow Sensors. Microvalves are the most important component at microfluidic scales among these 3 microfluidic systems [1]. Applications of the microvalves include flow regulation, on/off switching and sealing of liquids, gases or vacuums [8]. Microvalves can be classified into 2 general groups; active and passive microvalves, where passive microvalves can also be counted as a type of micropump [8]. Micropump devices are mostly used as a controlled transportation mechanism in other microsystems. The main importance of micropumps is the new pumping effects, which have much more effect on the microscale than the macroscale [1].

Microflow sensors could work with microvalves and micropumps in a control loop in the microsystems [1]. There are some huge advantages of microflow sensors; low energy consumption and the ability to measure very small flow rates on the order of microliters per minute to nanoliters per minute [1].

1.1.3 Microfluidics for life sciences and chemistry

Previously mentioned microfluidic system areas that are mentioned are mostly used for controlling the fluid transportation. The microsystems in this area are the devices that are used for analysis at microscales. These systems are mostly used as internal and external flow control systems for microsystems [1]. Most common devices that are used for life sciences and chemistry are micromixers, microreactors and microseparators. In biomedical and chemical analysis most of the time two different solutions have to be well mixed for enabling the reaction between them. At macroscale, mixing is achieved by turbulence character of the flow but at microscale, mixing is mainly caused by the diffusion on the laminar flow [1]. Quite low flow rates are needed to obtain a laminar flow at microscale. In microscale mixers, some obstacles or external forces can be used to increase the active diffusion rate on low flow rates [1].

One of the most common research area for microfluidic systems is microreactors. Microreactors offer relatively high throughputs and low-cost mass productions [1]. Some of the advantages of microreactors are; higher heat and mass transfer rates caused by the smaller size of the reactor, control systems that are faster and much more reliable than conventional reactors due to the scale of the flow and reactor, possibility of carrying out reactions without flames or explosions, small quantity of accidental chemical release, and the fact that laminar fluid flow in the microreactors can be handled by various CFD (Computational Fluid Dynamics) tools.

Small sizes of the microfluidic systems allow faster process and less reagent consumption. With these benefits, the small size of the devices also allows parallel processing which requires the separation application for being reliable [1]. These microseparator systems can be classified as active and passive systems depending on whether external force is used or not for separation [1]. Microseparator systems will be analyzed in detail in section 2.

1.2 Purpose of the Thesis

The main objective of this thesis is to manufacture a low cost polymeric passive microseparator device. These devices are designed based on both straight and circular channel geometry principles for obtaining low and high throughput devices. These microseparator devices will be used for analyzing biological samples. This project is funded by TUBITAK, with 109M298 project code.

2. MICROSEPARATOR SYSTEMS

Separation processes are used in many branches of the industry for several issues like purifying, concentrating or separating the components [9]. Filtration, centrifugation and electrophoresis are some of the most common separation techniques that are used in the industry [10]. Separation processes are quite dependent on the size of the particles that are intended to be separated [11]. These devices are mainly designed based on the particle size data. The main research about the microseparation devices is the understanding of the mechanism that leads to the separation. This understanding leads to the main classification on the microseparator technology which is either just dependent on the geometric effects of the microchannel or using an external force to increase the separation yield. These types of devices are named as passive and active microseparators respectively [10].

2.1 Active Particle Separation Techniques on Microfluidic Systems

2.1.1 Separation based on magnetophoresis

Magnetophoresis based microfluidic devices rely on separating particles that are responsive to magnetic effects, perpendicular to the fluid flow direction through applying an external magnetic force. In biological examinations, cells or proteins are coated with magnetic particles for generating the required magnetic properties. In this method, particles with magnetic properties or magnetically marked cells are entrapped in an externally applied magnetic field. Magnetic field that is applied to the particles is dependent on both gradient of the applied magnetic force and particle properties such as volume and magnetization [10, 12, 13]. Because of the applied external force on the system, observed particle trajectory is obtained by 2 different vector forces which are hydrodynamic velocity and magnetically induced velocity [10].

Because of the applied magnetic force, these types of microfluidic systems are

generally parallel flow systems without any obstacle in the main fluid flow direction. Therefore, it is an appropriate system to analyze magnetically induced biological particles without deforming their shapes [10].

2.1.1.1 Literature review about microfluidic systems with magnetophoresis

Deng et al. used this technique for the first time at miniaturized scale. In their experimental studies, they separated 6 μm non-magnetic particles and 4.5 μm magnetic particles with a high separation yield. The only problem they found was that the system had quite a low throughput [14]. In their study, Pamme et al. worked on particles with different magnetic properties and sizes such as 2.8 μm and 4.5 μm diameters. They applied a non-homogeneous magnetic force perpendicular to the main fluid flow direction. Because of the different properties, particles were focused on different positions in microfluidic device which can be seen in Figure 2.1 [15]. This point of view was used by further experiments by using side exit channels [16] and this method was used with biological cells to determine the system's yield on the biological cell separation processes [17].

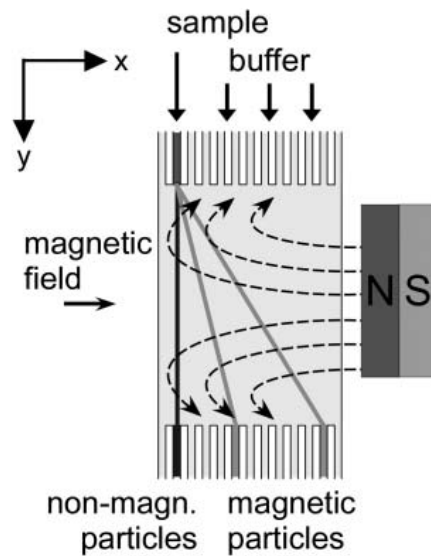


Figure 2.1: Microfluidic device with externally applied non-homogeneous magnetic force for separating particles in different outlets [11].

Inglis et al. replaced ferromagnetic bands in the microfluidic system with a slight angle to the fluid flow for separating magnetically marked cells. They observed that magnetically marked fluorescing leukocyte cells were entrapped in the ferromagnetic

bands that were generating the magnetic field at an angle of 9.6° to the main fluid flow, which can be seen in Figure 2.2 [18].

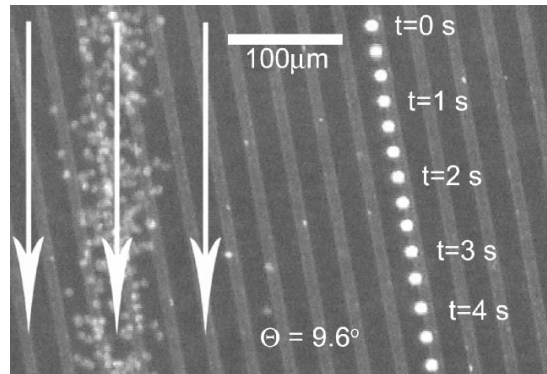


Figure 2.2: Magnetically tagged cells tracking a ferromagnetic band (fluid flow direction is indicated by white arrows) [19].

Magnetic forces are not only applied to the particles with magnetic properties either naturally or marked, they are also applied to non-magnetic particles. Under the magnetic field, non-magnetic particles are affected by a slight repulsion force. Furlani studied on this force to separate white and red blood cells in a magnetophoretic microfluidic system [19].

Han and Frazier also studied on red and white blood cells. A ferromagnetic wire was placed inside the microfluidic system parallel to the main fluid flow direction and this wire was activated with an external magnetic field. Red and white blood cells moved to or away from the ferromagnetic wire according to their magnetic properties [20].

Zborowski et al. used diamagnetic white blood cells and paramagnetic or diamagnetic red blood cells in their study. They tried to separate red blood cells from white blood cells with human lymphocyte marking [21].

Recently, Huang et al. studied on 2 module microfluidic system to remove the nucleotic red blood cells from a pregnant woman. In this system, white blood cells were gathered from the microfluidic system alone [22].

2.1.2 Separation based on acoustophoresis

Separation of particles and biological cells can be achieved with the usage of ultrasonic waves. A continuous sound wave should be applied perpendicular to the main fluid flow for obtaining a separation regime with ultrasonic waves. Particles that are affected

by the sound waves move to nodes or anti-nodes that occurred inside the channel because of the sound waves. Applied acoustic force is dependent on the acoustic field, particle properties and the environment. Required frequency of the acoustic field is determined by the channel width. Acoustic force is proportional to the particle volume and also compressibility of the particle and surrounding material's properties [10, 12, 13].

According to these properties, particles with different size, density and compressibility can be separated with this method [10].

2.1.2.1 Literature review about microfluidic systems with acoustophoresis

One of the first studies of microfluidic separation device with acoustic forces was made by Petterson et al.. They studied $5\ \mu\text{m}$ particles' and blood cells' behavior under the acoustic effects which can be seen in Figure 2.3. When the ultrasound was turned on, particles switched over to the clean medium and exited through the center outlet together with the clean medium. They produced sound waves by integrating a piezoceramic layer to the microfluidic device [23].

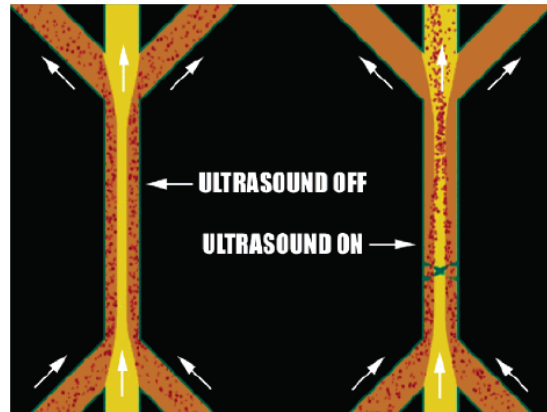


Figure 2.3: Schematic illustration of the medium exchange principle in acoustophoretic separation device [24].

In their study, Goddard et al. tried to gather $7.8\ \mu\text{m}$ particles and hamster cells at the center of the microfluidic system by using an externally applied ultrasonic acoustic energy which was generated by piezoceramic crystal [24, 25].

Shi et al. managed to create a bond with PDMS microchannel and piezoelectric substrate. With this microfluidic channel, they managed to focus $1.9\ \mu\text{m}$ particles

at the center of the microfluidic system in a low flow regime [26]. They also studied on cells and polymer particle separation with the same microfluidic channel [27,28].

2.1.3 Separation based on electrophoresis

Electrophoresis is one of the most powerful techniques that are used in particle and cell separations, but this technique did not take much attention because it has some technical problems such as convection that produces low separation yield and complexity on the teoretical background [29]. The most ideal way of electrophoresis application in microfluidic systems is applying free-flow electrophoresis.

In free-flow electrophoresis, particles change their direction inside the main fluid flow with a perpendicularly applied external homogeneous electrical field source. Charged sample components are deflected from the main fluid flow direction depending on their charge to size ratio. Particles will be forced by hydrodynamic forces on x axis and by electrical field on y axis which can be seen in Figure 2.4; sum of these two force vectors will define particle flow trajectories. [10].

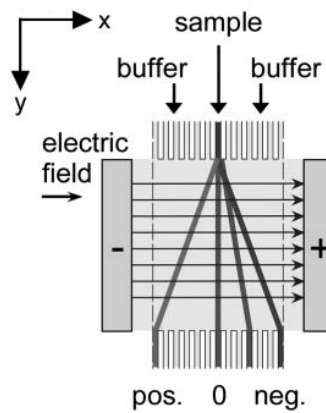


Figure 2.4: Schematic illustration of free-flow electrophoresis[11].

2.1.4 Separation based on dielectrophoresis

Separating particles or cells by using non-homogeneous electrical field is the main principle of Dielectrophoretic microfluidic system which is known as DEP. Particle that has been affected by an electric field is polarized because of the electrical charge throughout the electric field. In homogeneous electric field, opposite electrostatic forces will balance each other out and this will result with particles to stay still.

However, in non-homogeneous electrical field, these forces are not equal and this will result with particles to be affected and move. If the polarization of particles is more than the surrounding material, particles will move towards the electrical field, this is called as positive dielectrophoresis (pDEP). If the polarization of particles is less than the surrounding material, particles will move away from the electrical field, this is called as negative dielectrophoresis (nDEP). Because of these reasons, DEP force is dependent on the surrounding material's polarization and also on particle volume and gradient of the electrical field [10, 30]. A general schematic description of nDEP and pDEP can be seen in Figure 2.5 [10].

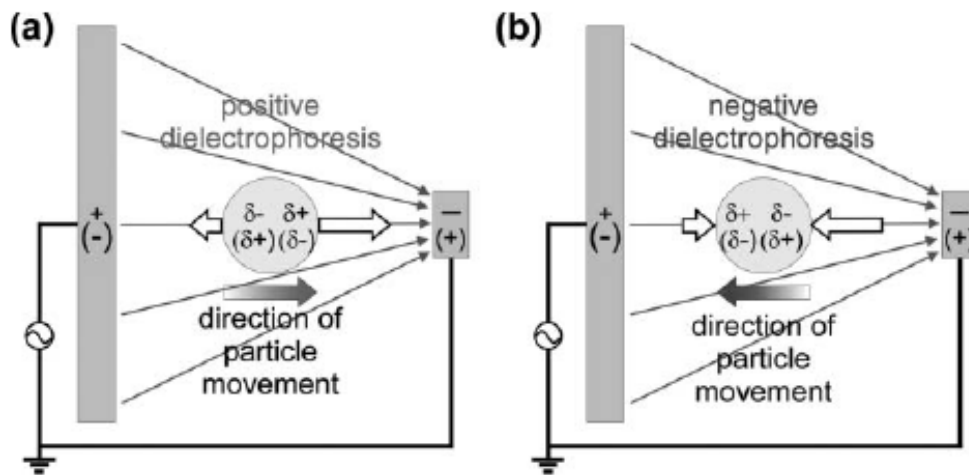


Figure 2.5: Schematic illustration of dielectrophoresis. (a) positive DEP situation (b) negative DEP situation [11].

Generally in dielectrophoretic microfluidic systems, non-uniform AC electrical fields and electrodes inside the micro channel are used for particle focusing purposes [10,30]. Microinsulators which are replaced inside the microfluidic system can also be used for particle focusing. With this method, when a DC electrical field is applied to the channel, particles will change their position because of the dielectrophoretic force field occurred around the microinsulators [31–33].

Negative dielectrophoresis is mostly used on the microfluidic systems that use electrodes for generating the dielectrophoretic force; particles will move away from the electrodes in this type of system [34, 35].

2.1.4.1 Literature review about microfluidic systems with dielectrophoresis

Cummings and Singh developed first dielectrophoretic system by using insulators [36]. They used cylindrical columns inside the microfluidic system as insulators and electrical field that occurred around these columns applied DEP effect on the particles. If dielectrophoretic movement surpassed electro-kinetic and Brownian hatches, particles gathered between these columns [37,38]. This method was tested on biomolecules in several studies [39–43], and was also applied to separation of polymer particles and biological cells with respect to their sizes [44–47].

Cummings and Singh also used dielectrophoretic particle separation mechanism on straight and curved microfluidic systems. They observed focusing of 200 nm particles by using positive dielectrophoresis inside a contraction and expansion channel [48]. Xuan et al. worked on a similar microfluidic channel by using negative dielectrophoresis, and observed that 40 μm particles were focused at the center of the channel [49].

Zhu and Xuan studied on particle focusing on a microfluidic system by using AC electrical field with DC influential, and they achieved to focus 10 μm polystyrene particles at the channel center [50]. Thwar et al. studied with oil for controlling electrical field and increasing yield of particle focusing [51]. Oil enhanced electrical field was also investigated in contraction and expansion type microfluidic systems for separating particles [52].

Xuan studied curved microfluidic system with DC electrokinetic flow for particle focusing mechanism [53–56]. Because of the low Reynolds number, inertial and dean forces were relatively low in this study. Electrical field was maximum at the inner wall and minimum at the outer wall in the entire microfluidic system. Because of this, particles were moving electro-kinetically through laterally on curves. Inner or outer wall focusing was dependent on the applied negative or positive dielectrophoresis [57,58].

Zhu et al. studied 5 μm particle focusing on spiral microfluidic channels with dielectrophoresis [55]. They observed that particles were moving towards the outer wall in negative DEP differently from the curved channels, and particle movements

were not affected by the curves. Zhu and Xuan studied on a double spiral channel geometry for particle focusing [53], then they combined this microfluidic system with dielectrophoresis and studied on separating particles with respect to their sizes [59].

2.2 Passive Particle Separation Techniques on Microfluidic Systems

2.2.1 Separation based on microfilters

It is possible to separate particles and cells with different sizes by using a filtering method, but this technique generally results in a low yield. There are 4 types of microfiltering techniques and these microchannels have some distinct geometries; weir, pillar, barrier and filter. A schematic view of these channel types can be seen in Figure 2.6 [60].

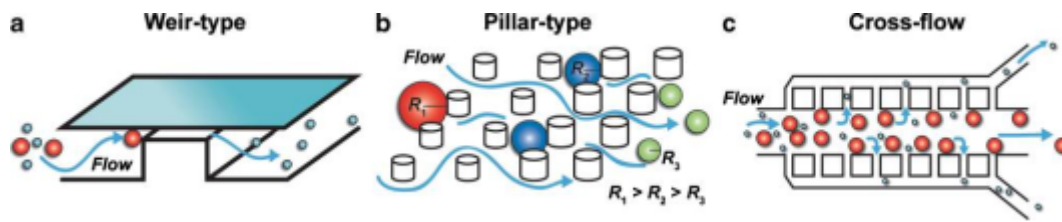


Figure 2.6: Microscale filter designs; (a) Weir type microfilters, (b) Pillar type microfilters, (c) Filter type microfilters [61].

2.2.1.1 Literature review about microfluidic systems with microfilters

In microfilters with threshold geometry, smaller particles are allowed to pass through the barrage type obstacles so that particles are separated. In their study Brody et al. used a capillary effect for separating blood plasma from the whole blood [61]. With the applied capillary effect, blood plasma passed through a narrow threshold while the blood cells could not. Gathering of blood cell yield was quite low in this study [62]. Later, high volumes of blood plasma was separated from the whole blood sample by improving this technique [63,64].

In microfilters with pillar geometry, flow and particles can be controlled with evenly separated pillars. However, problems like clogging of particles and deformation of particles may occur in this type of systems. In their study Mohammed et al. separated red blood cells of a child from the maternal circulation which also contained the

mother's red blood cells [65].

In microfilters with barrier geometry, flow and particle trajectories could be controlled with barrier type obstacles which were evenly placed on the microchannel perpendicular to the main fluid flow direction. Smaller particles could move from the sieves of these barriers where bigger particles could only follow the main flow directions. A schematic view of this type of microchannels can be seen in Figure 2.7 [66]. This type of microfilters are developed for decreasing the particle clogging problem. Separating blood plasma from the whole blood [62,64,67], separating white blood cells from whole blood [68,69] and purification of DNA [70] are studied with this type of microfilters.

