CHAPTER 2

BASIC CONCEPTS IN MICROFLUIDICS

2.1 INRODUCTION

Microfluidics is the science of manipulating fluid flow through channels having dimensions of less than 1 mm. The flow of a fluid through a microfluidic channel can be characterized by the Reynolds number, defined as

$$R_e = \frac{LV\rho}{\mu} \tag{2.1}$$

where L is the length of the channel, V is the average velocity flow, ρ is the density of the fluid, μ is the viscosity of the fluid. The Reynolds number, which determines the turbulence of flow, is extremely low at small scales, meaning that the fluid flow pretty much stays laminar. As the size of channels in which a liquid flows becomes smaller and smaller, local effects such as surface tension, laminar vs turbulent flow, Reynolds number and surface chemistry play a larger role in the physics and the chemistry of the reactions under investigation. Due to the small dimensions of microchannels, the Re is usually much less than 100, often less than 1.0. Laminar flow provides a means by which molecules can be transported in a relatively predictable manner through microchannels.

2.1.1 Importance of Microfluidics

The study of microfluidics becomes significant because of the following reasons.

- Reduction in size
- Handling of less amount of fluids
- The reduced consumption of chemical reagents
- Low power consumption
- Safety
- Reliability
- Portability
- User friendly

2.1.2 Advantages of Microfluidics

The advantages of microfluidics are summarized below.

- Work with small volume
- Increase in speed of reaction
- Lower power consumption and better performance
- Integrated with other devices – Lab on a Chip
- Ease of disposing of devices and fluids
- Reduction of cost for the reagent
- Higher surface to volume / Low Reynolds number
- Minimize the size of the chip

2.1.3 Applications of Microfluidics

2.1.3.1 Chemical synthesis

A microchannel reactor is a device in which chemical reactions take place in a confinement with typical lateral dimensions below 1 mm; the most typical form of such confinement are microchannels. Microreactors are studied in the field of micro process engineering, together with other devices (such as micro heat exchangers) in which physical processes occur. The microreactor is usually a continuous flow reactor in contrast to a batch reactor. Microreactors offer many advantages over conventional scale reactors, including vast improvements in energy efficiency, reaction speed and yield, safety, reliability, scalability, on-site/on-demand production, and a much finer degree of process control.

2.1.3.2 Separation and analysis

Many chemical and biochemical analysis methods involve performing a sequence of processes that can be broadly classified in terms of sample preparation, reactions, and product analysis. Since the reaction products often contain mixtures of multiple chemical species, subsequent analytical steps must be capable of separating and identifying the individual components. Electrophoresis, which relies on inducing detectable differences in migration behavior between charged species under the influence of an applied electric field, has proven to be a highly versatile analytical technique owing to a favorable combination of characteristics including relatively simple hardware design and compatibility with a wide range of analytes including biological macromolecules.

2.1.3.3 Biodetection

Biodetection refers to the field of medical diagnostics, food quality and biological warfare detection. The aim of microfluidic detection devices is to miniaturize and parallelize classical immunologic and genomic detection assays. Micro and nanofluidic devices dedicated to biodetection can be divided into two major classes: (i) sample preparation devices in which a preconditioning of the sample can be obtained (matrix change, preconcentration, cell lysis, purification, etc…) and (ii) biosensors devices in which the presence of the targeted analyte is transformed into an electrical or optical signal. On-chip real time PCR, enzyme or classic ELISA immuno-sensors, and microarrays are among the most promising technologies for biological agent or markers detection.

2.1.3.4 Single cell biology

Microfluidic is a well understood physic domain and can now be used to develop tools for cell biology. By simply miniaturizing macroscopic systems and taking advantage of the possibility of massive parallel processing, some microfluidic chips enable high-throughput biological experiments. Specific effects of laminar flow at the micron-scale also enable spatial control of liquid composition at subcellular resolution, fast media and temperature changes, and single cell handling and analysis. Microfluidic technology enables studies of cell behavior from single- to multi-cellular organism level with precise and localized application of experimental conditions unreachable using macroscopic tools.

