Microfluidic Mixing

Synonyms

Blending, homogenization.

Definition

Mixing is the process by which uniformity of concentration is achieved. Depending on the context, mixing may refer to the concentration of a particular component or set of components in the fluid.

Overview

Importance of mixing

A mixer is one of the basic building blocks in microfluidics, along with components such as pumps and valves, and is a critical component in several microfluidic devices. For example, mixing of reaction components is essential for providing homogeneous reaction environments for chemical and biological reactions. The efficiency of many devices such as biosensors depends on mixing. In other applications, rapid and controlled mixing is essential for studying reaction kinetics with much better time resolution as compared to microscale techniques. Microfluidic mixers are thus integral components essential for proper functioning of microfluidic devices for a wide range of applications.

Fundamentals of mixing

In the context of microfluidics, mixing is the process through which uniformity of concentration is achieved. Depending on the application, the concentration may refer to that of solutes (ions, small molecules, biomolecules, etc.), solvents, or suspended particles such as colloids. Microfluidics typically involves incompressible aqueous or organic solutions, and we will consider only these systems here.

Molecules in solution undergo random motions, giving rise to the process of diffusion. Under a concentration gradient, diffusion results in flux (J) of molecules that tends to homogenize the concentration (c) of that molecular species.

$$J = -D\nabla c \tag{1}$$

Here D is diffusivity of the species under consideration, and varies from approximately 10^{-9} m^2/s for small molecules and ions to 10^{-11} m^2/s for large biomolecules. Therefore, an isolated system with non-uniform concentrations ultimately achieves a state of uniform concentration, i.e. it will be completely mixed. The mixing time depends on the diffusivity (D) and length scale over which diffusion must act in order to homogenize the concentration, known as the striation length (l_{st}). The mixing time is then given by

$$t_{mix} \sim \frac{l_{st}^2}{D} \tag{2}$$

From this equation, it is clearly seen that for rapid mixing, it is necessary to reduce the striation length (Figure 1). This concept leads to two ideas intimately connected with the process of mixing: (a) the process of decreasing the distance over which diffusion must act, and (b) the process of diffusion itself. The former process of decreasing the striation length is accomplished by stretching and folding of the fluid or by breakup and rejoining. These processes decrease striation length and increase the area across which diffusion takes place, thus enabling diffusion to rapidly homogenize the solution.

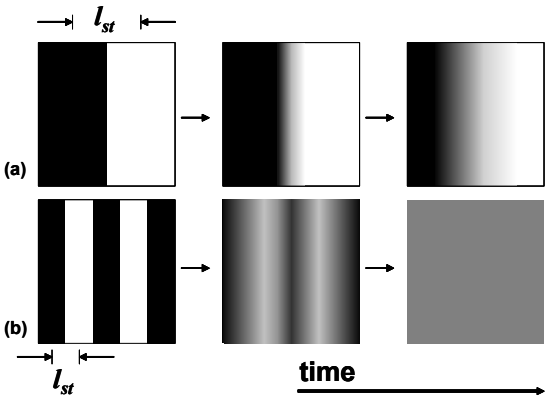

Figure 1. Striation length (l_{st}) and mixing time. The striation length characterizes the distance over which diffusion must act in order to homogenize the solution. (a) An unmixed solution with a large striation length takes time to mix by diffusion alone. (b) A 5-fold reduction in the striation length decreases the mixing time 25-fold.

Mathematically, the concept of mixing is rather unwieldy, and is built upon the concepts of ergodicity and dynamical systems theory. The reader is referred to Wiggins and Ottino [1] for an introduction to the mathematical treatment of mixing, and to Ottino [2] for a comprehensive treatment. Here we describe two types of flows or transformations with a mathematical basis that aid in understanding and designing mixers: The Baker's transformation is useful for understanding mixing involving the process of breakup, and blinking flows are useful for understanding the process of mixing in designs that do not involve breakup.

Consider a rectangular domain, with half of the domain marked with black points (Figure 2a). The Baker's transformation consists of stretching, cutting, and rejoining such that the striation length decreases uniformly everywhere in the domain. In the first step, the domain is stretched uniformly in one direction. In the second step, the domain is cut and rejoined. The striation length decreases by a factor of two each time the transformation is applied, therefore an exponential decrease in the striation length is achieved (Figure 2b). Mixing achieved in this transformation satisfies the strongest mathematical definition of mixing and is therefore highly desirable [1]. The Baker's transformation illustrates how the process of breakup can be used to exponentially decrease the striation length, and is useful for designing systems where fluid streams or droplets split and rejoin.