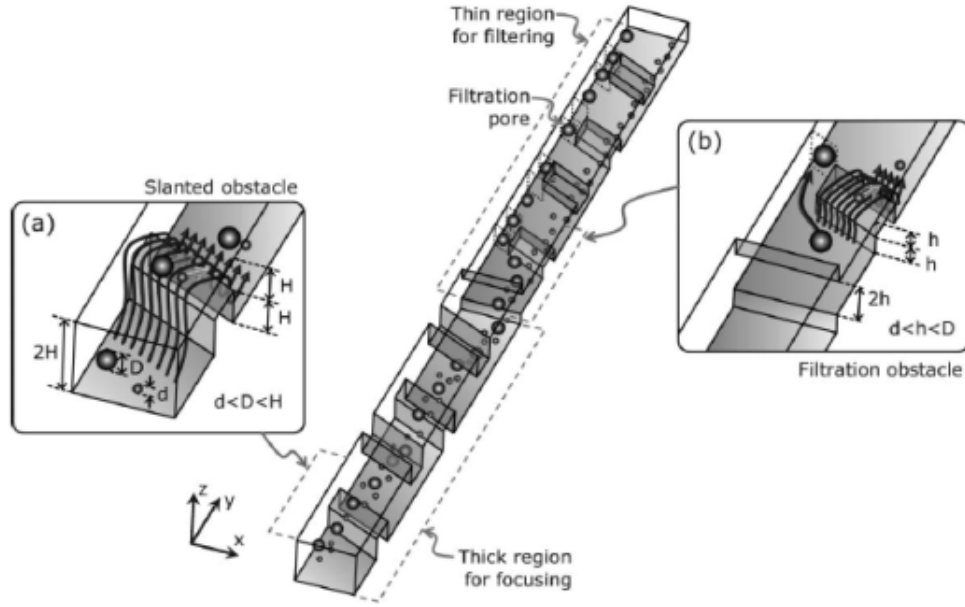


Figure 2.7: Hydrophoretic filtration by using barrier type microfilters [67].

Holes with specific sizes that allow some particles and cells pass through the filter are used in microchannels with filter geometry. Particle clogging was a quite important problem in this type of microfilters. By using microfilters with round and egg shaped holes, Zheng et al. tried to separate tumor cells from the whole blood sample [71].

2.2.2 Separation based on hydrodynamic filtration

Hydrodynamic filtration technique is used for separating particles with the channel properties and flow characteristics. In this method, microchannel has a main flowing channel and side channels that are placed perpendicular to the main flowing channel.

A general schematic view of this type of microchannels can be seen in Figure 2.8. Smaller particles in the flow tend to come closer to the main channel walls than the bigger particles. Collecting smaller particles with side channels from the main channel is dependent on the flow rate of the near wall part of main channel. When this flow rate is low, small particles cannot be collected from the side channels. With mediocre flow rates, only small particles can be collected from the side channels. In the case of high flow rates, both particles can be collected from the side channels [10].

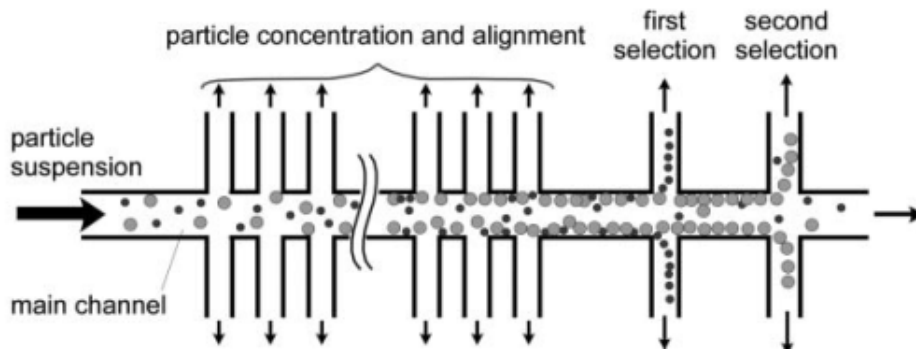


Figure 2.8: Design of hydrodynamic filtration channel network for enrichment of small and large particles [11].

2.2.2.1 Literature review about microfluidic systems with hydrodynamic filtration

Yamada and Seki, was the first group that studied this type of passive microseparation technique. They managed to separate particles with 1 and 2 μm by using a flow rate of 1 $\mu\text{l/min}$ [72]. By changing channel design, they obtained a higher yield to separate 1, 2 and 3 μm particles from different exits [73]. Then, Yamada et al. used this method to separate liver cells from parenchymal tissue with a flow rate of 50 $\mu\text{l/min}$ [74]. They also worked on spherical and non-spherical particle separation with hydrodynamic filtration technique in a wide range of flow rates [75].

Aoki et al. used side channels for introducing a new flow to the main fluid flow for focusing the particles at the center of the main flowing channel [76].

2.2.3 Separation based on pinch flow fractionation (PFF)

At least 2 different feeding solutions are used in this method. One of the entrances is used for feeding the sample solution with particles in it while the other entrance

is used for feeding only the carrier fluid. In this channel geometry, these 2 different flows are merged on a narrow main flowing channel. The channel design uses a sudden expansion after the main narrow flowing channel. A general schematic view for this type of microfluidic systems can be seen in Figure 2.9 [10].

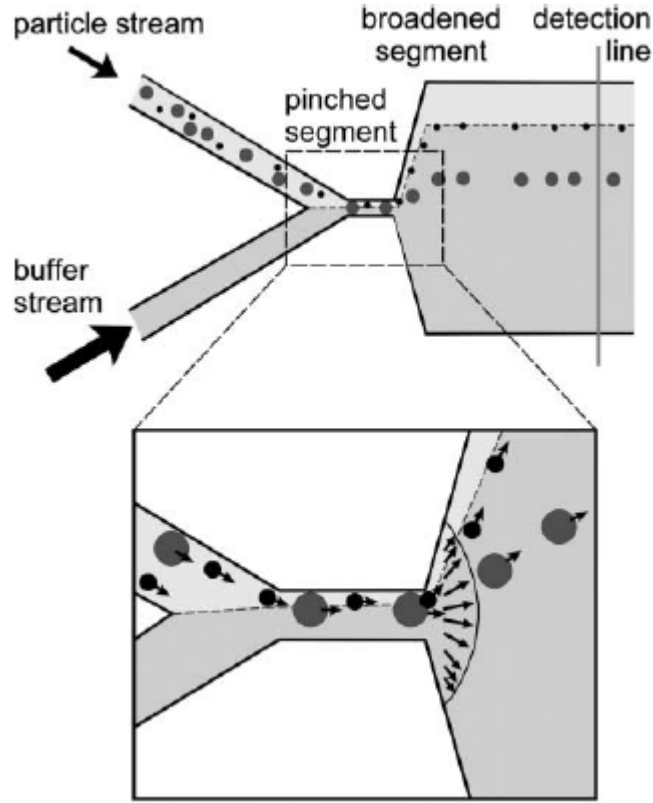


Figure 2.9: Schematic illustration of Pinch Flow Fractionation device [11].

Flow rate of the fluid with particles should be more than flow rate of the carrier fluid. With this difference at narrow channel, smaller particles are focused on the near wall section. When channel suddenly expands, particles can be gathered from separate exits because they will follow flow trajectories which are appropriate for their flow rate [10].

2.2.3.1 Literature review about microfluidic systems with pinch flow fractionation

This method was also first studied by Yamada et al. [77]. In this study they studied with 12 and 30 μm polystyrene particles for separation. They also studied on this method with different geometries [78]. They also increased the yield of separation by introducing check valves to the channel design and obtained quite high separation yields like 90% [79].

3. PARTICLE SEPARATION MECHANISM WITH INERTIAL EFFECTS ON PASSIVE MICROFLUIDIC SYSTEMS

This separation technique relies on the influence of inertial forces which allow neutrally buoyant particles to flow in a microchannel migrating to a stable equilibrium position along the channel periphery. This single particle stream can later be extracted by employing bifurcated outlets. The first experiment about inertial forces was performed by Segre and Sildenberg in which they observed the particles that tend to migrate from the axis of the pipe to a radial equilibrium position at pipe radius of 0.62, this effect is known as "Tubular Pinch Effect" [80].

Working with a wide range of Reynolds number, Matas et al. experimentally confirmed the tubular pinch effect and found that equilibrium positions shifted towards the wall with increasing Reynolds number [81]. Kim et al. observed that particles focused to a narrow band along the perimeter, which was about $0.2 D_h$ (Hydraulic diameter, Equation 3.1) in low Reynolds number ($Re < 20$) [82]. Di Carlo et al. investigated the inertial focusing in a straight microchannel and showed that uniformly distributed particles in rectangular channels migrated across the streamlines of four symmetric equilibrium positions at the center of the sides as shown in Figure 3.1 and moved closer to the walls as particle Reynolds number increased [83]. Di Carlo et al. also mentioned that the focusing positions that occur in straight channels can be determined by the fold symmetry of the channel's cross section. Therefore, the flow would only have 2 focusing positions in a rectangular system [84]. Di Carlo et al. also studied the equilibrium positions of cells by comparing the expansion channel types. They determined that the equilibrium positions moved closer to the channel centerline in a rapid expanding channel while they were closer to the channel wall in the gradual expanding channel [85]. Recently, Asgar et al. found that the inertial focusing positions of particles in a straight microchannel also depend on the channel aspect ratio which is the ratio between width and height which is schematically explained in Figure 3.2. They found that the particles equilibrated into two focused streams along

the longer sidewalls for both $H/W > 1$ (H: Height, W: Width) and $W/H > 1$ at the same channel Reynolds number [86].

$$D_h = \frac{4(\text{Area})}{(\text{Perimeter})} = \frac{4HW}{2(H+W)} \quad (3.1)$$

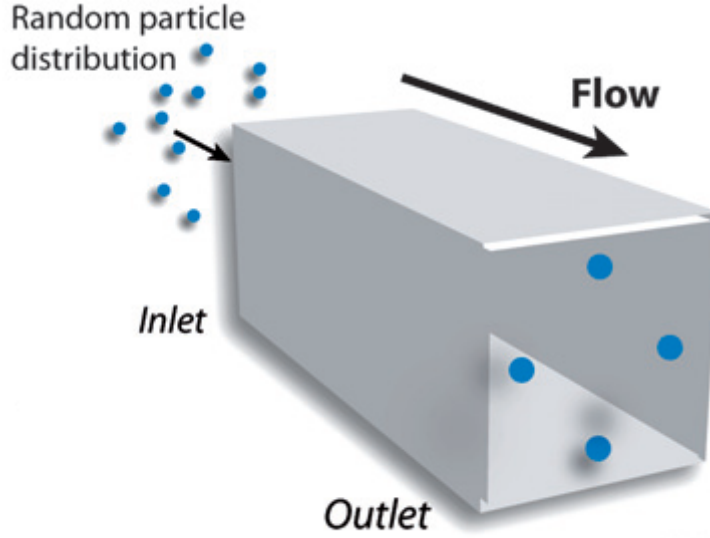


Figure 3.1: Equilibrium positions of randomly distributed particles in a rectangular microchannel after the tubular pinch effect [88].

3.1 Theoretical Background

There are 2 main forces that affect the particles in a flow depending on shear and normal stresses acting over the particle surface. These forces are the drag forces which are parallel to the main flow direction and lift forces which are perpendicular to the main flow direction. Mostly, drag forces will only accelerate the particles along the fluid flow. Lift forces are mostly cause the particle migration in lateral axes [87].

Segre and Sildenberg introduced the "Tubular Pinch Effect" which is the main focusing mechanism for straight passive microfluidic systems. Tubular pinch effect is generated by 2 inertial lift forces that act in different directions which can be seen in Figure 3.3. Wall induced inertial lift force is higher near the wall section of the channel and lower at the center of the channel, Shear-Gradient induced inertial lift force is higher at the center of the channel and lower near the wall section of the channel.

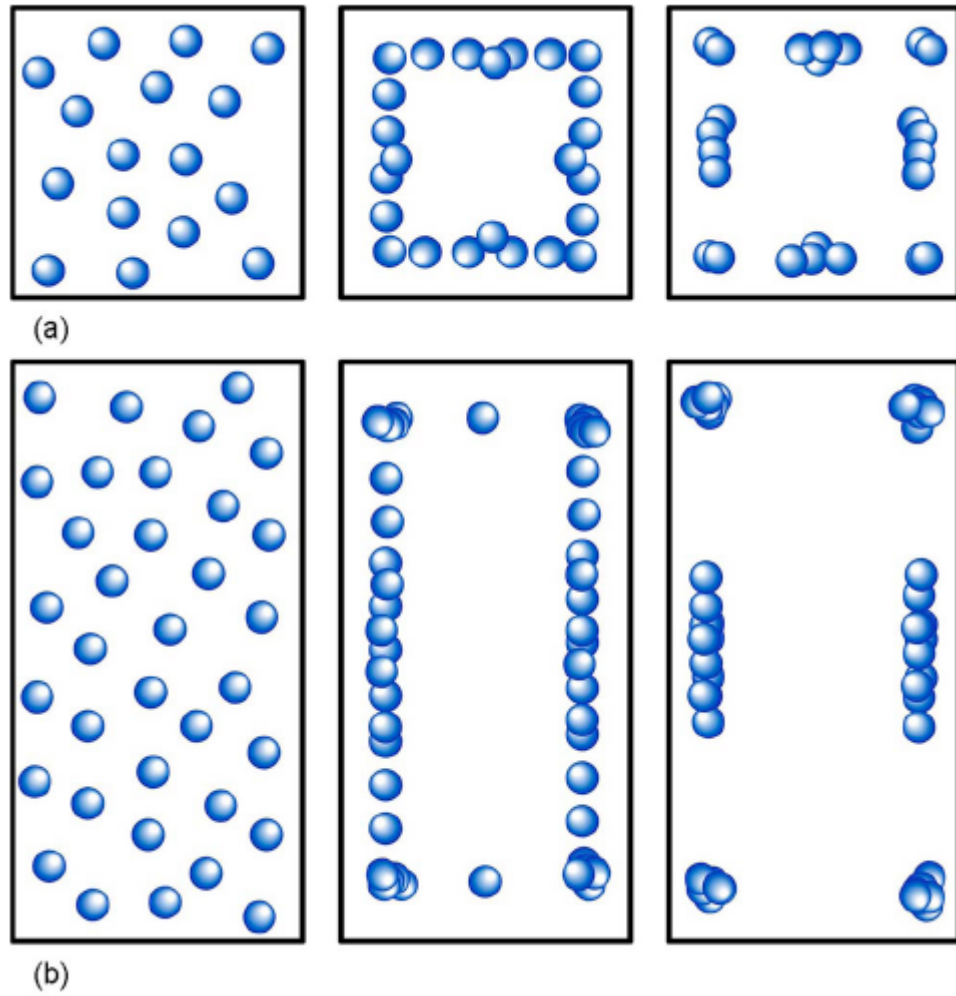


Figure 3.2: Equilibrium positions of randomly distributed particles in microchannels with different aspect ratio; (a) Aspect ratio = 1, (b) Aspect ratio $\neq 1$ [87].

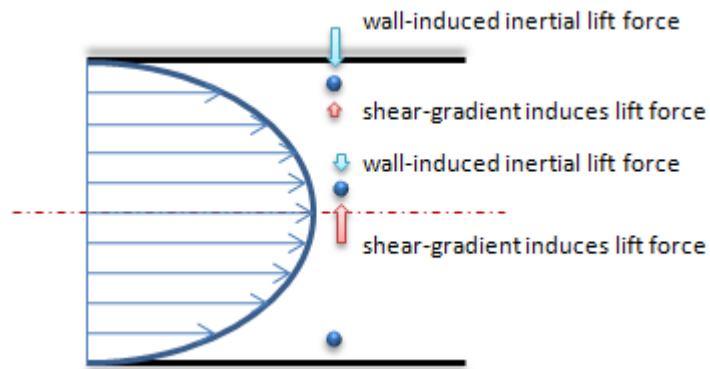


Figure 3.3: Inertial lift forces that apply on the particles in a fluid flow.

Segre and Sildenberg observed that randomly distributed spherical particles focused at a position of 0.6 times the radius of a cylindrical pipe shown in Figure 3.4. In consequence of further investigations, F_L (Lift force) is scaled with $\rho U^2 a^4 / H^2$ [87].

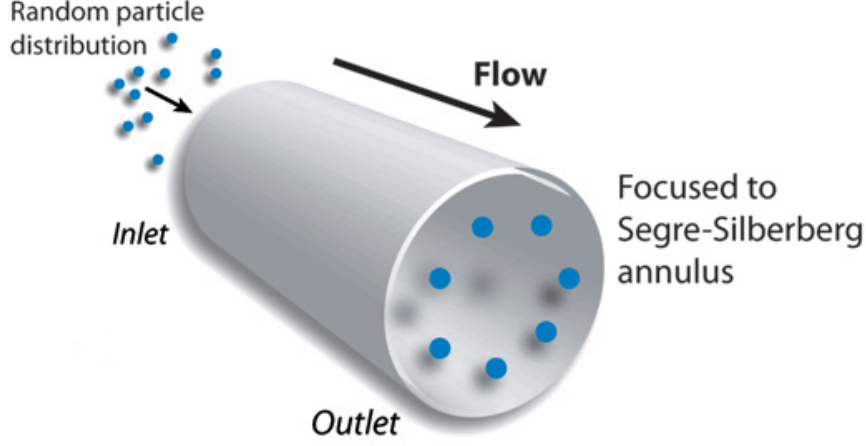


Figure 3.4: Equilibrium position in a cylindrical pipe. Observed by Segre and Sildenberg [88].

Theoretical investigations in inertial migration of particles proved that lift force has an additional dependence on Reynolds number. With this additional dependence on Reynolds number, the lift force formula is turned into Equation 3.2

$$F_L = f_L(Re, x/h) \times \rho U^2 a^4 / H^2 \quad (3.2)$$

These experiments also showed that similar forms of lift forces were observed for cylindrical channels and parallel plates which can be seen in Figure 3.4 and Figure 3.1. For all of these theoretical explanations, an assumption of small particle Reynolds number (Equation 3.3) and $a/H \ll 1$ was used so that the particle does not disturb the underlying flow field [87].

$$Re_p = Re \times \left(\frac{a}{H}\right)^2 = \frac{\rho U a^2}{H} \quad (3.3)$$

Particle Reynolds number is a measure of the ratio of inertial forces to viscous forces of the disturbance from the channel flow at the particle length scale.

At the recent studies of Di Carlo et al. they showed that this model changed throughout the lateral scaling of the channel. They indicated the lift force scaling as in Equation 3.4 [87];

$$\begin{aligned} F_L &\propto \rho U^2 a^3 / H && \text{near the channel centerline} \\ F_L &\propto \rho U^2 a^6 / H^4 && \text{near the channel wall} \end{aligned} \quad (3.4)$$

These differences in scaling between channel wall and center suggest that two disparate fluid dynamic effects are physically acting to create inertial lift equilibrium positions, which are wall induced lift force and shear gradient induced lift force [87].

Shear gradient induced lift force is linked to the flow velocity profile at the location of the particle. Due to its weight and size, the particle moves a little more slowly than the surrounding fluid and relative velocity is higher at the center part of the particle. Because of this slight difference in relative velocity, a pressure difference acts on the particle to push it towards the wall [87]. The second lift force, which is called as wall effect induced lift force is linked to the vicinity of the solid surface. The relative velocity near the wall side of the particle is reduced by the presence of the wall and the pressure on the wall side is larger than that on the centerline side. A lift force is exerted on the particle towards the channel center [87].

Focusing equilibrium positions caused by inertial lift forces are also dependent on the channel symmetry. Particles in a cylindrical channel tend to focus on an annulus following the channel symmetry which is shown in Figure 3.4. However, it has been observed that particles in a square or rectangular channel tend to focus on equilibrium positions following the 4-fold symmetry which is shown in Figure 3.1. Also, as the aspect ratio of the channel becomes larger, focusing follows the symmetry but reducing two equilibrium positions centered at the long face of the channel.