2.1.3.5 Micro droplets

Multiphase flows generate a high interest in microfluidics as the laminar flows facilitate the generation of monodisperse droplets. Emulsions and double emulsions can be used for nanoparticle synthesis, drug microencapsulation (lipid vesicles), and active substance encapsulation. Microdroplets can also be used as single microreactors in biodetection system. The amplification of single DNA strands can be obtained to increase the sensitivity of the biodetection schema.

Alternatives to the above closed-channel continuous-flow systems include novel open structures, where discrete, independently controllable droplets are manipulated on a substrate using electrowetting. Following the analogy of digital microelectronics, this approach is referred to as digital microfluidics (Velve-Casquillas et al 2007).

2.1.3.6 Microfluidic rheology/rheometry

Working with low Reynolds numbers enables to properly investigate viscous liquids especially non linear visquous effects. A number of microfluidic rheometry systems have been investigated and they enable an alternative to conventional characterization methods. The study of fluids transport across micro-nanofluidic porous media is also of high interest for oil recovery applications. Finally, a number a fundamental questions around the slip velocity at the solid liquid interface can also be investigated using microfluidic devices together with particle velocimetry techniques.

2.1.3.7 Optofluidics

Optofluidics refers to manipulation of light using fluids, or vice-verse, on the micro to nano meter scale. By taking advantage of the microfluidic manipulation, the optical properties of the fluids can be precisely and flexibly controlled to realize reconfigurable optical components which are otherwise difficult or impossible to implement with solid-state technology. In addition, the unique behavior of fluids on micro/nano scale has given rise to the possibility to manipulate the fluid using light.

2.2 MICROFLUIDIC DEVICES

A Microfluidic device consists of various components such as, microchannels, micoronozzles, micropumps, micromixers and microvalves. These devices handle very small volumes of fluid and can be integrated into microfluidic chip or Lab-on-a-Chip. The following figure shows a microfluidic device which consists of microfluidic valves and hydrophobic vents fabricated by Mathies and Lagally (2001). In this device, sample is loaded from the right by opening the valve using vacuum (30 mmHg) and forcing the sample under the membrane using pressure (10-12 psi); vacuum is simultaneously applied at the vent to evacuate the air from the chamber. The sample stops at the vent, and the valve is pressure-sealed to enclose the sample. Dead volumes for the valves and vents are ~50 nL.

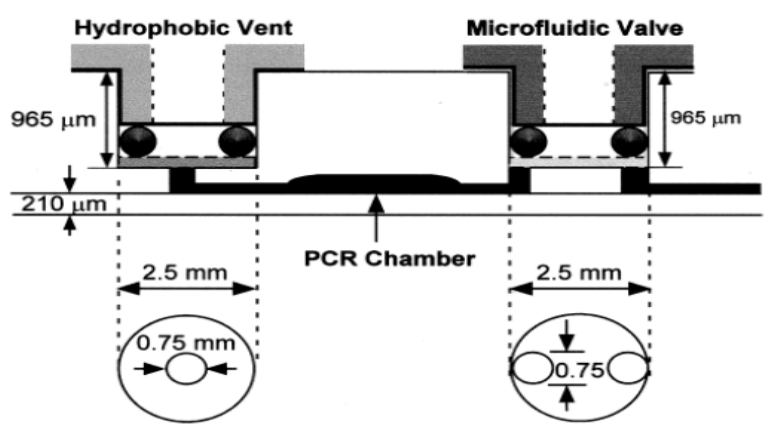

Figure 2.1 Schematic diagram of micro TAS (Lagally 2001)

2.2.1 Microvalves

Microvalves are used to rectify fluidic flows, used in pairs in directing fluid flow in and out of a micropump or individually in a microchannel. Microvalves can be classified into static and dynamic. Static microvalves are mostly mechanical check valves consisting of a micromachined orifice and a deflectable sealing element. This sealing element can be a plate, a ring mesa, a cantilever or a float. Dynamic microvalves have micronozzles and microdiffusers functioning as valves. These are known as dynamic passive valves. The electrostatic valves can be used to direct pressure to pneumatic microvalves that reduce the ancillaries typically needed to operate pneumatic actuators (Tice et al 2011).