In a seminal paper in 1984, Aref [3] pointed out that simple time-varying two-dimensional flows can result in non-integrable particle trajectories, beautifully illustrated in the book by Ottino [2] (Figure 2c). This concept was the starting point of what is now widely called chaotic advection. While chaotic advection is not precisely defined, it is associated with exponential stretching and folding of the fluid. Aref considered mixing in an idealized bounded two-dimensional domain with blinking flows. Blinking flows switch instantaneously from one

streamline pattern to another in a periodic fashion. The relevance of this idealized concept to continuous-flow mixing in microfluidics is that flows transverse to the primary flow direction can be made to switch between two patterns as the fluid travels along the channel. Thus, a three-dimensional steady flow with periodicity in space may be understood in terms of a two-dimensional blinking flow with periodicity in time. An intuitive design criterion for such flows is that effective mixing corresponds to maximum crossing of streamlines of the two flows of the blinking flow. The mathematical basis of this design criterion is the linked twist map, described by Wiggins and Ottino [1]. Proper design of mixers incorporating the principles of chaotic advection can result in striation lengths that exponentially decrease in time.

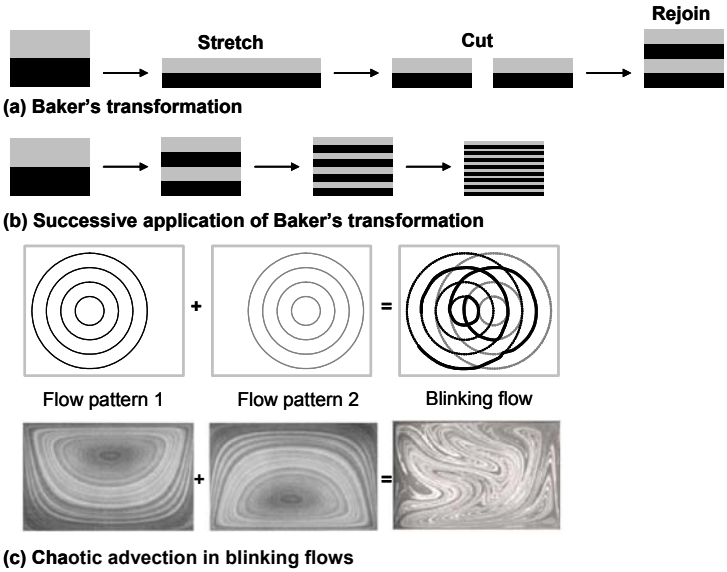

Figure 2. (a) Baker's transformation consists of stretching, cutting, and rejoining the domain. After each transformation, the striation length decreases by a factor of 2. (b) Successive application of the Baker's transformation results in exponential decrease of the striation length. (c) Blinking flows alternate periodically between two flow patterns. While each flow pattern exhibits simple streamlines and particle trajectories, the blinking flow itself exhibits chaotic advection and non-integrable particle trajectories. Images of cavity flow are reproduced from Ottino [2] with permission of Cambridge University Press.

Basic Methodology

Mixing in Microfluidics

The design and implementation of mixers in microfluidics differs considerably from than that on the macroscale. The small length scale leads to different physical phenomena being dominant at the microscale: First, inertial effects that typically result in turbulence and good mixing on the macroscale are weak in microfluidics, while methods of actuation based on electrokinetics, surface tension or other phenomena that are not relevant on the macroscale become feasible on the microscale. Secondly, many mechanical designs such as stirrers that can be easily implemented on the macroscale are very difficult to implement on the microscale. A useful mixer is therefore often the one that is simple to fabricate and integrate with other microfluidic components.

The Reynolds number (Re) characterizes the relative importance of inertial to viscous forces, and is given by

$$\mathrm{Re} = \frac{\rho U l}{\eta} \tag{3}$$

Here ρ is the density, U is flow velocity, l is the characteristic length scale (e.g., channel height), and η is the dynamic viscosity of the fluid.

In macroscale systems, the effect of inertia is often significant, resulting in a large Re and turbulence, which can be harnessed for mixing. However, due to the small channel size (l), microfluidic flows are characterized by a low Reynolds number, typically in the range of 0.01 to 100, and the effects of inertia are often negligible. Turbulence is therefore typically not encountered and microfluidic flows are usually laminar. Mixing due to diffusion alone is also not sufficient for rapid mixing in microfluidics. For example, a small molecule with a diffusivity of 10^{-9} m^2/s will take approximately 10 s to diffuse across a 100 μm microchannel, while a large macromolecule with a diffusivity of 10^{-11} m^2/s will require about 1000 s.