Asgar et al. indicated that the lateral migration of particles mainly depends on the ratio of the particle diameter to the channel hydraulic diameter (a_p/D_h). Inertial effects are significantly large and particle focusing occurs in short distances at $a_p/D_h > 0.07$ criterion [87]. To determine microchannel length required for particles to equilibrate at a given flow rate, particle lateral migration velocity (U_L) and minimum microchannel length (L_p) necessary for a particle to completely migrate to its equilibrium position can be derived by using Stokes' Law as,

$$U_L = \frac{F_L}{3\pi\mu a_p} = \frac{2\rho U_f^2 a_p^3}{3\pi\mu D_h^2} \quad (3.5)$$

When L_p is the maximum required particle migration distance approximated as $0.5 L_c$ and U_{max} is the maximum flow velocity.

$$L_p = \frac{3\pi\mu}{2\rho U_f} \left(\frac{L_c}{a_p}\right)^3 \quad (3.6)$$

Thus, microchannel length required for migration to the equilibrium position shows a strong dependence on the a_p/L_c

3.2 Secondary Flow in Curved Channels

In curved channels, improved mixing and precise control over fluid can be achieved by utilizing flow transverse to downstream fluid streamlines. Key parameters for controlling these flows include the channel dimension, radius of curvature and flow rate. Secondary flow occurs in fluid flow through a curved channel because of a mismatch between fluid in the center and near wall regions of the channel. Fluid layers near the channel centerline have higher inertia than fluid layers near the channel walls and would tend to flow outward around a curve. Because the channel is enclosed, stagnant fluid elements near the side wall of the channel re-circulate inward due to the movement of fluid layer near the centerline. This centrifugal phenomenon creates 2 symmetric vortices which can be seen in Figure 3.5 [87].

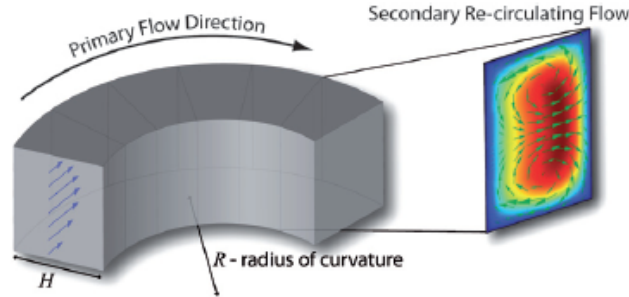


Figure 3.5: Dean flow which occurs in curved channels [88].

W. R. Dean introduced a dimensionless number for describing the magnitude of this secondary flow and Berger et al. introduced a more generally accepted form of this Dean number. Dean number described by Berger et al. can be seen in Equation 3.7 [87].

$$\kappa = (H/2R)^{1/2} Re \quad (3.7)$$

Berker et al. also notified that the radius of curvature has also important effect on the secondary flow. Following these studies, Squires and Quake described the velocity of the secondary flow velocity as Equation 3.8 [87].

$$U_D \sim \kappa^2 \mu / (\rho H) \quad (3.8)$$

For particles flowing in curved channels, inertial effects and secondary flow act together as shown in Figure 3.6. Dean drag force acts to entrain particles in the secondary flow in competition with lift forces directed towards the inertial lift positions. Di Carlo proposed that the ratio between these 2 forces is a key parameter which describes the behavior of this type of systems [87].

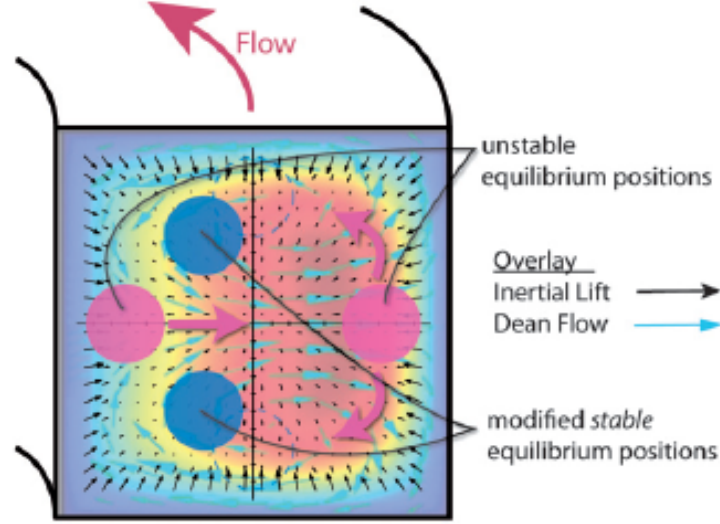


Figure 3.6: Superposition of inertial lift and Dean flow in curved channels.

They introduce an inertial force ratio that can be seen in Equation 3.9 which describes the order of magnitude scaling between these forces. This dimensionless group can be used for predicting particle behavior by 2 limiting cases which are shown in Equation 3.10.

$$R_f = a^2 R / H^3 \quad (3.9)$$

$$\begin{array}{ll} R_f \rightarrow 0 & \text{particle stream will neglect inertial equilibrium positions} \\ R_f \rightarrow \infty & \text{particle will move to inertial equilibrium positions} \end{array} \quad (3.10)$$

3.3 Literature Review of Microfluidics with Inertial Forces

After the observations of Segre and Sildenberg, separating particles from the main flow trajectories and stabilizing them at specific equilibrium positions by using the effect of inertia became quite a popular topic but commercial applications for this mechanism was quite low. This method is used on particle and cell separation applications because of its low response time but it is not preferred for applications with low amounts of sample [87].

After Segre and Sildenberg introduced the particle stabilization with the effect of inertia, Matas et al. studied this theory with a straight microfluidic channel design and observed that the equilibrium positions of the particles tend to move towards the channel walls with increase on Re number [81, 88, 89].

Equilibrium positions of the particles are also dependent on the geometry of the microchannel. Kim and Yoo used a straight channel with square profile for their experiments and on particles gathered on a thin equilibrium position along the channel perimeter at low Reynolds numbers ($20 < Re < 30$) [82]. Chun and Ladd also worked on a similar study. In their experiments with $10 < Re < 1000$, with a constant flow rate increment, they observed that there are 8 equilibrium positions at the range of $Re > 100$, and that 8 equilibrium positions decreased to 4 at the channel sides at the range of $Re > 500$. They explained this phenomenon with uniform shear gradient on 4 sides of the channel geometry [90].

Asgar et al. studied with straight microchannels with rectangle profile and they observed that particles gather on the equilibrium positions along the longer side of the channel [86, 91]. With the increasing Re number, equilibrium positions changed to 4 at the corners and 2 at the longer side of the channel which is shown in Figure 3.2. When observing this channel from top of the smaller side, only 2 distinct lines can be seen because of the overlap. Bhagat et al. also studied on straight microchannels with square profiles and observed that equilibrium positions on the rectangle profile were much more dependent on smaller side of the channel than the hydraulic diameter. The reason for this phenomenon is that the lift forces on the smaller side are higher than the lift forces on the bigger side because of the shear gradient rate. For this reason, separation on rectangle profile microchannels is only possible at low Re numbers or short channel lengths [86, 91].

Park et al. designed a straight microchannel with 80 contraction and expansion parts, a schematic view of this microchannel can be seen in Figure 3.7 [92]. They observed that vortices which occurred at the expansion part of this continuum affect the particle focusing positions. They fixed the geometry and added another expansion to the exit part of the microchannel. In their experiment, they worked with 2, 7, 15 μm particles at $Re = 70$ and observed that 15 μm particles focused around the center and 7 μm

particles focused near the channel walls [93]. Faivre et al. also studied on a similar microchannel for separation of blood plasma [94].

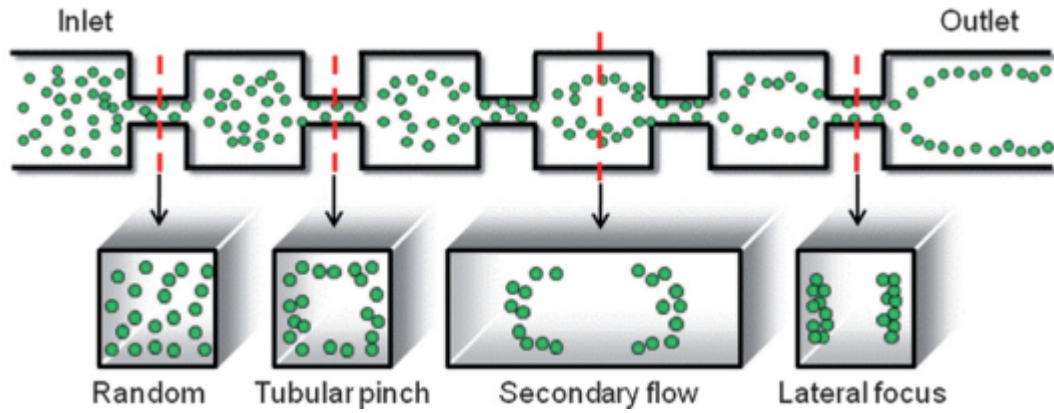


Figure 3.7: Schematic view of multi orifice microchannel that is described by Park et al. [94].

Wu et al. separated E. Coli bacteria from the blood by using kinetic inertial effects [95]. Blood cells in the sample were affected by higher quantity of inertial forces because of their larger volumes. For this reason, Wu et al. focused on a different equilibrium than E. Coli bacteria. They managed to separate the bacteria from the blood with a percentage of 99%.

Hur et al. designed a particle separation device by using 256 high aspect ratio straight microchannels [96].

3.4 Literature Review of Microfluidics with Dean Flow

Dean flow occurs at the curved channel geometry and is formed by 2 different flows which turn on opposing directions along the channel profile. Dean flow is mainly used for mixing the solutions inside a channel. In microchannels, it is quite hard to create a turbulence with just flow properties because of the low scales. The effect that occurs on the Dean flow is a kind of turbulence. Also, mixing with only diffusion principle requires quite a time in microchannels. Using Dean flow in mixing systems results on high mixing yield.

First studies on this area were performed by Liu et al. with their design of 3 dimensional curved microchannel for benefiting from chaotic advection [97]. They observed that, mixing yield increased to its maximum value when $Re > 25$, with the

increase in Re number. They also observed that dean flow was not effective and only diffusion controlled the mixing inside the microchannel when $Re < 6$.

Howell et al. studied dean flow effect on circular microchannels with different heights. They observed that high mixing yield was obtained at higher heights [98].

Sudarsan and Ugaz designed a spiral microchannel for increasing the mixing yields on the curved microchannels [99]. They observed that dean flow was negligible when $Re < 1$ and mixing was only dependent on the diffusion, and they observed that the dean vortices occurred and increased the yield of mixing when $Re > 10$. In another study, they studied on a curved microchannel with sudden expansion and contraction parts which can be seen in Figure 3.8 [100].

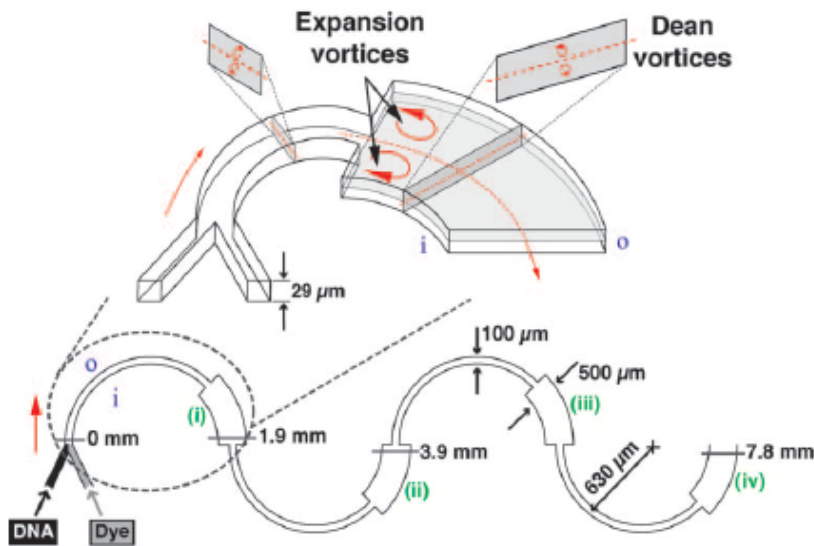


Figure 3.8: Schematic view of expansion channel design that Sudarsan used on curved microchannels [101].

They also observed that centrifugal forces were quite low for creating a secondary flow and when De number was below 1, and a movement of fluid occurred through the outer wall of the channel when the De number was over 10.

Yoon et al. studied on microchannels with single turn and separated 20 and 40 μm glass and nickel particles after the turn [101]. At $De = 28.87$, nickel particles which had smaller size but were 3 times heavier than the glass particles focused at the inner wall of the channel after U-turn and glass particles focused at the outer wall of the channel.

3.5 Literature Review of Microfluidics Using Inertial Forces with Dean Flow Together

Dean drag force and inertial lift forces are recently studied particle focusing situations, but the effectiveness of the system and the design parameters are not clear yet.

Blatter et al. worked with a curved microchannel with 90° curvature for separating the blood plasma and used 2 distinct channels after the curvature [102]. They observed that the separation yield increased at lower curvature degrees and nearly 80% separation yield was obtained.

Gregoratto et al. studied on a spiral microchannel with high aspect ratio ($H / W = 10$) with 1, 8, 10 μm particles. They indicated that 10 micron particles focused at outer wall of the microchannel at 2 ml/min while 1 μm particles' concentration on the outer wall of the microchannel is negligible [103].

Di Carlo et al. performed a comprehensive particle focusing study by using straight, symmetrical and asymmetrical microchannel geometries. They studied with particles in the range of 2 - 17 μm ranges, channel hydraulic diameters in the range of 10 - 87 μm ranges and Re number in the range of 0.1 - 255 ranges. They observed 2 discrete focusing at symmetrical microchannels and single focusing at asymmetrical microchannels [83].

They also observed that, particle focusing only occurs when $a_p / D_H > 0.07$. After this discovery, they designed an asymmetrical geometry microchannel with a changing width in the range of 350 - 650 μm and 5 exit channels which can be seen in Figure 3.9. They studied with 3.1 and 9 μm particles at 0.9 ml / min flow rate and observed that 9 μm particles focused at the outer wall of the microchannel [104].

Gossett and Di Carlo studied particle focusing mechanisms on single U-turn microchannels at $Re > 270$ and developed the design criteria for these types of microchannels [105].

Kuntaegowdanahalli et al. achieved 90% separation yield on spiral microchannels by using 10, 15 and 20 μm particles [106].

Bhagat et al. studied on a microchannel that has 5 turns, 2 entrances and 2 exit positions with 1.9 and 7.32 μm particles at low Dean numbers. They achieved to separate bigger particles at the outer wall and smaller particles at the inner wall of the microchannel at

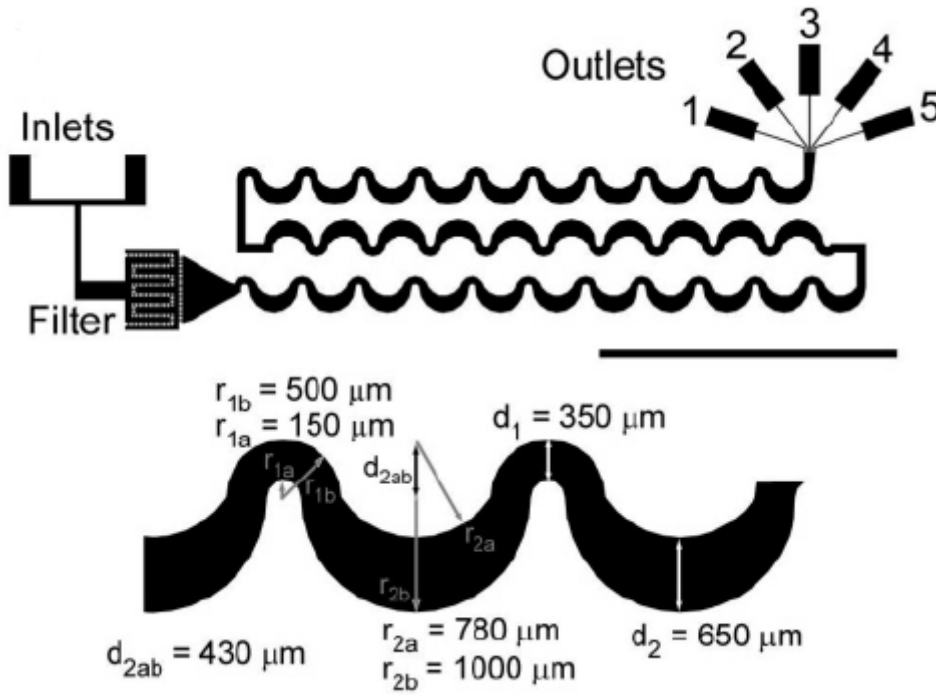


Figure 3.9: Schematic view of the asymmetrical channel design generated by Di Carlo et al. [105].

$De = 0.47$ [107].

Oozeki et al. used arc shaped microchannels with 30° , 60° , 90° (Figure 3.10) and 180° angles for studying on $1.8 - 30 \mu\text{m}$ particles at $300 - 1200 \text{ Re}$ number ranges [108]. They observed that single focusing pattern was obtained at the channel with 20 mm diameter and 180° arc angle, and observed that this particle focusing pattern moved through the outer wall of the channel with increased Re numbers. This result does not match with the results of high aspect ratio studies on spiral microchannels. Using these data, it is understandable that particle focusing patterns distance from the inner wall of the channel is dependent on the aspect ratio of the channel, and increased aspect ratio will allow particle focusing positions to move towards the inner wall of the channel [87].

Russom et al. designed a spiral microchannel widening along the width of the microchannel and used 2 different exit sections with 50 and $950 \mu\text{m}$ widths. They worked with 3 and $10 \mu\text{m}$ particles at 3.5 ml/min . They observed that nearly 98.5% of the $10 \mu\text{m}$ particles focused on the inner wall of the channel and gathered through

narrow exit while nearly 92.5% of 3 μm particles focused on and gathered at the other part of the channel [109].

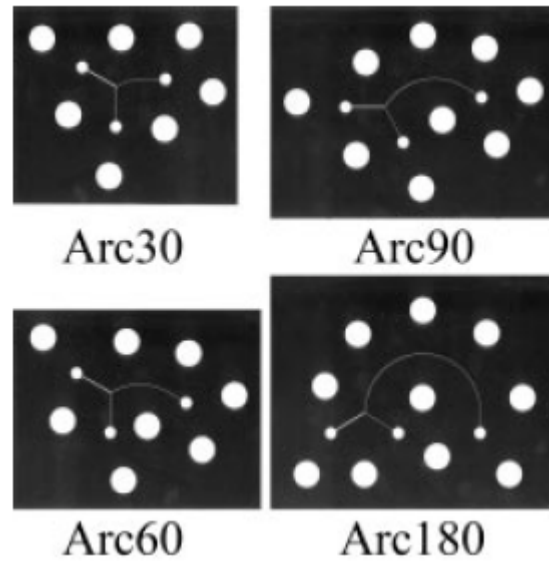


Figure 3.10: Arc shaped microchannel designs generated by Oozeki et al. [109].