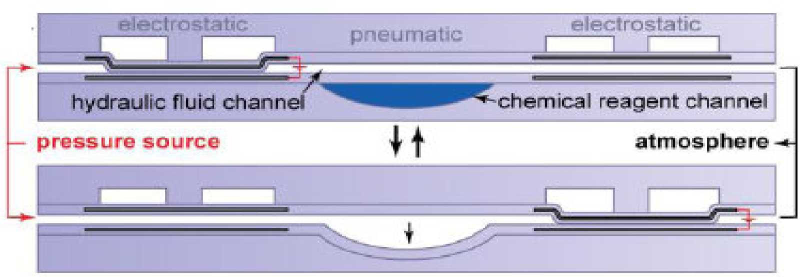

Figure 2.2 Micro Valve (Tice et al 2011)

2.2.2 Micro Mixer

A mixer must have the ability to mix two or more fluids thoroughly and in a reasonable amount of time. For effective mixing, the contact area between the fluids must be increased and the distance over which diffusion acts must be decreased. In biomedical and chemical analysis, a sample solution is often to be tested with a reagent. The two solutions should be well mixed to make the reaction possible. While in macroscale, mixing is achieved with turbulence, mixing in microscale relies mainly on diffusion due to the laminar behavior at low Reynolds numbers.

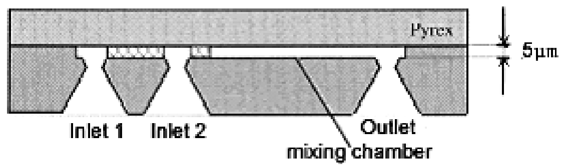

Figure 2.3 Micro Mixer designed by Nguyen et al (1998)

2.2.3 Micropump

Micropumps are used in numerous fields such as chemical process control, medical drug delivery systems, environmental control, and biotechnological applications to name a few. In all of these applications, the main requirement is that of low energy consumption needed so that systems can be portable and battery-powered. The ability to turn off the flow or to deliver small and precise amount of liquid is needed for drug delivery system, such as microsyringes for diabetics or in a chemical analysis system.

Figure 2.4 A valveless micropump manufactured by IDEX corporation

2.2.4 Micronozzle

The micoronozzles were designed to be operated with supersonic gas flows. In the initial stages of this investigation, however, they were operated with a liquid in order to assess the spatial resolution capabilities of the µPIV technique without having to push the temporal envelope simultaneously (Nam-Trung Nguyen 2006). Consequently, the converging-diverging geometry of the micronozzle served as a very small venturi. The micronozzles were fabricated by Robert Bayt and Kenny Breuer (now at Brown University) at MIT in 1998.

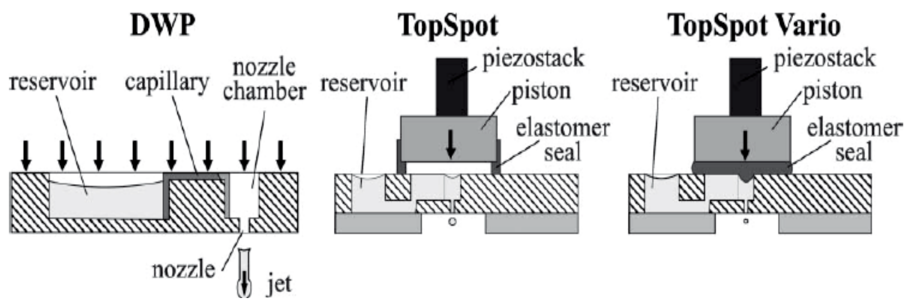

Figure 2.5 a)DWP b) and c) Micro nozzle (developed by TopSpot technologies)