4. PDMS BASED MICROFLUIDIC DEVICE PRODUCTION

In this study, PDMS based microfluidic devices have been produced with soft lithography techniques. This production method has 3 basic steps; master producing with lithography, PDMS mold production and plasma bonding. A basic production scheme can be seen in Figure 4.1

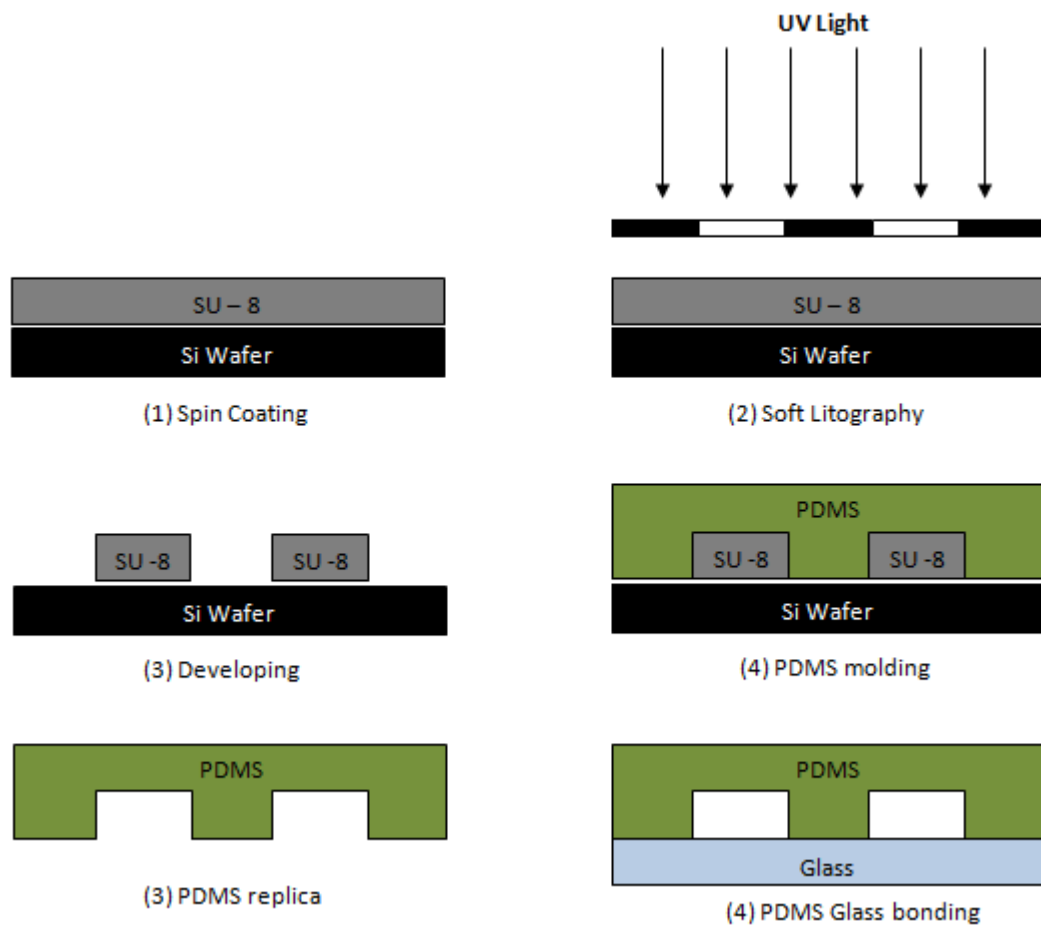


Figure 4.1: Schematic flow diagram for PDMS based microfluidic device production.

4.1 Acetate Mask Preparation

Because of its low cost and mass production options, acetate based negative mask has been chosen for this study. A sample of the acetate mask can be seen in Figure 4.2.



Figure 4.2: Acetate mask with microfluidic channel design.

4.2 Resist Coating on the Wafer

Single side polished Silicon wafers are prepared with DI water (Deionized water) cleaning and dried with N₂ gas. SU-8 3025 and 3050 are used as resist materials in this study. Some of the SU-8 properties can be listed as [110];

1. Improved adhesion
2. Reduced coating stress
3. High aspect ratio imaging
4. Vertical sidewalls
5. Greater than 100 μm film thickness in a single coat

Because SU-8 has high viscosity, covering whole wafer body equally requires a lot of time in which even solidification can result before the lithography phase. Therefore, a spin coating device is used for SU-8 coating of the wafer surface.

Wafer is placed at the center of the spin coater to assure having uniform thickness of the resist coating.

After the wafer is placed on the spin coating device, nearly 4 ml SU-8 is directly poured on the center of the wafer. After pouring, it is required to remove any air bubbles that occurred inside the SU-8 which happened because of the pouring.

Developer company of SU-8, MicroChem, provides process information for 3000 series of SU-8 resist and spin coating process information is given in Figure 4.3 [110]. Among this information, for obtaining a desired coating thickness, the spin coater steps should be set to;

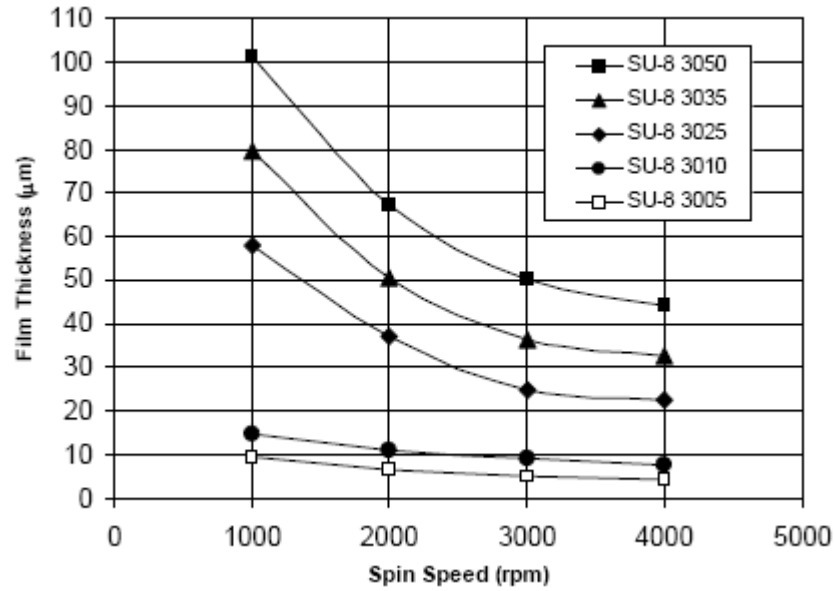


Figure 4.3: Spin speed vs. Thickness data for SU 3000 resists [111].

1. Acceleration with 100 rpm to a maximum of 500 rpm in 10 seconds
2. Acceleration with 300 rpm to a maximum of 3000 rpm in 30 seconds

First step is used to distribute the resist which is poured on the center of the wafer, over the wafer body and second step is used to obtain a desired resist thickness. This process can produce 25 μm thickness with SU-8 3025 and 50 μm thickness with SU-8 3050.

4.3 Soft Bake of Resist

After the spin coating step of production, wafer is baked at 95 °C on a hot plate for 15 minutes. This process step is quite essential and it allows SU-8 resist to create strong bonds with wafer. Process information that is provided by MicroChem can be seen at Table 4.1 [110].

It is required to perform a second spin coating step after soft baking the first layer of resist to obtain a coating thickness of 50 μm by using SU-8 3025.

Table 4.1: Soft bake times provided by MicroChem [111].

Thickness μm	Soft Bake Time minutes @ 95 °C
4 - 10	2 - 3
8 - 15	5 - 10
20 - 50	10 - 15
30 - 80	10 - 30
40 - 100	15 - 45

4.4 Soft Lithography

After the soft bake step, wafer is exposed to UV light through using the acetate mask. Intensity and energy of the UV light is quite important in this step. Lithography device that is used in this study can provide 25.50 MW/cm² for 365 nm wavelength. Process information for this step is provided by MicroChem and can be seen in Table 4.2 [110].

Obtaining the desired height of channel walls can be achieved with 8 seconds of UV processing which is determined with experimental studies in a range of 2-30 seconds.

Table 4.2: Lithography data provided by MicroChem [111].

Thickness μm	Exposure Energy mJ/cm ²
4 - 10	100 - 200
8 - 15	125 - 200
20 - 50	150 - 250
30 - 80	150 - 250
40 - 100	150 - 250

4.5 Post Exposure Bake

After lithography process, wafer is baked on hot plate in 2 steps which allow the solidification of the UV affected part on the wafer body to be finished. Process information for post exposure bake step is provided by MicroChem and can be seen in Table 4.3 [110].

Table 4.3: Lithography data provided by MicroChem [111].

Thickness μm	Post Exposure Bake Time (65 °C) minutes	Post Exposure Bake Time (95 °C) minutes
4 - 10	1	1 - 2
8 - 15	1	2 - 4
20 - 50	1	3 - 5
30 - 80	1	3 - 5
40 - 100	1	3 - 5

For obtaining the desired coating thickness of 25 μm and 50 μm , wafer is post exposure baked as;

1. for 1 minute at 65 °C
2. for 5 minutes at 95 °C

4.6 Developing SU-8 Master

The design is produced on the wafer body as a solid structure after the UV exposure and post exposure bake. Chemical development method is used to remove the residual SU-8 from the wafer and finishing the development of the microchannel on the wafer. Processing time information for this step is also provided by MicroChem and can be seen in Table 4.4 [110].

Table 4.4: Developing SU-8 Master data provided by MicroChem [111].

Thickness μm	Development Time Time
4 - 10	1 - 3
8 - 15	4 - 6
20 - 50	5 - 8
30 - 80	6 - 12
40 - 100	7 - 15

For cleaning the residual SU-8 from the wafer body and not damaging the solidified design, the wafer is processed for about 7 minutes as shown in Figure 4.4. After 7 minutes, residuals of the removing solution should be cleaned with IPA and DI water respectively and then wafer should be dried with N_2 gas.

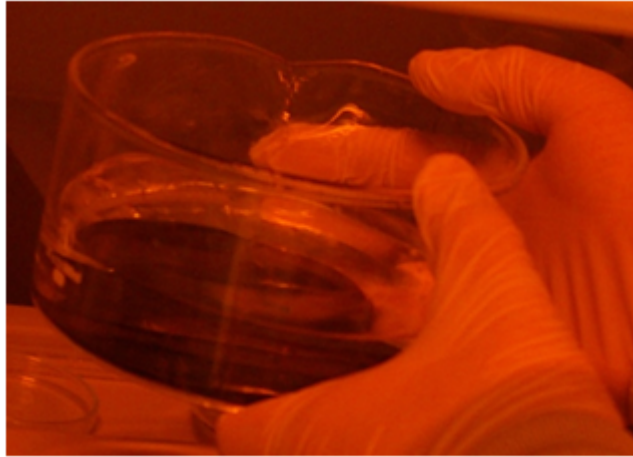


Figure 4.4: Developing SU-8 master on the wafer.

4.7 Hard Bake (Curing of the Developed SU-8 Master)

After the development stage, design of the microchannel can be seen on the wafer easily. As a last processing step, the wafer is baked in an oven at 150 °C for 2-4 hours. Hard baking of the wafer will increase the chemical and physical properties of the produced resist matter. SU-8 resist and wafer is called as "Master" or "SU-8 Master" after this step.

4.8 Characterization of SU-8 Master

It is essential to characterize the produced SU-8 master for checking whether there is any structural failure over the microchannel design by using a microscope and profilometer. In Figure 4.5 and Figure 4.6, examples of microchannels can be seen.

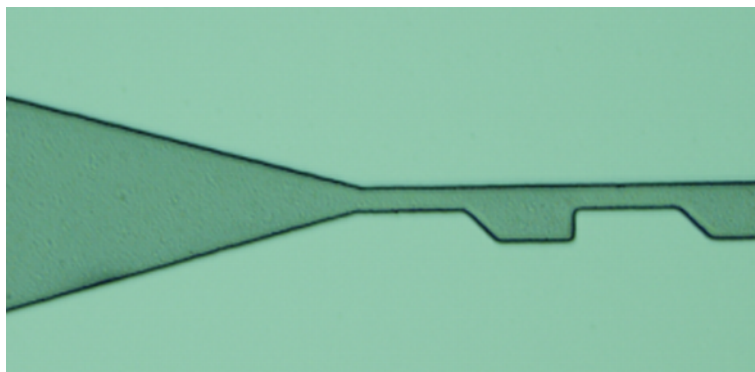


Figure 4.5: No defect on microstructure.

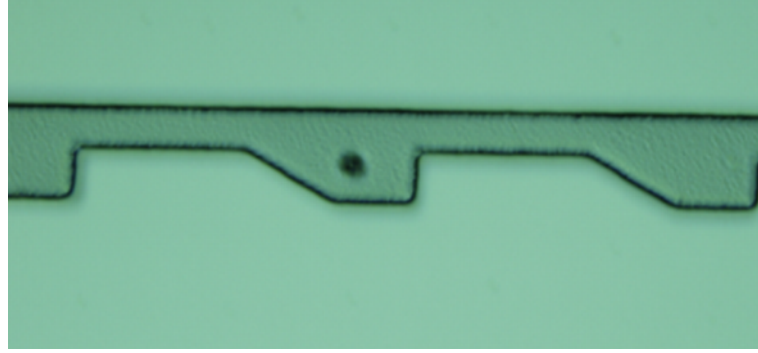


Figure 4.6: Defect on microstructure.

Along with the structural test, SU-8 master is also analyzed with a profilometer for determining channel height that has been obtained at the production stage.

SU-8 thicknesses may vary over the SU-8 master body, but this variation must have quite a narrow range. An example of profilometer analysis for straight channels that have been studied in this project can be seen in Figure 4.7.

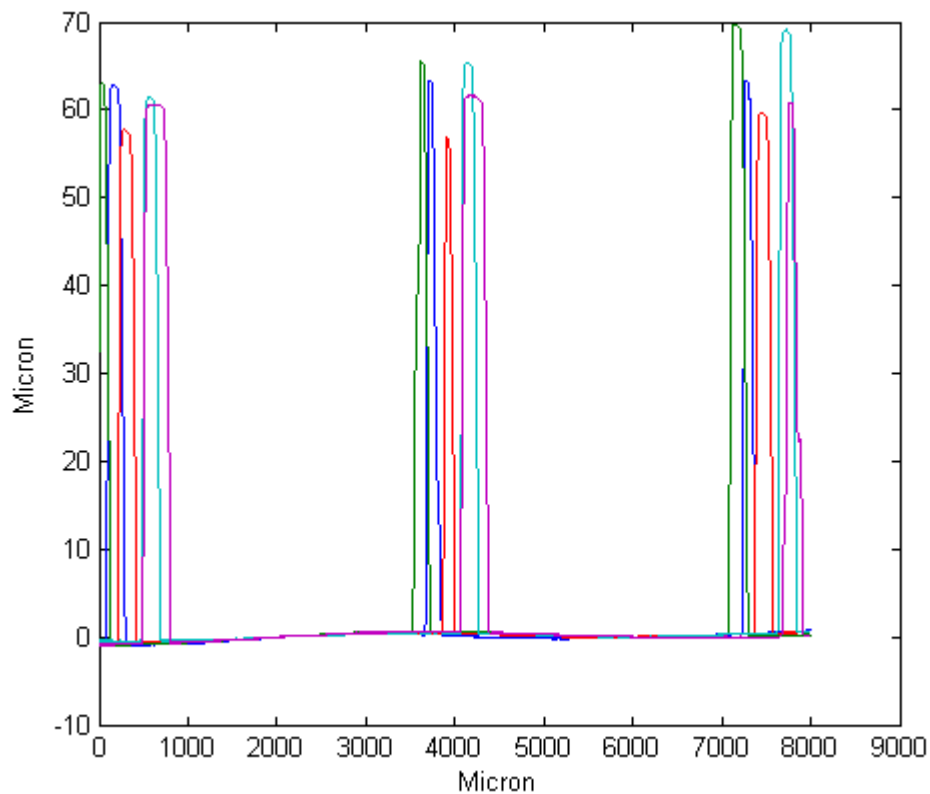


Figure 4.7: Profilometer analysis of straight microchannels.

4.9 Production of PDMS Mold

PDMS is used as mold material for microfluidic channel because of its transparency and high bonding force with glass surface. Liquid PDMS and its solidification agent is mixed with 10/1 weight ratio respectively. Mixed PDMS is poured at the center of the SU-8 master. The bubbles that occur on the PDMS are removed by using a vacuumed atmosphere. After bubble removing, PDMS is solidified at 65 °C for at least 2 hours. For peeling the PDMS from the SU-8 master surface easily, it is kept at this temperature for at least 12 hours in this study.

After the solidification process, PDMS is peeled off the SU-8 master and cleaned. SU-8 master can be stored for later uses. Fitting holes on the PDMS mold are punched with a 2 mm biopsy punch and microchannel design area is cut from the whole PDMS mold. After these steps, PDMS mold is cleaned with IPA and DI water and dried with N₂ gas.

4.10 O₂ Plasma Bonding of PDMS with Glass Surface

Glass and PDMS are cleaned with IPA and DI water and dried with N₂ gas before this step. They are placed on a hot plate at 45 °C for 15 minutes with their bonding sides up. After this baking process, PDMS and Glass are placed inside the oxygen plasma device. Plasma environment is vacuumed and then pure oxygen gas is introduced to the vacuum chamber with a low rate. After 45 seconds of RF plasma application, PDMS and Glass are removed from the plasma device and placed on each other. With the help of oxygen plasma process, these 2 different materials will produce a powerful bond which results in the final product. For increasing the bonding power that is obtained between PDMS and glass, the device should be placed on a hot plate at 75 °C for at least 15 minutes.

5. CHARACTERIZATION OF MICROFLUIDIC SYSTEMS

Fluidic characterization of the microchannels is performed with Olympus BX 51 fluorescence microscope with a DP 72 camera for imaging the fluorescence particles. This camera head has 3 different fluorescence filters for detecting different fluorescent colors (red, green, blue color filters). Images that are obtained with the microscope have 1360 x 1024 resolution and 50 image accumulation with variant exposure times. Image accumulation technique is used for analyzing the system in a time span by merging 50 pictures that has been captured in 1 second. A view of the microfluidic system integrated to the microscope can be seen it Figure 5.1 and an example of particle analysis result can be seen it Figure 5.2.

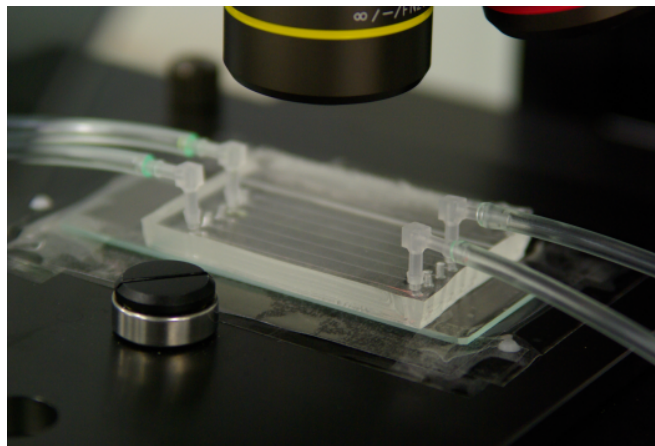


Figure 5.1: Microfluidic system integrated for particle analysis.

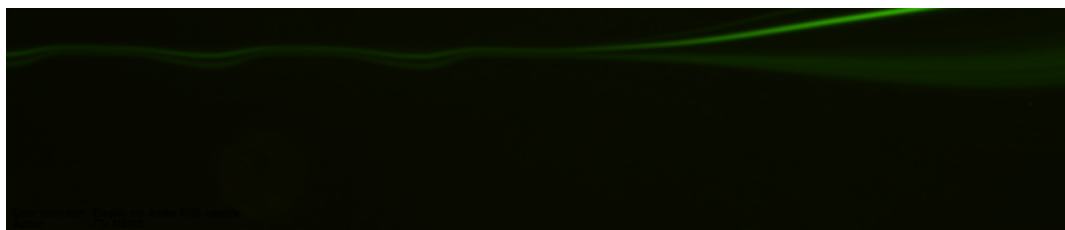


Figure 5.2: Example of particle analysis result.

An integrated line profile option of microscope software is used for analyzing the particle focusing behaviors. An example of the line profile analysis can be seen in

Figure 5.3. This graph contains the fluorescent color intensity value of different particles on y axis and the length of analysis on the x axis.

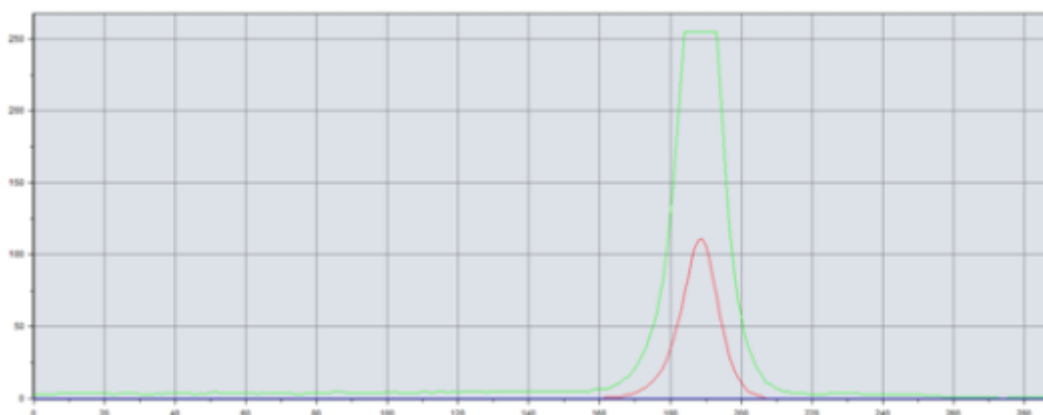


Figure 5.3: Example of line profile result.

Polystyrene spherical microparticles that are commercially produced by Thermo Scientific with precise sizes are used to characterize microfluidic systems. These particles are solved in DI water with different concentrations for different experiments. Two different particles have been used in this study; $9.9\ \mu\text{m}$ green fluorescent particles and $3.0\ \mu\text{m}$ red fluorescent particles. A view of green fluorescent particles under the appropriate filter can be seen in Figure 5.4. Before each experimental study, particle solution is mixed with a magnetic shaker for at least 5 minutes to obtain homogeneity at the solution.

A syringe pump is used for pumping the solution to the system.

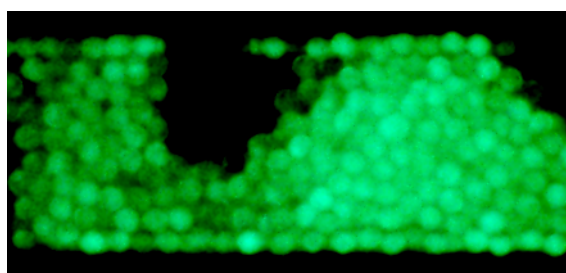


Figure 5.4: Green particles ($9.9\ \mu\text{m}$) view under the microscope.

6. EXPERIMENTAL RESULTS

6.1 Particle Focusing in Straight Microchannel

Particle focusing in straight channel systems has been introduced by Segre and Sildenberg [80]. Later, Asgar et al. indicated that a particle's focusing in a microchannel system is dependent on the particle diameter (a_p) and hydraulic diameter (D_h) of the microchannel [87]. For understanding this effect a microfluidic system designed and studied with $9.9\ \mu\text{m}$ and $3.0\ \mu\text{m}$ particles at 3 different flow rates. Designed microchannel can be seen in Figure 6.1 and its features can be seen in Table 6.1.

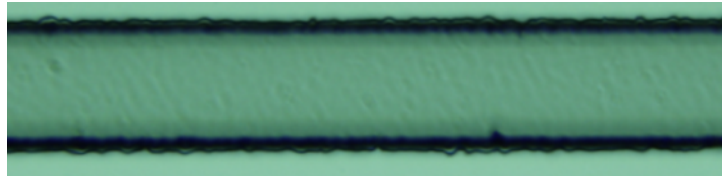


Figure 6.1: Straight microchannel for determining particle diameter effect on focusing.

Table 6.1: Straight microchannel design properties.

Channel Length	80 x 400 μm
Channel Width	100 μm
Channel Height	60 μm
Obstacle type	None

Asgar et al. indicated that particle focusing with inertial effects occurs at short distances when $a_p/D_h > 0.07$ criterion is obtained. For this purpose, the microchannels are designed with 100 μm width and produced with nearly 60 μm height at the production stage. For achieving the aimed height, production with double SU-8 3025 coating method is used, and an average of 60 μm is obtained. With this study, main flow velocity is also studied for its effect on the particle focusing when inertial effects have potential. 10, 50 and 100 $\mu\text{l/min}$ flow rates are used. Experimental data can be

seen in in Table 6.2 and analysis results can be seen at Figure 6.2. D_h calculations are performed with Equation 3.1.

Table 6.2: Experimental data for particle focusing in straight microchannel.

Flow Rate ($\mu\text{l/min}$)	D_h (μm)	a_p (μm)	a_p/D_h	Velocity (m/sec)	Reynolds Number	Particle Reynolds Number
10	75	3.0	0.04	4.63×10^{-4}	3.0×10^{-2}	5.56×10^{-5}
25	75	3.0	0.04	2.31×10^{-4}	1.7×10^{-1}	2.78×10^{-4}
100	75	3.0	0.04	4.63×10^{-3}	3.5×10^{-1}	5.56×10^{-4}
10	75	9.9	0.132	4.63×10^{-4}	3.0×10^{-2}	6.05×10^{-4}
25	75	9.9	0.132	2.31×10^{-4}	1.7×10^{-1}	3.03×10^{-3}
100	75	9.9	0.132	4.63×10^{-3}	3.5×10^{-1}	6.05×10^{-3}

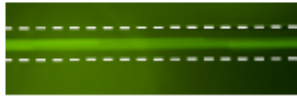
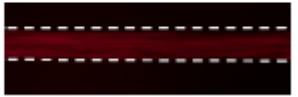
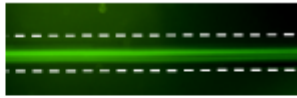
Flow Rate ($\mu\text{l/min}$)	Green Fluorescent Particle 9.9 μm	Red Fluorescent Particle 3.0 μm
10		
25		
100		

Figure 6.2: Fluid flow analysis of these systems with fluorescence microscope.

The data of a_p/D_h which is given in Table 6.2 shows that green particles with bigger size should focus in this microchannel design and red particles with smaller size should not focus in this microchannel design. With respect to the particle analysis images of this experiment, $a_p/D_h > 0.07$ criterion is proven to be true and particle focusing in systems with dominant inertial effects is quite dependent on the particle diameter (a_p). These results also indicate that particle focusing mechanism is not too dependent on the fluid flow rate, but this variable affects the particle focusing position inside the microchannel and the width of the focused particle streamline.

6.2 Particle Focusing Positions in Straight Microchannel

According to the literature, particles tend to focus at the center of the channel walls in a microfluidic system as shown in Figure 3.1. For determining particle focus

positions, microfluidic systems whose properties given in Table 6.1 has been used. In this experimental setup, particle focusing positions have been observed similar to literature, at 140 $\mu\text{l}/\text{min}$ flow rate. Particle focusing positions can be seen in Figure 6.3 and Figure 6.4. These images are captured at the exit part of the microchannels with 50 frame accumulation. These images indicate that red particles ($3.0\ \mu\text{m}$ - $a_p/D_h = 0.04 < 0.07$) is spread along the microchannel width but green particles ($9.9\ \mu\text{m}$ - $a_p/D_h = 0.132 > 0.07$) focused on 3 visible positions at this flow rate.

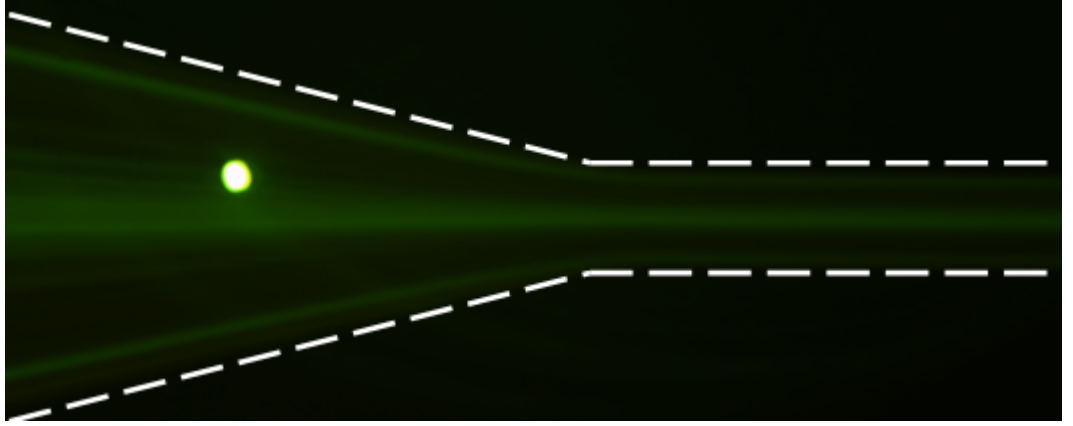


Figure 6.3: Green particle ($9.9\ \mu\text{m}$ - $a_p/D_h = 0.132 > 0.07$) focusing image in straight microchannel at 140 $\mu\text{l}/\text{min}$ flow rate.

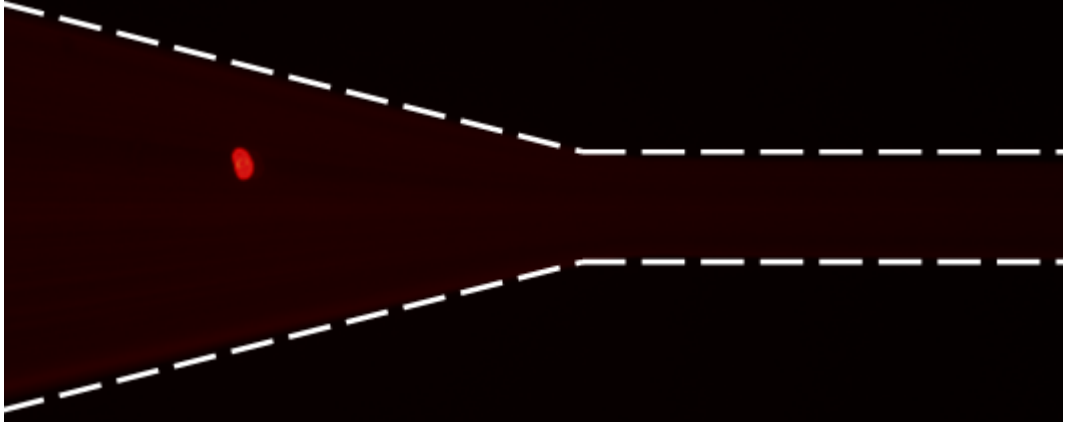


Figure 6.4: Red particle ($3.0\ \mu\text{m}$ - $a_p/D_h = 0.04 < 0.07$) focusing image in straight microchannel at 140 $\mu\text{l}/\text{min}$ flow rate.

In Figure 6.3, only 3 particle focusing positions can be seen, but actually there are 4 particle focusing positions in this experimental result. Because image capturing of microscope only works from the top of the channel, 2 particle focuses are overlap to form the particle focus which is seen at the center of the Figure 6.3. These 2

particle focuses are top and bottom particle focuses. Because of the overlap of these focuses, the centerline focus which is seen in Figure 6.3 has more intensity value than the side focuses. This intensity difference can be seen in Figure 6.5. With this

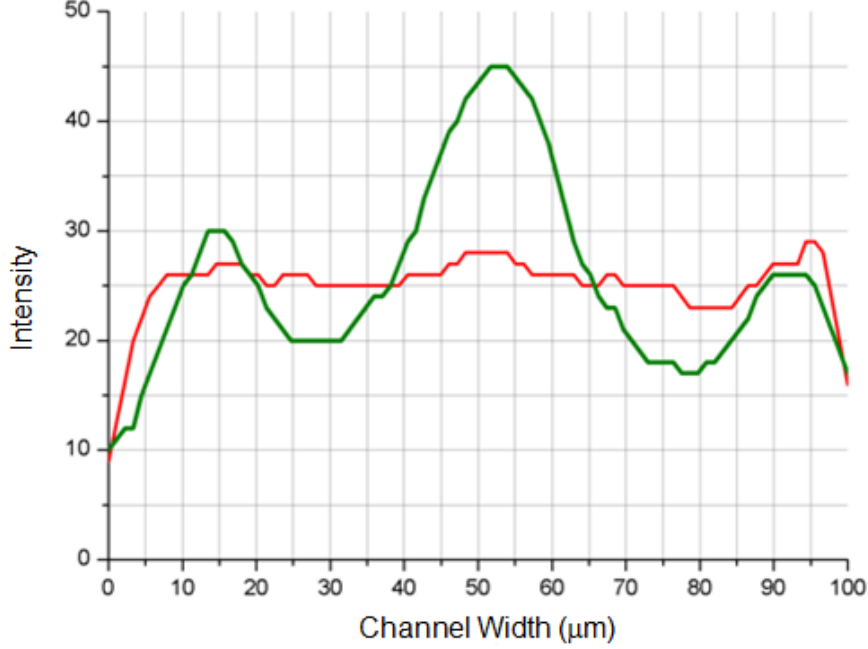


Figure 6.5: Line profile data for Figure 6.5 - Green particles line profile is shown with green line and red particles line profile is shown with red line.

experimental study, 4 different particle focusing positions of green particles ($9.9 \mu\text{m}$ - $a_p/D_h = 0.132 > 0.07$) have been obtained at the exact positions of the microchannel which are indicated in literature.

6.3 Particle Focusing Mechanism in Contraction - Expansion Straight Microchannels

In this experimental study, straight microfluidic channels with contracting and expanding geometry are studied. The angles in the entrance of contraction part of these channel designs are varied and studied for determining whether this angle has an effect on the inertial forces that apply to the particles. Particle focusing is measured at various fluid flow rates.

The angle of the entrance to contraction part was varied on this study while other geometric parameters were kept constant. Schematic view of the designed channel geometry can be seen at Figure 6.6 and geometric data is given in Table 6.3.

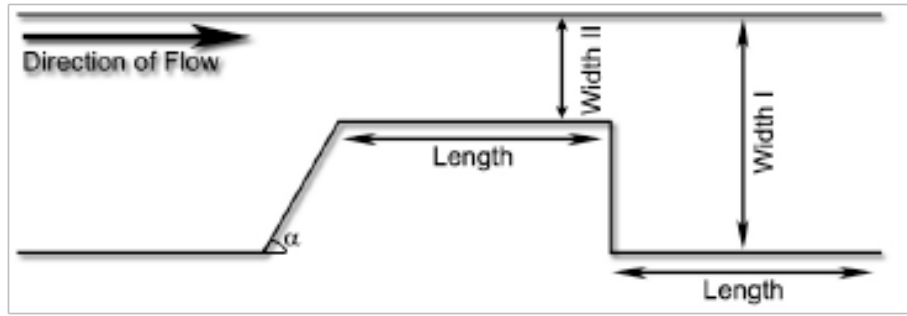


Figure 6.6: Schematic view of designed channel geometry for determining contraction and expansion geometry effects on inertial focusing along with the effects of the contraction part entrance angle.

Table 6.3: Geometric data of designed channel geometry for determining contraction and expansion geometry effects on inertial focusing along with the effects of the contraction part entrance angle.

Width I	100 μm			
Width II	40 μm			
Length	200 μm			
Depth	60 μm			
α	30	45	60	90

For characterization of this setup, a mixture of 0.04 ml solution containing 1% of 9.9 μm green fluorescent particles and 70 mL DI was used. Flow rates were determined with respect to the particle Reynolds numbers (Re_p). It has been shown that particle inertial lift forces are dominant when $\text{Re}_p > 1$ causing particles to migrate laterally inside the channels [87]. Flow rates and particle Reynolds numbers used in this study can be seen in Table 6.4.

Table 6.4: Flow and particle Reynolds numbers in Expanding - Contracting parts of the microchannel.

Flow Rate ($\mu\text{l}/\text{min}$)	Re_p (expansion part)	Re_p (contraction part)
105	0.38	1.49
120	0.44	1.70
140	0.51	1.99
160	0.58	2.27
180	0.65	2.55

Images that were captured in this experimental study will be introduced angle by angle with results responding to that angle. For this experimental study, the flow inside the

microchannels was captured with 50 frame accumulation and line profile analysis has been performed in 2 different ways;

- Position of focuses has been investigated
- Intensity/Width value of focuses has been investigated

6.3.1 Results and discussion about 90° design

Captured images of flow for this type of design can be seen in Figure 6.7.

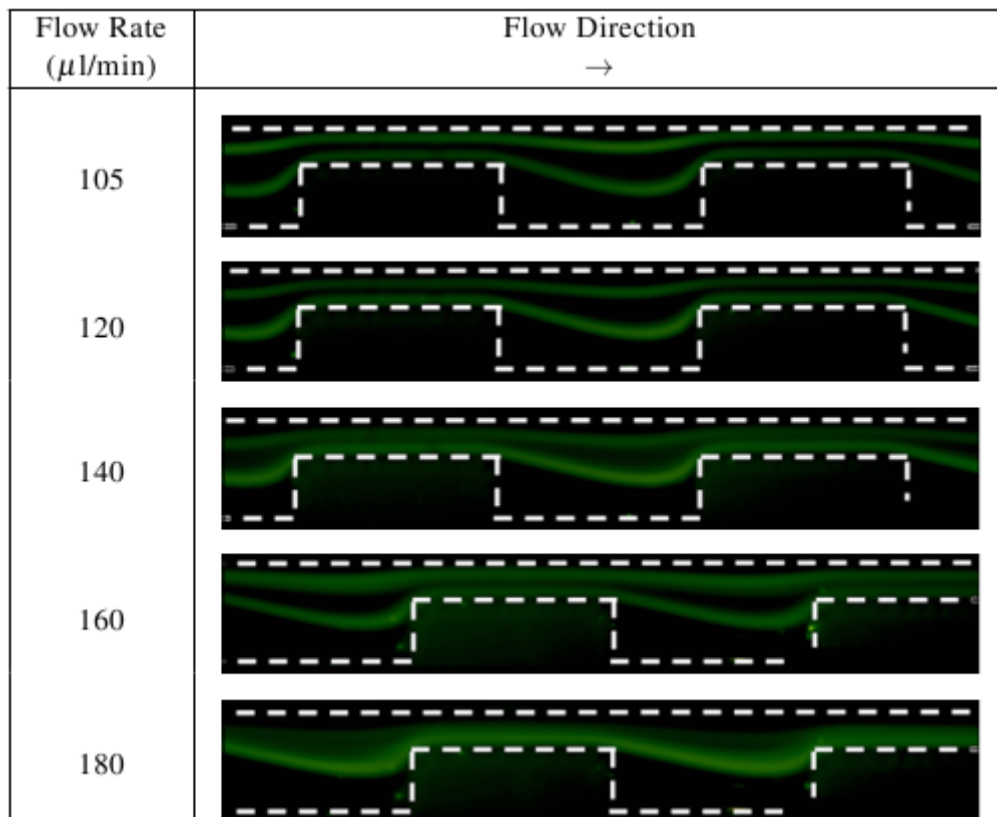


Figure 6.7: Fluorescent particle images of 90° design.

It can be seen that this type of channel produced 2 focused particle streamlines inside the microchannel. Results of these experimental studies match with Park et al.'s double sided contraction - expansion channel except that this microchannel produced non-symmetrical focuses along to the channel width [92]. Positions of the focuses with respect to the Re_p can be seen in Figure 6.8.