The above figure shows the Dispensing Well Plate which is used for pressure-based actuation dispensing from 10 nL up to several mL (Stefan Haeberle et al 2007). The TopSpot is a pressure-based actuation for dispensing volumes in the lower nL range, TopSpot Vario uses direct displacement principle via an elastomer, a polymer having low Young's modulus, for dispensing of volumes from 100 pL to 1400 pL.

2.3 FLUID FLOW IN MICRODEVICES

In macroscopic scale, liquid flow in a pipe can be laminar, transitional or turbulent, depending on the Reynolds number (Re). When the Re is small (less than 2100), the flow is laminar and when it increases the flow reaches a transitional phase where the flow is partly laminar with intermittent bursts of irregular behaviour. When the Re is further increased (above 4000), the flow becomes turbulent, having random fluctuations with particle mixing. The velocity has unsteady components normal to the channel axis as well as the predominant component along the channel (Munson et al 1998). For microdevices, which has dimensions in the order of microns, the Re is very small (less than 1), even if the velocity is not. The flow is laminar, moving in smooth streamlines. It is rarely turbulent. In this analysis, only liquid flow is considered, so compressibility effect is neglected. The flow is treated as incompressible flow. In incompressible flow, density is constant with respect to pressure as well as temperature. Although density is sensitive to temperature changes, in this analysis the temperature is regarded as a constant. The flow is further restricted to Newtonian fluid, specifically water, in which case the viscosity is constant.

2.3.1 Microchannels

As a fluid enters a microchannel, it undergoes two distinct regions of flow. In the beginning, it goes through the entrance region where the flow profile undergoes changes from flat shape to a more rounded and eventually to the characteristic parabolic shape. Once it reaches this position where the profile is parabolic, it is in the fully developed region of the flow.

2.3.1.1 Entrance Region

The entrance region of a microchannel is one in which the flow is not fully developed. It is also know as the inlet flow region. The length from the inlet to the fully developed flow region is known as the entrance length. For a circular duct, the entrance length L_{FD} is given by (Shah and London 1978) in (Schetz, 1993):

$$\frac{L_{FD}}{D} = \frac{0.6}{1 + 0.035\,\mathrm{Re}} + 0.56\,\mathrm{Re} \tag{2.2}$$

If the entrance is well-rounded, the velocity profile is nearly uniform. As the fluid enters the channel, boundary layers form at the entrance. Fluid at the walls of the channel slows down while the fluid in the centre accelerates, according to the continuity law. Due to viscous effects, the boundary layers thicken downstream and join together until the channel is filled with these boundary layers. At a certain position in the channel, x_L, the flow profile develops into a parabolic shape. There is an excess pressure drop across the entrance length due to the increased shear forces in the entrance boundary layers as well as the acceleration of the core.

2.3.1.2 Fully Developed Laminar Flow

Once the fluid enters this fully developed region, the velocity flow profile remains the same parabolic shape. The pressure gradient is constant throughout this region. The velocity profile and pressure gradient is independent of the inlet conditions. The flow rate for laminar flow in a circular pipe is given by the Hagen-Poiseuille equation (Zengerle and Richter 1994):

$$Q = \frac{\pi r^4}{8\mu L}\Delta p \tag{2.3}$$

where r is the radius of the pipe, l is its length, Δp is the applied pressure difference and μ is the viscosity of the fluid. Although equation (2.3) is for circular pipe, it can be applied to channels with square as well as rectangular cross-sectional areas of aspect ratios close to 1 if the radius is replaced by hydraulic diameter D_h given by:

$$D_h = \frac{4bh}{2(b+h)} \tag{2.4}$$

2.3.2 Diffusers and Nozzles

Nozzles and diffusers form part of the non-moving part micropump, acting as passive valves. Passive valves aim to have the fluid flow in one direction only. It should ideally have zero resistance in one direction and infinite resistance in the other direction. Nozzles are the channels that have slowly converging walls while diffusers have gradually expanding walls. Diffusers were designed to increase pressure and reduce kinetic energy. As a fluid enters the diffuser, its flow velocity decreases and the static pressure increases. Diffusers can be conical, pyramidal or planar. The flow in a diffuser is complex and is dependent on several factors such as the diffuser's geometric parameters, inlet Reynolds number, inlet boundary- layer blockage factor, inlet turbulence, and pulsations. The three most important parameters of diffusers and nozzles are area ratio, angle and inlet boundary-layer blockage factor $B_t = A_{BL}/A_1$, where A_{BL} is the wall area blocked or displaced by the retarded boundary-layer flow in inlet. Its performance decreases with blockage (White 1994).

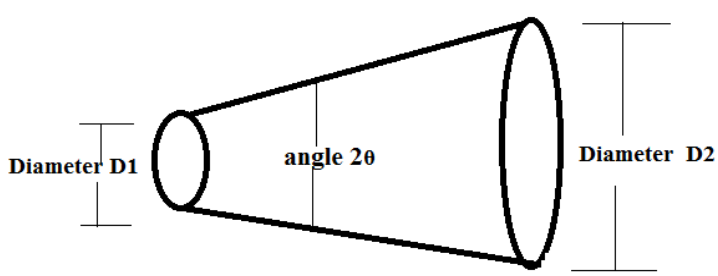

Figure 2.6 Geometry of Conical Diffuser

Nozzles transform pressure energy into kinetic energy. As a fluid goes through a nozzle, its flow velocity increases while its static pressure along the axis decreases. The fluid accelerates through the nozzle and the inlet velocity profile distortions become smoothed. Since the pressure decreases and the length is too short, fully developed flow cannot form in the nozzle. The effect of friction and turbulence is also reduced (Schetz and Fuhs 1999). The Geometry of nozzle is presented in Figure 2.6.

Diffusers transform kinetic energy into pressure energy. Since the velocity decreases and the pressure increases in the flow direction, boundary layer separation can occur at the wall, especially when the area ratio between inlet and outlet A_2/A_1 is large. The fluid particles are moving through higher pressure area. If the Reynolds number is large, a boundary layer forms close to the wall where the particles velocity is smaller than the average velocity, due to dissipation. As they move further in, the pressure increases until they reach a point at which they can no longer advance and will eventually flow backwards. This forms a boundary layer separation where vortices form and are kept in motion by friction stresses and by turbulent stresses exerted by the unseparated flow. This separated flow is usually unsteady. As for the particles in the unaffected core, they are in effect flowing in a smaller cross-section of the channel, experiencing a smaller pressure increase than expected. The friction stresses experienced by the separated flow leads to additional pressure loss. The ratio of the actual pressure increase to that of the theoretical pressure increase is the diffuser efficiency and is given by (Spurk, 1997):

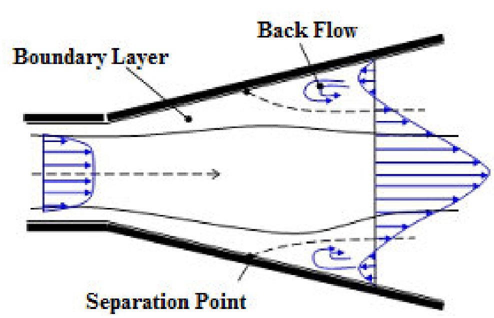

Figure 2.7 Boundary Layer Separation in Diffuser

2.4 BASIC DEFINITIONS

2.4.1 Electric Double Layer

Most substances acquire a surface electric charge when brought into contact with an aqueous electrolyte solution (Ronald F. Probstein 1995). Any aqueous electrolyte solution, such as sodium chloride (NaCl) or potassium chloride (KCl) can conduct electricity. Such electrolytes even exist inside the human body, in the form of salts, containing sodium and potassium ions. When dissolved in an aqueous solution, the salts dissociate completely into ions. The pH of the aqueous electrolyte determines the charge on the surface of the solid.