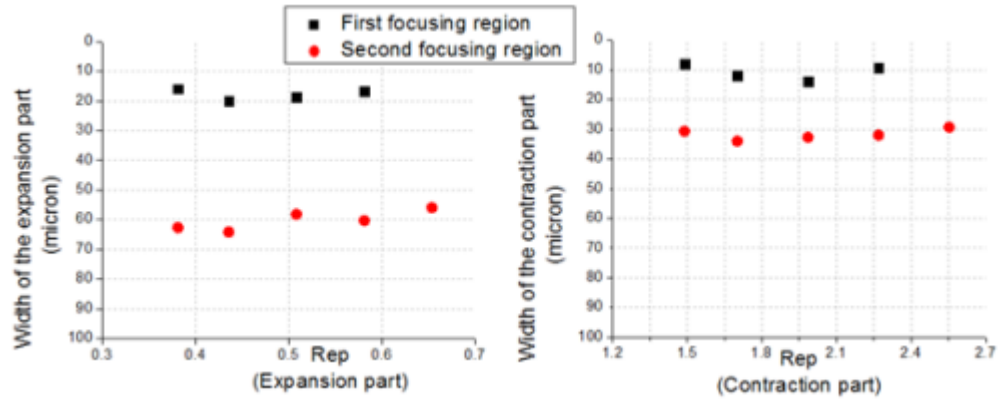


Figure 6.8: Particle focus positions of 90° design.

6.3.2 Results and discussion about 30° design

Captured images of flow for this type of design can be seen in Figure 6.9.

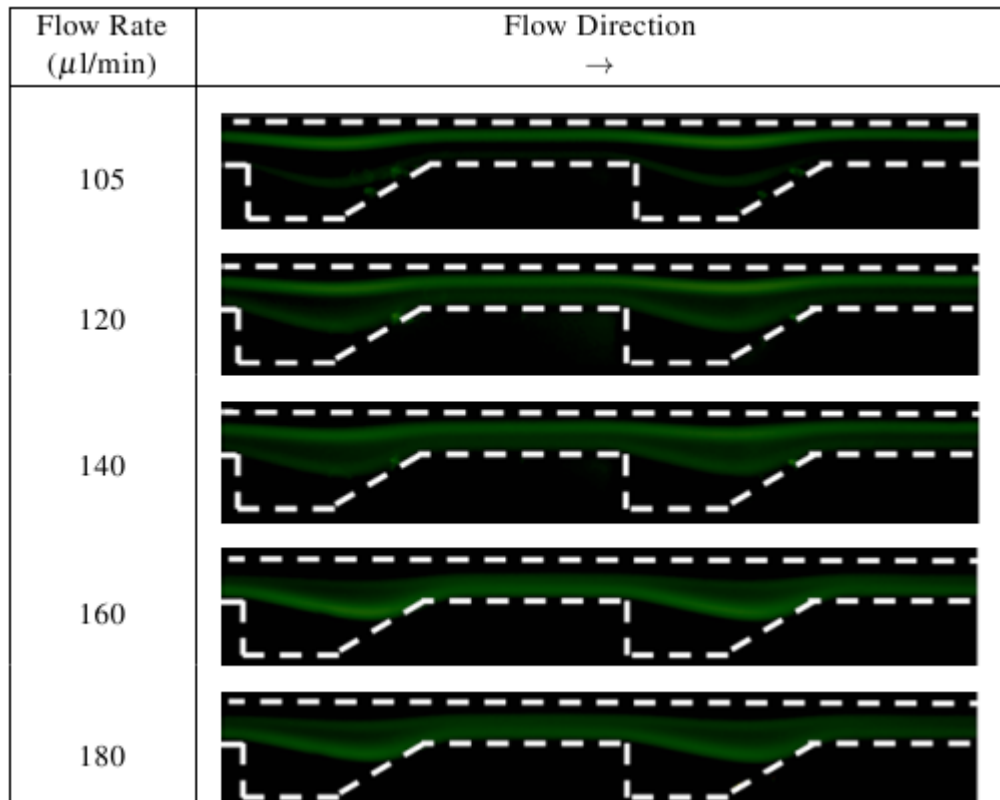


Figure 6.9: Fluorescent particle images of 30° design.

It can be seen that this type of channel produced single focused particle streamlines inside the microchannel at 105 $\mu\text{l}/\text{min}$ at the contraction part and this single particle streamline is quite intense in expansion parts which can allow the second visible

particle streamline to be neglected. This situation will be explained in details on Intensity/Width analysis. This single focused particle trajectories are divided into 2 different focuses at higher flow rates. Obtaining a single focused particle streamline in this type of microchannel means that higher separation yield can be achieved. Positions of the focuses with respect to the Re_p can be seen in Figure 6.10.

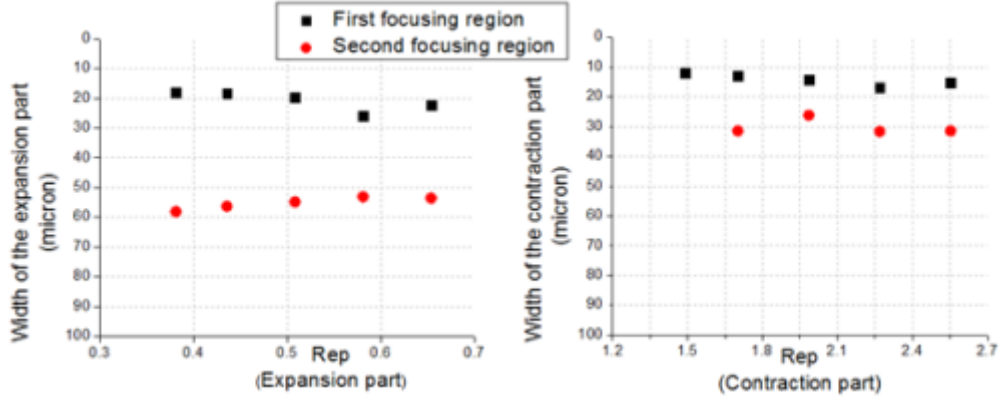


Figure 6.10: Particle focus positions of 30° design.

6.3.3 Results and discussion about 45° design

Captured images of the flow for this type of design can be seen in Figure 6.11.

It can be seen that this type of microchannel produced single focused particle streamline at 105 $\mu\text{l}/\text{min}$ at the contraction and expansion parts of the microchannel. Also it produced single focused particle streamline at 120 $\mu\text{l}/\text{min}$ only at the contraction part of the microchannel. These single particle trajectories are quite intense at expansion parts which allows the second visible focused particle streamline to be neglected. This situation will be explained in details at the Intensity/Width analysis. This single focused particle streamline was divided into 2 different focuses at higher flow rates.

After changing the design from 90° to 30°, the system produced a single focused particle streamline at 105 $\mu\text{l}/\text{min}$ at the contraction part. After that, through changing the design from 30° to 45°, the system produced a pure single focused particle streamline at 105 $\mu\text{l}/\text{min}$ and a single focused particle streamline at 120 $\mu\text{l}/\text{min}$ at the contraction part. With these results, it can be predicted that 60° design may produce

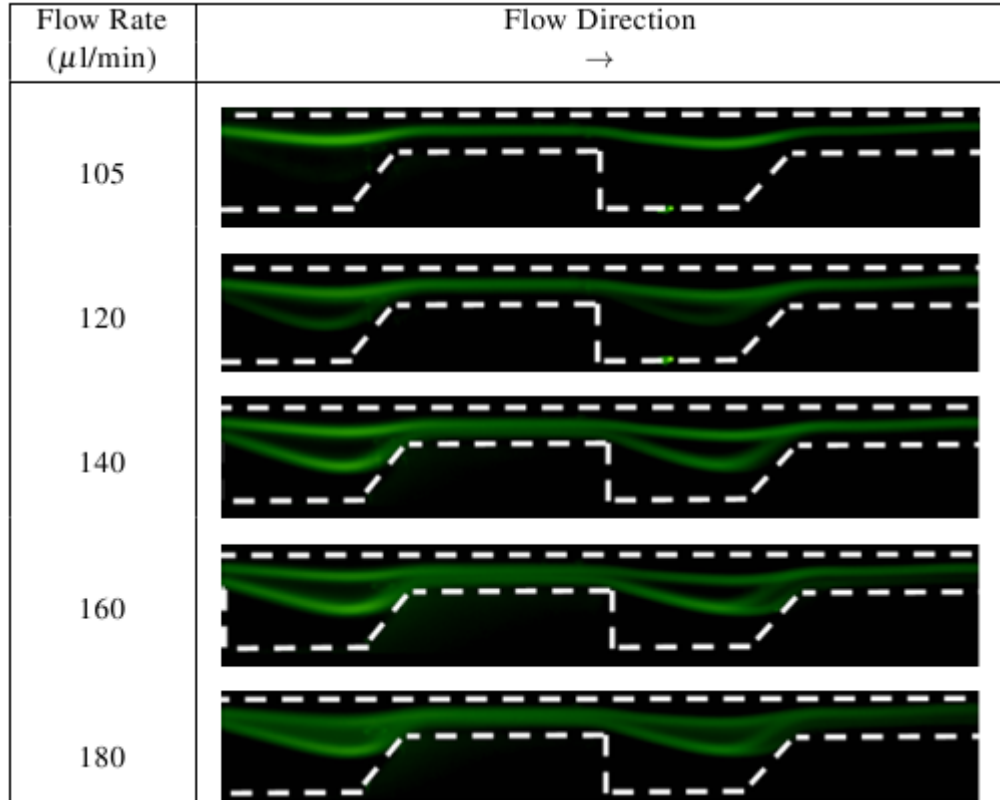


Figure 6.11: Fluorescent particle images of 45° design.

pure single focused particle streamlines at 105 and 120 $\mu\text{l/min}$. Positions of the focuses with respect to the Re_p can be seen in Figure 6.12.

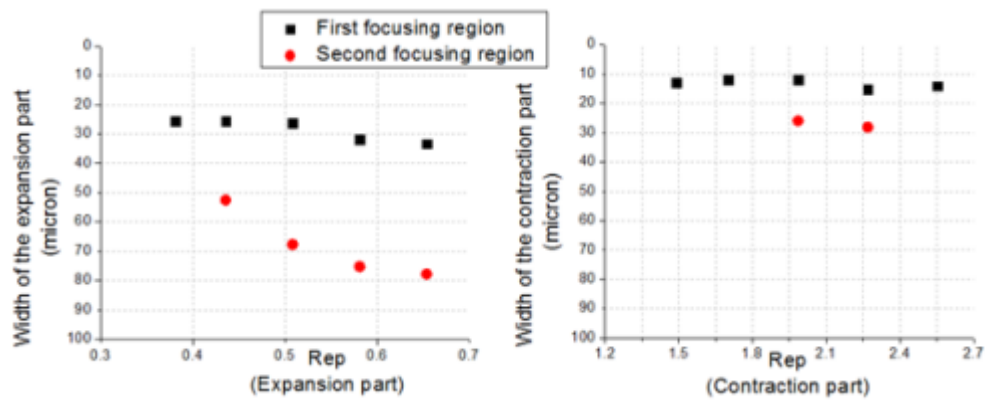


Figure 6.12: Particle focus positions of 45° design.

6.3.4 Results and discussion about 60° design

Captured images of the flow for this type of design can be seen in Figure 6.13.

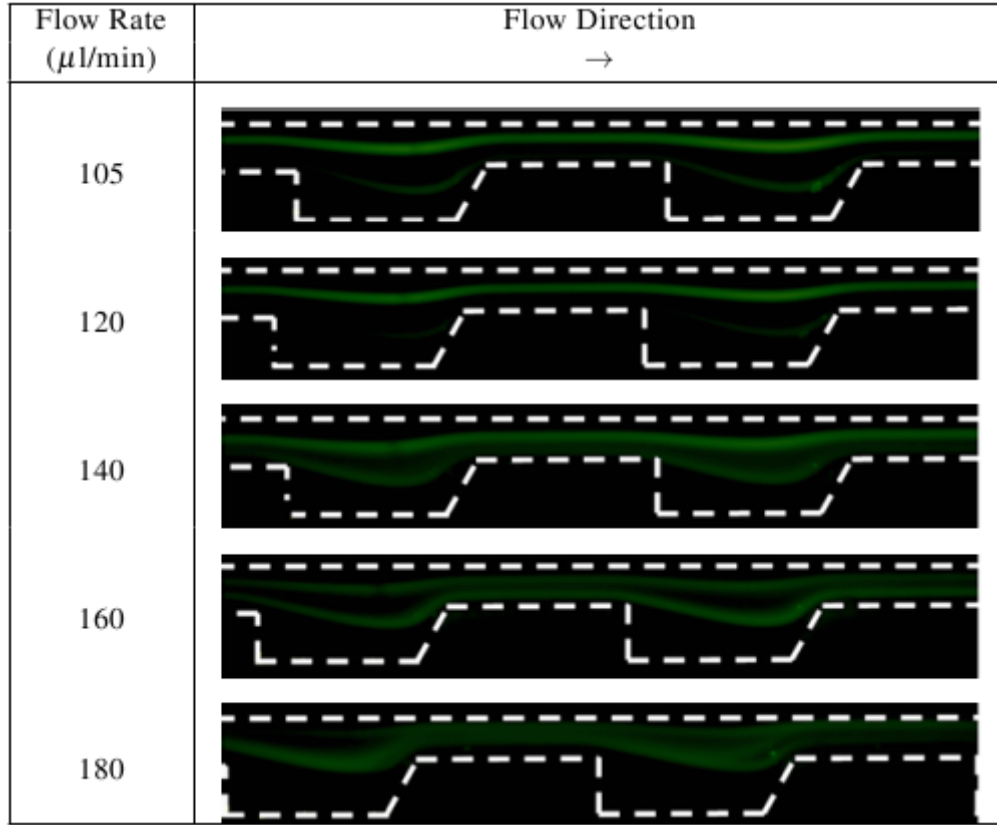


Figure 6.13: Fluorescent particle images of 60° design.

It can be seen that the prediction that has been made in previous section is partially correct. Through changing the design from 45° to 60° , the system produced a pure single focused particle streamline at $120 \mu\text{l/min}$ and a single focused particle streamline at $105 \mu\text{l/min}$ at the contraction part. This means that, through changing the channel design in the direction of $30^\circ \rightarrow 45^\circ \rightarrow 60^\circ$, pure single focused particle will occur and move towards the higher flow rates. In this design, $105 \mu\text{l/min}$ seems to have a second focused particle streamline at the contraction parts of the channel, but the single particle trajectories that are alone at the contraction parts are quite intense at the expansion parts which allows the second visible particle streamlines to be neglected. This situation will be explained in details at the Intensity/Width analysis. This single focused particle streamline was divided into 2 different focused particle streamline at higher flow rates.

Positions of the focuses with respect to the Re_p can be seen in Figure 6.14.

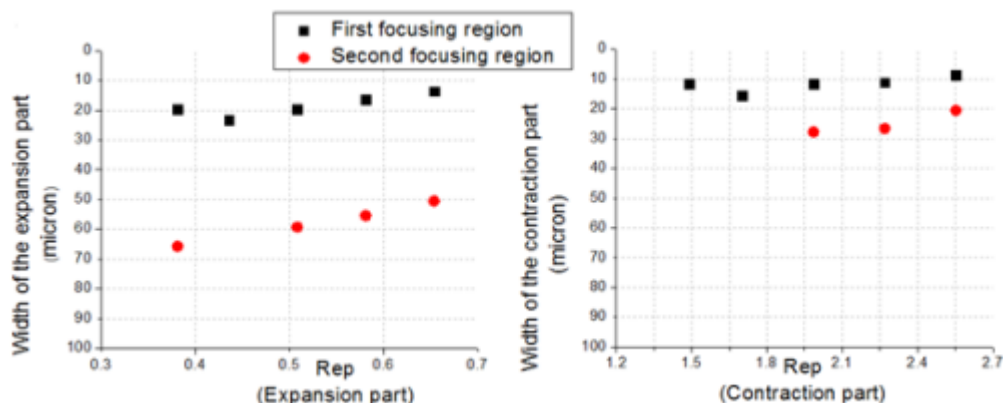


Figure 6.14: Particle focus positions of 60° design.

6.3.5 Intensity results and analysis

In this experimental study, line profile that is obtained from the microscope software is quite essential for determining that if a particle streamline can be neglected from being a focused particle streamline. For this purpose, line profile data is collected for all of the captured images. An example line profile data can be seen in Figure 6.15.

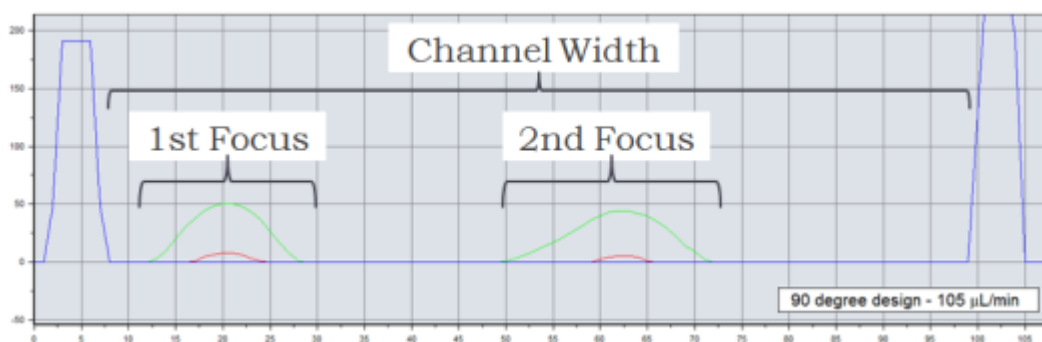


Figure 6.15: An example of line profile data.

The X axis of the shown graph is given as pixels in microscope software, so it requires a correction for determining the real width value of the focused areas. Channel width is known as a design parameter, all the width data is corrected for their realistic value by using this information. As it can be seen, focuses with different regions have different values of Y axis, which is the intensity value. Because of the accumulation that is used for capturing the images, intensity also means that the amount of particles that is pass in a position in that time manners. Therefore, this value can be used to compare

different angles at the same flow rate.

Obtaining a single focused particle streamline with high intensity alone is important but obtaining a narrow single focused particle streamline with high intensity is much more important. For this reason, the comparison between different angles is performed by using the Intensity/Width value. For increasing this value, either intensity should be increased or width should be decreased.

Intensity/Width value can be used for comparison between same angles alone, but for comparing different flow rates at least one more parameter is needed to be added to this value. For this reason, this value is divided by flow rate for obtaining the comparison value which is defined in Equation 6.1.

$$ComparisonValue = \frac{Intensity}{Width \times FlowRate} \quad (6.1)$$

Data gathered from the line profiles is analyzed with this comparison value and Figure 6.16 and Figure 6.17 are drawn. Both expansion and contraction parts of each design's data has been introduced in the same graph for easy access to the data. Upper focus means that focused particle streamline is close to the straight wall side and lower focus means that focused particle streamline is close to the contraction and expansion parts. Single focus means that either there is a single focused particle streamline or the secondary focused particle streamline is negligible.

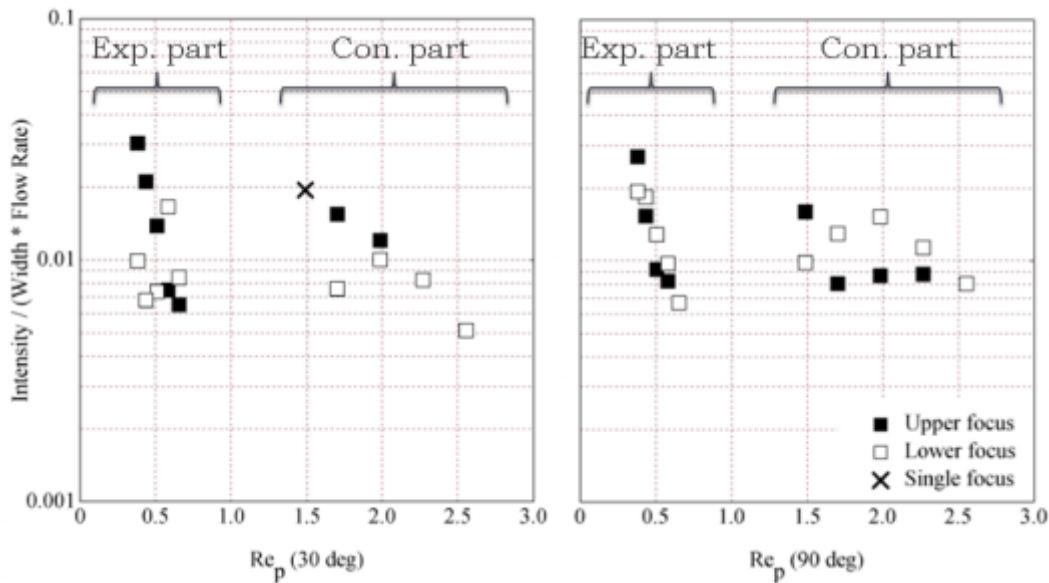


Figure 6.16: Intensity/(Width x Flow Rate) - Re_p graph for 30° and 90° designs.

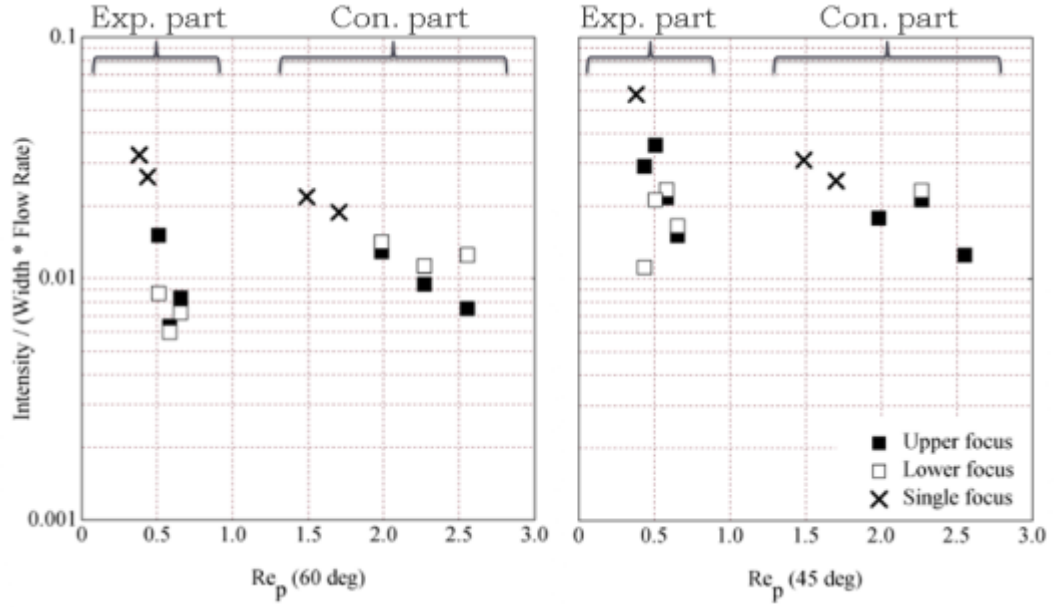


Figure 6.17: Intensity/(Width x Flow Rate) - Re_p graph for 60° and 45° designs.

Analyzing these graphs, we can conclude that;

- 90° design has no real single focused particle streamline and only contains two distinct but nearly equally focused particle streamlines. In 90° design graph, differences between data at the same Re_p is negligible and they can be counted as nearly equal.
- 30° design has only a single focused particle streamline in contraction part at 105 $\mu\text{l}/\text{min}$. At the same flow, expansion part of this system has two distinct focused particle streamlines with a slight difference; because of that it can not be negligible. It can be said that the ratio between these two focused particle streamlines is nearly 3:1, which can not be counted as a high yield focusing situation.
- 45° design has single focused particle streamline at 105 $\mu\text{l}/\text{min}$ and there is not even a secondary focused particle streamline that has significance in this situation. But at 120 $\mu\text{l}/\text{min}$, only the contraction part of the channel has a single focused particle streamline and expansion part has a secondary focused particle streamline which has nearly 1/3 of the main focused particle streamline. Therefore, this situation can not be counted as a high yield focusing situation also.

- 60° design has single focused particle streamline at both 105 and 120 $\mu\text{l}/\text{min}$ flow rates. When the captured images of this design are analyzed, a secondary focused particle streamline can be seen at 105 $\mu\text{l}/\text{min}$ and even this data is also marked in the position graph in Figure 6.14, this value has quite a lower value of Intensity/(Width x Flow Rate) than the main focused particle streamline at the expansion parts of the microchannel for the same flow rate. For this reason, this value is negligible.

6.3.6 Theory for single particle focusing mechanism in single sided contracting - expanding straight microchannel with different entrance angular paths at contraction part

With this study, particle focusing mechanism in the straight channels is altered to obtain a single and stable focused particle streamline. This situation can be explained with 2 component of inertial effects, which are wall effect induced inertial lift force and shear gradient induced lift force.

Park et al. mentioned that when a rapid expansion occurs in a narrow channel, wall effect induced inertial lift force component will be reduced to 0 directly and this will be resulted in particles moving inside the expansion parts to equilibrate the shear gradient induced lift force component [92,93]. But in these designs, one side of the microchannel always has the wall effect induced lift force component when the other side has expansion behavior. This is the main reason why there is two stable focused particle streamlines in 90° design similar to Park et al.'s study, because even when the top part of the system is not introduced to an expansion, both sides still have a stable focused particles streamline which cannot be changed easily.

By introducing the angular path before the contraction parts of the microchannel designs, the force balance of the entire system is altered. Because the wall effect induced lift force is perpendicular to the channel walls, it will not affect the particles directly with the angular system.

All of the forces and their components are schematically described in Figure 6.18, Figure 6.19, Figure 6.20 and Figure 6.21. As seen in these figures, wall effect is reintroduced to the system instantly in 90° design; this leads to the situation two focused particle streamlines.

In 30° , 45° and 60° designs, this effect is introduced to the system with its x and y components. Y component of the wall effect induced lift force is creating a disturbance in the focused particle streamline at the bottom and this streamline may no longer stabilize itself at the bottom side of contraction parts. Therefore, particles which focused at the bottom side of the microchannel tend to move top side of the microchannel to stabilize this wall effect induced inertial lift force. This theory explains the single focused particle streamline situation but it does not explain the affect of different angles.

X axis component of the wall effect induced inertial lift force is used to explain why single focused particle streamlines occur at different flow rates at different angles. This component is at the opposite direction of the fluid flow and it decreases the main fluid flow's effects on the particle. This x component has different values based on the angle values, so their effect on different angle values is different too. It can be seen that 60° design has the highest x component of wall effect induced inertial lift force, so the decreasing effect on this design is higher than 45° design and 30° design. For this reason, these x components reduce the overall force that affects the particles in the direction of their main movement; higher x components will decrease particles' movements a lot more. This is the main reason why 60° design has stable single focused particle streamlines at higher flow rates. Because of the affected higher x component of the wall effect induced inertial lift force, y component of the system is affects the particles more. Thus, particles can be forced to move to the top part of the microchannel even at higher flow rates.

6.4 Effects of Aspect Ratio on Inertial Focusing at Contraction - Expansion Microchannels

Until now, effects of single sided contraction and expansion geometry, effect of the angle at contraction part entrance and effect of flow rate on inertial focusing has been identified. In literature, it is also indicated that aspect ratio of the channel has an effect on the inertial focusing. For this reason, a microchannel series with different height but same geometrical properties has been designed. Detailed geometrical data for those 2 systems can be found in Table 6.5 and the design can be seen in Figure 6.6.

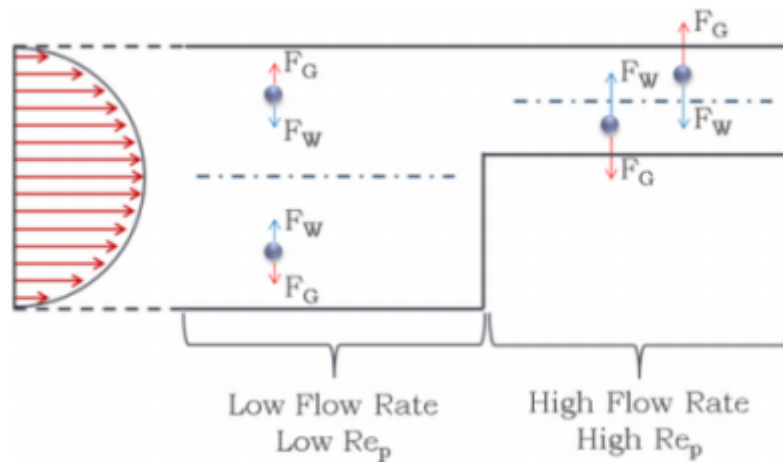


Figure 6.18: Components of Inertial forces that occur in 90° design - F_G : Shear gradient induced inertial lift force, F_W : Wall effect induced inertial lift force.

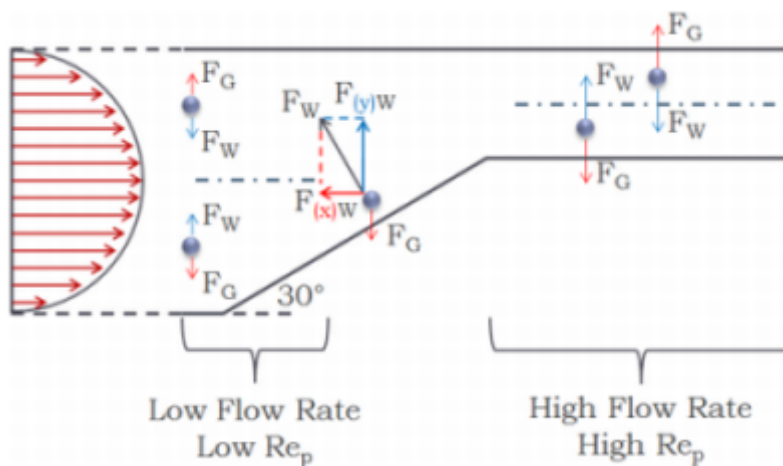


Figure 6.19: Components of Inertial forces that occur in 30° design - F_G : Shear gradient induced inertial lift force, F_W : Wall effect induced inertial lift force.

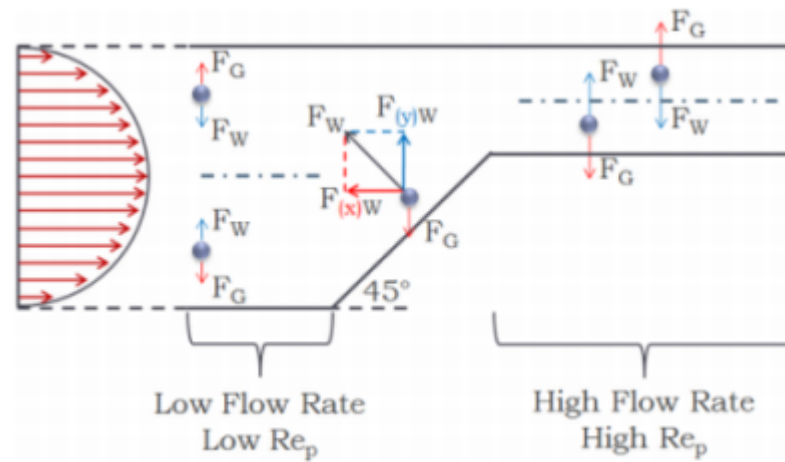


Figure 6.20: Components of Inertial forces that occur in 45° design - F_G : Shear gradient induced inertial lift force, F_W : Wall effect induced inertial lift force.

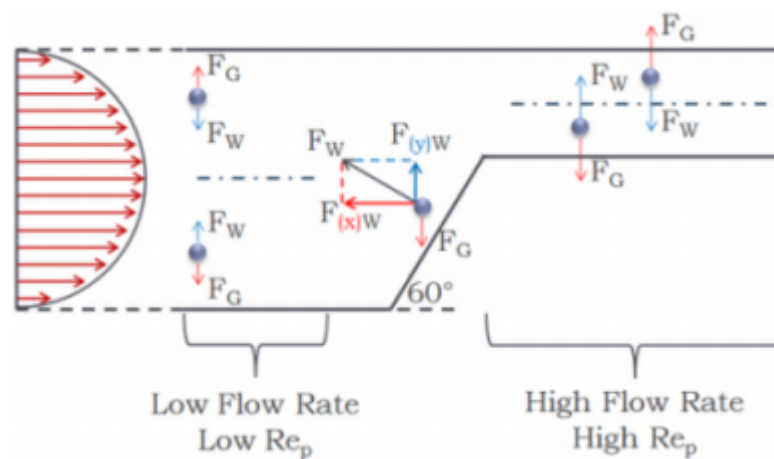


Figure 6.21: Components of Inertial forces that occur in 60° design - F_G : Shear gradient induced inertial lift force, F_W : Wall effect induced inertial lift force.

Table 6.5: Geometric data of designed channel geometries for detecting aspect ratio effects on inertial focusing.

	Design I				Design II		
Width I	100 μm				100 μm		
Width II	40 μm				40 μm		
Length	200 μm				200 μm		
Depth	60 μm				40 μm		
α	30	45	60	90	30	45	60

Design I is the microchannel system that has been used for the analysis given in section 6.3. Design II is the microchannel system that has been produced with SU-3050 resist and obtained an average height of 40 micron. Aspect ratio of these systems in both contraction and expansion channels can be seen in Table 6.6.

Table 6.6: Aspect ratio of Design I & II at contraction and expansion parts.

	Aspect Ratio of Design I	Aspect Ratio of Design II
Contraction part	$40/60 = 2/3$	$40/40 = 1$
Expansion part	$100/60 = 5/3$	$100/40 = 5/2$

6.4.1 Captured images and position data about Design II microchannels

Design I microchannel system captured images are given and analyzed in Section 6.3. In this section, Design II microchannel systems captured images are introduced and analyzed.

Captured images of 30° design with Design II parameters can be seen in Figure 6.22 and position data of the focused particle streamlines can be seen in Figure 6.23.

Captured images of 45° design with Design II parameters can be seen in Figure 6.24 and position data of the focused particle streamlines can be seen in Figure 6.25

Captured images of 60° design with Design II parameters can be seen in Figure 6.26 and position data of the focused particle streamlines can be seen in Figure 6.27

From the position data of each angle, it can be seen that this system tends to focus at lower half of the microchannel at low flow rates, and tends to obtain a single focus at high flow rates. There are some differences in focusing mechanism between Design II and Design I, these are;

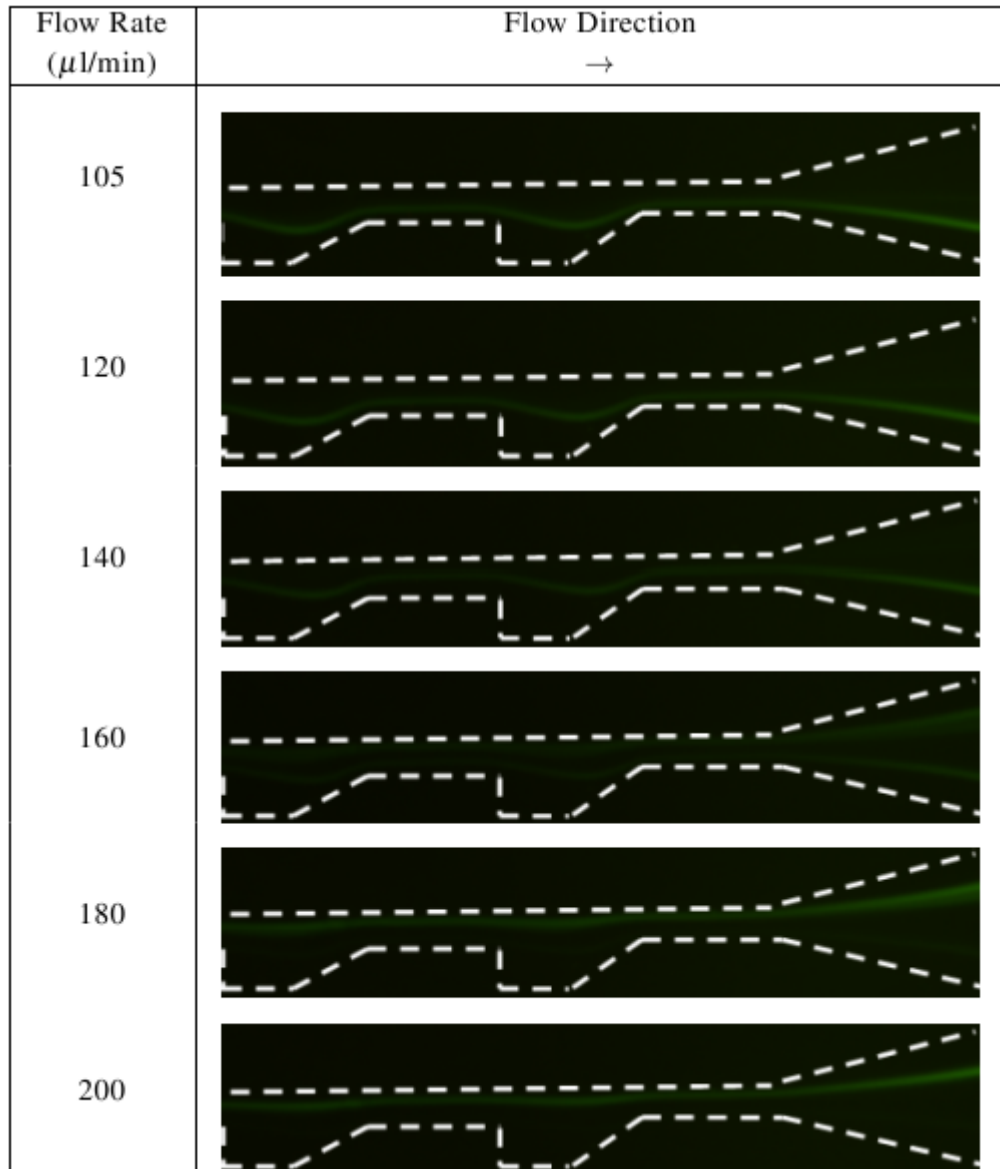


Figure 6.22: Fluorescent particle images of 30° design with Design II parameters.

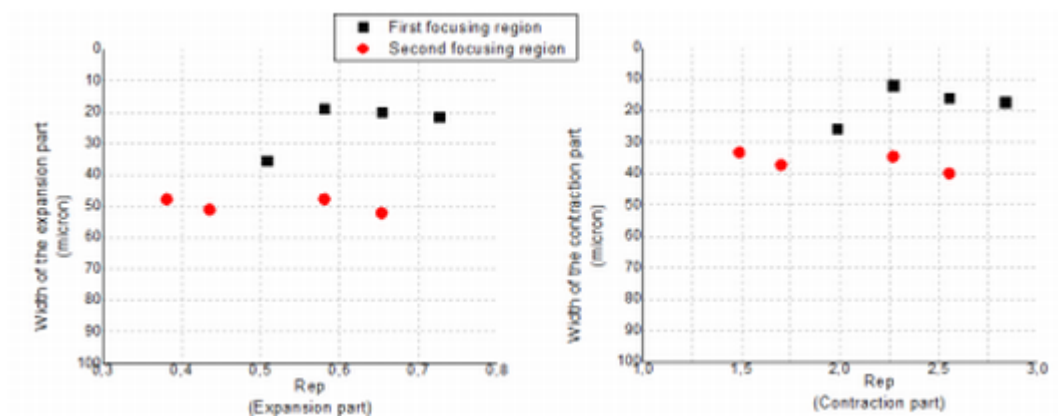


Figure 6.23: Position data of focused particle streamlines for 30 ° design.