When considering silicon oxide as the solid substance, a fraction of the silanol group SiOH at the surface, change to SiO- or SiOH2+, creating a negative or positive charged surface respectively. The term zeta potential can be given to the charge, which appears on the surface of the solid.

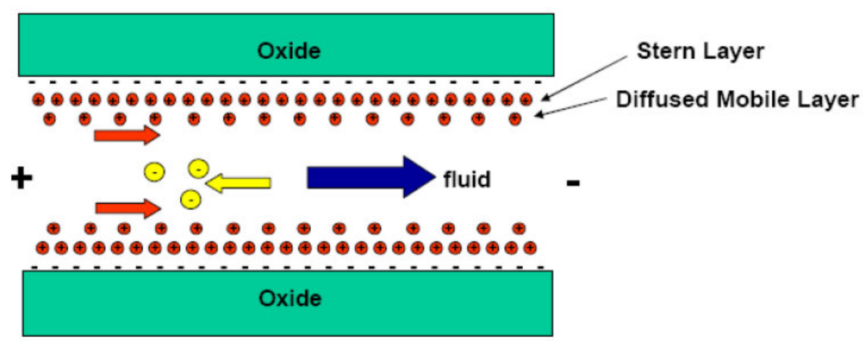

Figure 2.8 Electric Double Layer

The charged surface affects the distribution of ions inside the fluid, by attracting ions of opposite charge (counter-ions) and repelling ions of similar charge (coions). This results in a high concentration of counter-ions in a layer close to the wall, known as the inner diffuse layer or Stern layer as the idea was proposed by Stern in 1924. This layer is typically around 1 nm

(Ren et al 2001) thick and the ions are not mobile, they adsorb to the silicon through Coulomb forces as well as chemical affinity for the surface. Further away from the surface, lies another layer, where the concentration of counter-ions is also higher than that of the co-ions. This layer is known as the outer diffuse layer. Ions in this layer are mobile and attracted through electrical forces. The inner and outer layers lying close to the wall are known collectively as the Electrical Double Layer (EDL), this can be seen in Figure 2.8. The thickness of the EDL is determined by the strength of the electrolyte.

2.4.2 Electrokinetic

Electrokinetic (Henry Bruus 2008) is the description given to the four phenomena resulting from attempting to shear off the outer diffuse layer of the EDL.

2.4.2.1 Electroosmosis

When the microchannel is filled with the electrolyte solution, counter ions (+) are gathered into very thin Debye layers by channel surface charges (-). When an electric field is applied from outside, the counter ions are pulled into the electrode (-). The motion of the ions is transferred to the electrolyte solution, and the solution moves to the electrode along with the counter ions because the microchannel flow is a viscous flow, the Reynolds number of which is far less than 1. This is the electroosmosis phenomenon.

2.4.2.2 Electrophoresis

If particles with neutral surface charges are exposed to an external electric field, the charges are separated from the particle surface through polarization. If this external electric potential is uniform, the forces on both electrodes become equal and accordingly, no movement is made. However, if the external electric potential has a gradient - that is, if it is a non-uniform or asymmetric electric field - even neutral particles are subject to a move by the generated net force. This is known as electrophoresis.

2.4.2.3 Streaming potential

The generation of an electric field by ionised liquid flowing past a solid surface is streaming potential which is the opposite of electro-osmosis.

2.3.2.4 Sedimentation potential

The generation of an electric field by charged particles moving with respect to a stationary solid surface is called sedimentation potential that is the opposite of electrophoresis.

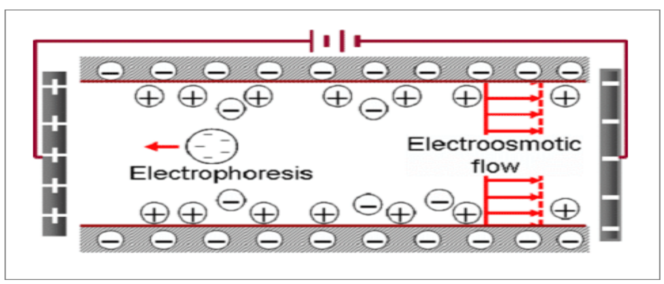

Figure 2.9 Electroomosis and Electrophoresis

All the electrokinetic effects occur as a result of the EDL, however the importance of including how the electrokinetic forces affect the fluid flow through channels is dependent on the length scales of the channel (Patankar and Hu 1998). Traditional fluid dynamics does not take into account the electrokinetic effects, as they are negligible at this scale, however at micro-scale, it is important to include these effects. In this thesis, it is assumed, as in (Dutta P et al 2002) that the fluid is a continuum and has a Knudsen number $<$

0.1. The Knudsen number is defined as the ratio of mean free path of molecules to characteristic dimension.

Electroosmotic flow occurs when the ions in the outer diffuse layer of the EDL move in response to an externally applied electric field. The electric field acts upon the ions in this layer, forcing them to move towards the appropriate electrode. The bulk of the fluid, in the center of the channel, is dragged along by the moving ions through viscous forces. This creates a plug-like flow, characteristic to electroosmotic flow as seen in the following figure.

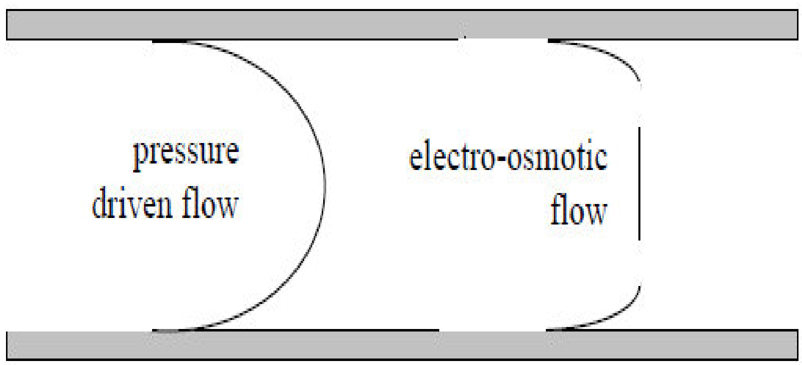

Figure 2.10 Diagram outlining the difference between the plug-like velocity profile, characteristic of EOF and the velocity profile generated by pressure driven flow.

The flat profile is created through the driving force, which in electro-osmosis is the internal potential distribution of ions, being uniformly distributed throughout the channel. The pressure drop encountered in laminar flow due to frictional forces along the walls is not present in EOF. The flat plug-like profile minimises the dispersion of substances, hence allowing efficient transport of substances through long micro-channels. If mixing was the aim, extra objects could be incorporated into the flow path, so as to break up the smooth flow produced by electroosmosis.

2.4.3 Zeta Potential

The zeta potential (given the Greek symbol ζ) is defined as the value of the electrical potential on a plane located between the inner diffuse layer or Stern layer, and the outer diffuse layer. The plane between the Stern layer and the outer diffuse layer is called the Stern plane. Hence, the potential at the Stern plane can be called the zeta potential (Hunter 1981). The zeta potential can be varied through the pH of the buffer solution; therefore, in order to produce effective pumping through electroosmosis, the choice of buffer is important.

2.5 SUMMARY

In this chapter the basic concepts of microfluidics is described. The importance, advantages, applications are elaborately discussed. The use of microfluidic devices such as, microvalves, micromixer, micropump and micronozzle are analysed. Fluid flow through different microfluidic devices is also referred.