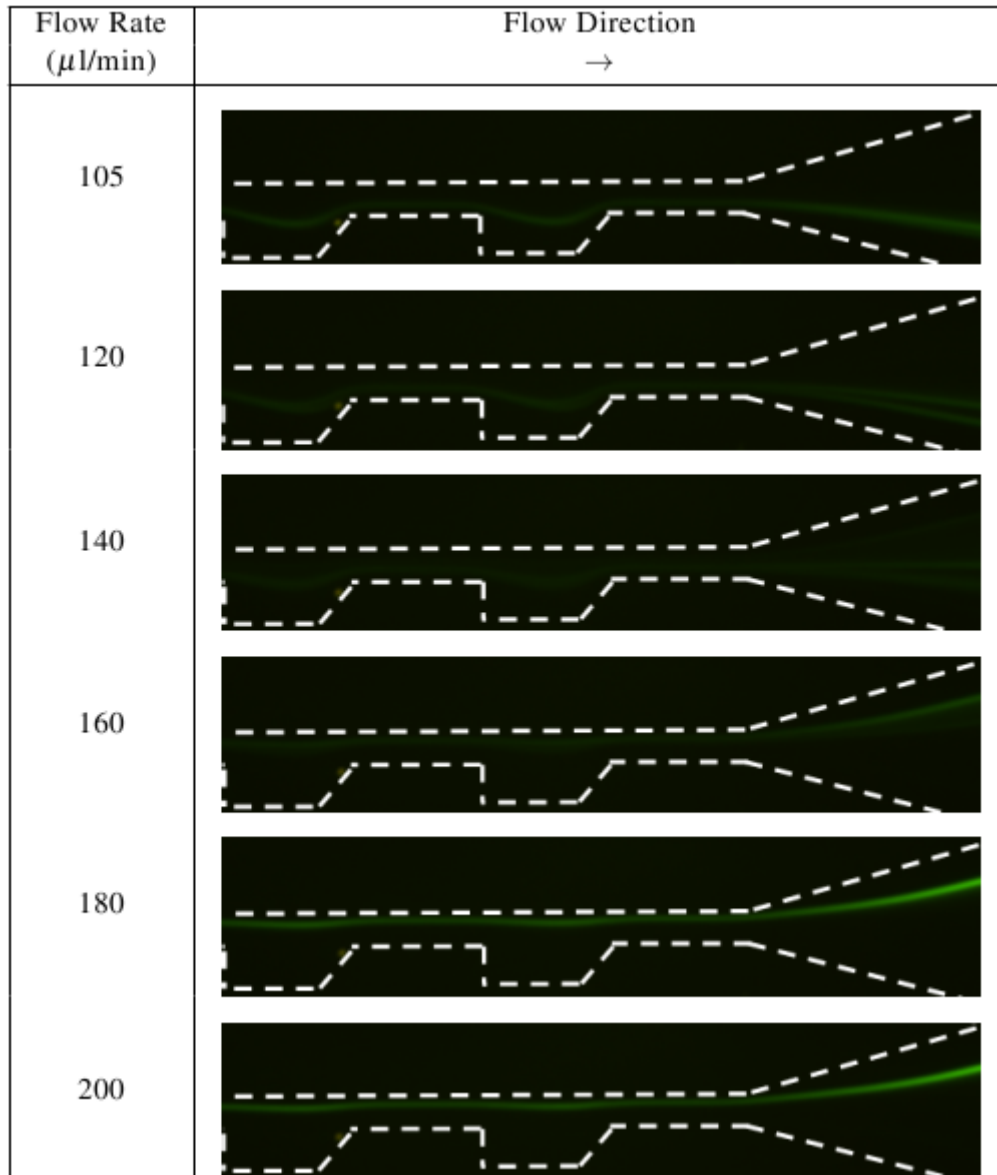


Figure 6.24: Fluorescent particle images of 45° design with Design II parameters.

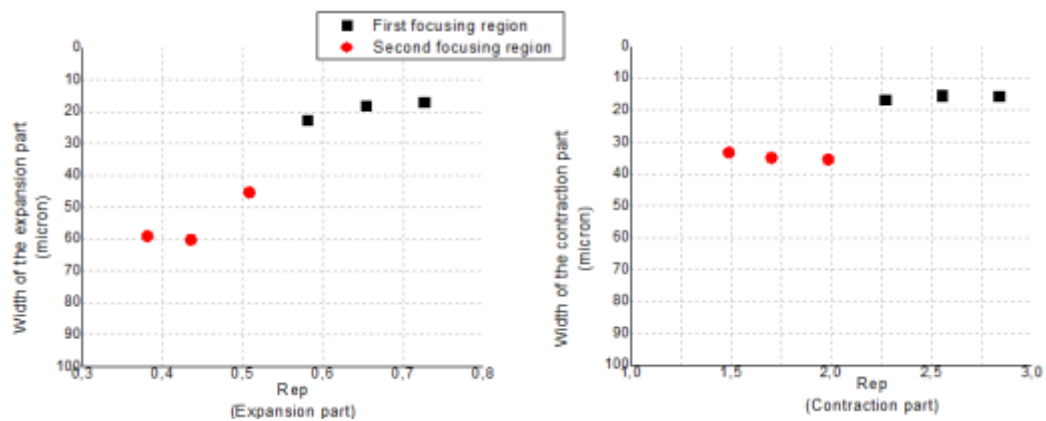


Figure 6.25: Position data of focused particle streamlines for 45° design.

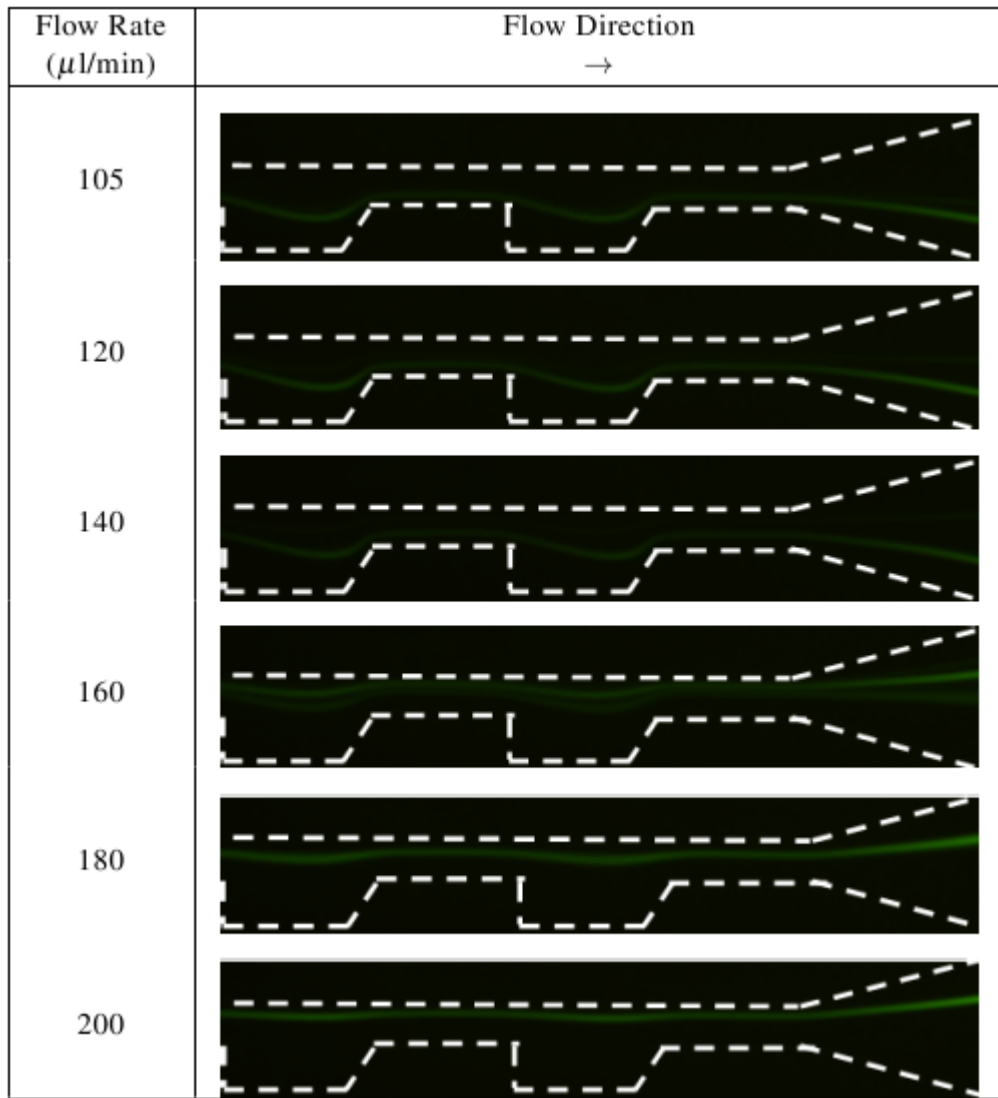


Figure 6.26: Fluorescent particle images of 60° design with Design II parameters.

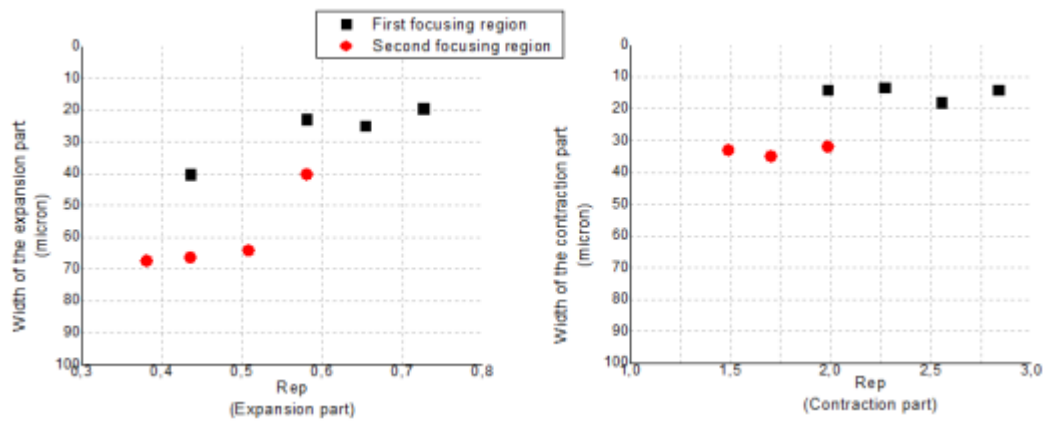


Figure 6.27: Position data of focused particle streamlines for 60° design.

- Design I has two distinct focused particle streamlines in low flow rates like 105 $\mu\text{l}/\text{min}$, but especially at this flow rate each angle on Design II has a single focused particle streamline at the bottom part of the microchannel.
- In Design I, as the flow rate increased, single focused particle streamline is deformed and two different focused particle streamlines are formed at the top and bottom part of the microchannel. But in Design II, as the flow rate increased, single focused particle streamline at the bottom tends to move to the top part of the microchannel.
- Expansion parts of the microchannel in Design I have quite an effect on the single focused particle streamline as breaking or expanding them. But in Design II, expansion parts of the microchannel only push focused particle streamlines to more bottom parts.

6.4.2 Intensity results and analysis on Design II

Besides the position data of Design II experiments, Intensity/(Width x Flow Rate) analysis is needed to determine the quality of focused particle streamlines. Intensity/(Width x Flow Rate) data of focused particle streamlines of 30° design can be seen in Figure 6.28, 45° design can be seen in Figure 6.29 and 60° design can be seen in Figure 6.30.

Single focused particle streamline occurs at the bottom part of the microchannel at low flow rates and with increased flow rate this focused particle streamline tends to separate on 2 distinct but nearly equally focused particle streamlines at moderate flow rates like 140 - 160 $\mu\text{l}/\text{min}$. Above these flow rate values, the system obtains a new single focused particle streamline at the top part of the microchannel. It can be assumed that these two distinct focused particle streamlines are created for transition phase. Besides this transition phase, there is no real two distinct focused particle streamlines in Design II. Below 105 $\mu\text{l}/\text{min}$, particles imitate the behavior of 105 $\mu\text{l}/\text{min}$ and this is also the same for over 200 $\mu\text{l}/\text{min}$ flow rates.

Increasing aspect ratio of the channels created more reliable single focused particle streamline even at high flow rates. Also, increase in aspect ratio decreased the effects

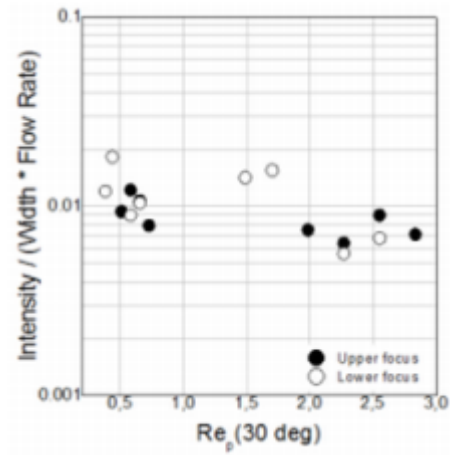


Figure 6.28: Intensity/(Width x Flow Rate) data of focused particle streamlines for 30° design.

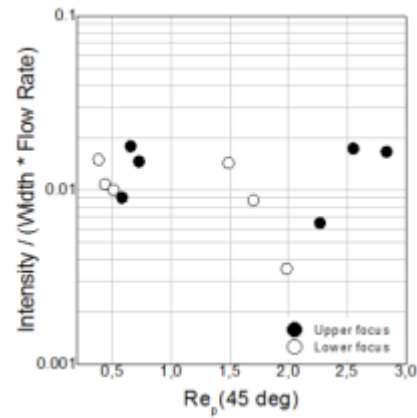


Figure 6.29: Intensity/(Width x Flow Rate) data of focused particle streamlines for 45° design.

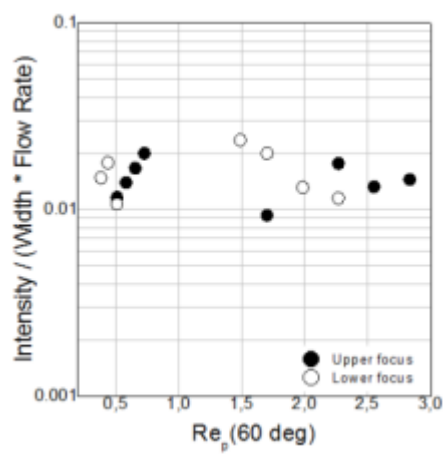


Figure 6.30: Intensity/(Width x Flow Rate) data of focused particle streamlines for 60° design.

of angular path slightly, but still 60° design tends to obtain single focused particle streamline at the top of the microchannel at much lower flow rates than 45° design and 30° design. This situation can be explained with the same theory as Design I.

7. CONCLUSIONS AND DISCUSSIONS

In this study, particle focusing mechanism in straight microfluidic channels with contraction and expansion geometry has been studied at different flow rates. Particle focusing in straight microfluidic channels is mainly due to the inertial lift forces applied to the particles by flow characteristics. It has been indicated that particle diameter and microchannel's geometric details (aspect ratio - hydraulic diameter) are quite important for determining whether inertial lift forces are enough for obtaining a focused particle streamline or not ($a_p/D_h > 0.07$ must be achieved for obtaining a focused particle streamline) [29].

Theory for this particle focusing mechanism is given in Section 6.3. 4 different microchannel designs (different angle at the angular path before contraction parts) have been studied for 5 different flow rates. In the Sections from 6.3.1 to 6.3.4; captured images for 90° , 30° , 45° and 60° angular paths are analyzed. According to the given images, it can be concluded that angular entrance at the contraction parts is the key factor for obtaining single focused particle streamline in straight microchannels. In Section 6.3.1, captured images for 90° angular path are analyzed; this geometry provides 2 focused particle streamlines also as indicated in a similar study by Park et al. [92]. With the exception of the 90° design, all other designs have single focused particle streamline at situational flow rates. According to the given images, these 3 designs have single focused particle streamline at low flow rates of 105 and 120 $\mu\text{l}/\text{min}$. Increase in flow rates causes the single focused particle streamline to split into 2 distinct focused particle streamline till a higher limit of 160 and 180 $\mu\text{l}/\text{min}$. After this limit, particles tend to break the focused particle streamline formation.

In these 3 designs;

- 60° design has stable single focused particle streamline at 105 $\mu\text{l}/\text{min}$ and 120 $\mu\text{l}/\text{min}$.

- 45° design has stable single focused particle streamline at 105 $\mu\text{l}/\text{min}$ and unstable single focused particle streamline at 120 $\mu\text{l}/\text{min}$.
- 30 45° design has unstable single focused particle streamline at 105 $\mu\text{l}/\text{min}$.

These results are also supported by the Intensity/(Width x Flow Rate) analysis given in Section 6.3.5.

Theory for the angle effect on particle focusing mechanism is explained in Section 6.3.6. By using an angular path at the entrance of the contraction part, wall effect induced inertial lift force is introduced to the system earlier than 90° design. Because of the angular path, wall effect induced lift force does not only apply to y direction but also applies to x direction at the opposing direction of fluid flow causing a negative drag behavior. This x component's value is dependent on the angle and it has the highest value in 60° design. It can be concluded that the x component of wall effect induced inertial lift force acts against the drag force which is created by fluid flow, so the particles tend to move slower than their regular speed inside the carrier fluid. Single focused particle streamlines are stable at much higher flow rates than other designs since 60° design has the highest value on the x component of wall effect induced inertial lift force.

Aspect ratio effect on the particle focusing mechanism in straight microchannels has also been studied. It has been found that increasing the microchannel's aspect ratio alters the particle focusing mechanism so that particles tend to obtain single focused particle streamline at both the bottom and top part of the microchannel at different flow rates with an increased aspect ratio, the captured images of these studies are given in Section 6.4.1.

At low flow rates of 105 and 120 $\mu\text{l}/\text{min}$, particles tend to focus at the bottom of the channel where they obtained 2 distinct particle streamline at higher aspect ratio. Increasing the flow rate splits focused particle streamline into 2 distinct particle streamlines but at high flow rates of 180 and 200 $\mu\text{l}/\text{min}$, particles tend to obtain single focused particle streamline at the top of the microchannel again.

Increasing the aspect ratio of the channel decreases the effects of angle at the entrance of the contraction part. Difference in angular path at the entrance of contraction part

creates a difference in the flow rates where particles focused at 2 different streamlines. These flow rates can also be described as transition region between focused particle streamline at the bottom of the microchannel and focused particle streamline at the top of the microchannel. In 60° design, this transition region is more narrower than the other designs at the same fluid flow rates.

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List of Publications and Patents:

PUBLICATIONS/PRESENTATIONS ON THE THESIS

- Kızıl, H., Trabzon, L., Yobaş, L., **Yılmaz, M.**, Özbey, A. (2010) “Computational analysis of microparticle separation in straight channels”, in MME 2010, *Proceeding of 21st Micromechanics and Micro systems Europe Workshop*, 26 – 29 September 2010, Enschede, Netherlands
- **Yılmaz, M.**, Cengiz, M., Kızıl, H., Özbey, A. Trabzon, L. (2011) “Geometry induced microparticle separation in passive contraction expansion straight channels”, in ICQNM 2011, *Proceeding of 5th International Conference on Quantum, Nano and Micro Technologies*, 21 – 27 August 2011, Nice, France
- Trabzon, L., Kızıl, H., Yobaş, L., **Yılmaz, M.**, Özbey, A. “The effect of asymmetry on particle focussing in microchannels”, *Advanced Materials Research*, pgs 482 – 485, Vol. 403-408 (2012)