The Peclet number (Pe), a dimensionless number that characterizes the relative importance of diffusion to convection, is often used in the context of mixing of continuously flowing streams. The Peclet number is given by

$$Pe = \frac{l^2/D}{l/U} = \frac{t_{diff}}{\tau_{conv}} = \frac{lU}{D} \tag{4}$$

Here D is diffusivity, l is the characteristic length scale (typically channel height) and U is the flow velocity. The Peclet number can thus be viewed as the ratio of characteristic time for diffusion (t_{diff}) to the characteristic convection time (τ_{conv}). When mixing occurs only via diffusion in a microchannel, $t_{mix} = t_{diff} = \tau_{conv} Pe$. The channel length required for mixing (l_{mix}) is then given by

$$l_{mix} = U t_{mix} = lPe \tag{5}$$

A linear relationship between the mixing time and the Peclet number implies that the channel length needed for mixing increases linearly as the flow velocity is increased, or as the diffusivity is decreased (for different species). In order to minimize the channel length required for mixing, it is desirable to design mixers in which the mixing time increases only weakly with the Peclet number. For a microchannel with l = 100 μm, the Peclet number is 1000 for diffusivity (D) of 10^{-9} m^2/s (typical of small molecules) and flow speed of 1 mm/s. If mixing occurs purely due to diffusion, the channel length must be 1000 times the channel height for two streams to mix in the channel, i.e. the channel length must be 10 cm. However, if larger biomolecules with a diffusivity of 10^{-11} m^2/s are to be mixed, the required channel length increases 100-fold to 10 m!

Clearly, in the absence of turbulence, other methods of microfluidic mixing must be devised. Since mixing ultimately occurs by diffusion, the goal of all mixers must be to decrease the striation length across which diffusion takes place in order to mix more efficiently.

Mixer Performance

The criteria used to measure mixing vary widely. One of the more common measures for mixing known as the mixing variance coefficient (MVC) [4] is based on the concentration distribution inside the channel or volume. For this purpose, the volume under consideration is divided into sub-volumes, and the deviation of concentrations in each sub-volume from the average concentration in the volume is computed as follows:

$$MVC = \frac{1}{N}\sum\left(c_i - c_{avg}\right)^2 \quad (6)$$

Here N is the number of sub-domains, c_i is the concentration in the i^{th} sub-domain, and c_{avg} is the average concentration for the entire domain. MVC approaches zero when mixing is complete. Division of the domain into sub-domains for computing the MVC is shown in Figure 4a.

Experimentally, a commonly used method for characterizing mixing uses chemical reactions with fast kinetics. Such reactions may include reactions such as ion-binding fluorescent dyes that change fluorescence intensity upon binding the ion or pH indicators that change color. However, it must be noted that mixing characterized using these methods depends on reactant concentrations as well as diffusivities. Therefore, care must be exercised when attempting to evaluate mixing of the molecular species of interest using other species as indicators.

The criteria for evaluating the performance of microfluidic mixers vary widely depending on the application. However, for many applications, the most important criterion that determines the usefulness of the mixer is ease of fabrication. Mixers that can be easily incorporated with other microfluidic components are more likely to be used than those that require special fabrication procedures. Active mixers are generally more difficult to fabricate than passive mixers, and therefore find use only in certain applications. Apart from ease of fabrication, different applications may have different requirements that may be used to judge the performance of the mixer. Applications such as study of reaction kinetics demand rapid mixing and ease of observation of the ensuing reaction. Here, the primary consideration is usually mixing time. For combinatorial synthesis or other applications, it may be necessary to have a small space footprint and ease of integration with other components. In certain cases, pressure drop in the mixer may be important.

Key Research Findings

Mixer classification

Mixers are broadly classified as active or passive mixers based on the method of actuation. Active mixers employ “active” elements such as external pressure perturbations, small actuators, or other methods in addition to the applied pressure that drives flow. Passive mixers rely solely on the pressure gradient (or other mechanisms such as electroosmosis) that drives the flow in combination with “passive” elements such as channel geometry or other properties in order to achieve mixing. Note that the definition of passive mixers applies only to continuous flow systems, and mixers that mix stationary and bounded volumes of fluid are typically active mixers. Some passive mixers may operate at moderate Reynolds numbers and use inertial effects for mixing, while others use channel geometry or other effects to mix effectively at low Reynolds numbers. Typically, passive mixers are easy to fabricate and more robust than active mixers, and are therefore more widely used by researchers. Other methods of classification may be based on the physical phenomena driving the flow (electrokinetics, magnetohydrodynamics, ultrasound, inertia, etc.), single phase or multi-phase flows, fabrication complexity, continuous flow versus discrete volumes, etc. The following sections classify mixers as active/passive and further based on flow patterns, and other classifications are either self-evident or pointed out in specific cases of interest.

Passive Mixers

Passive mixers may be broadly classified as focusing/injection mixers, lamination mixers, and chaotic advection mixers. Focusing/injection mixers rely on diffusion alone to cause mixing. These mixers are effective if one stream with a small flow rate is to be diluted into another stream with a large flow rate. Lamination mixers typically split the streams to be mixed into multiple streams that are then interdigitated and brought together. Splitting into several streams decreases the striation length and therefore enhances mixing. In these cases, the striation length remains fixed during the process of mixing, and mixing time is approximately independent of the flow rate. Chaotic advection mixers, on the other hand, cause exponential thinning of the striation length. Achieving chaotic flows in passive microfluidic mixers typically requires three-dimensional channel geometry, use of weak inertial effects, or two-phase flows.

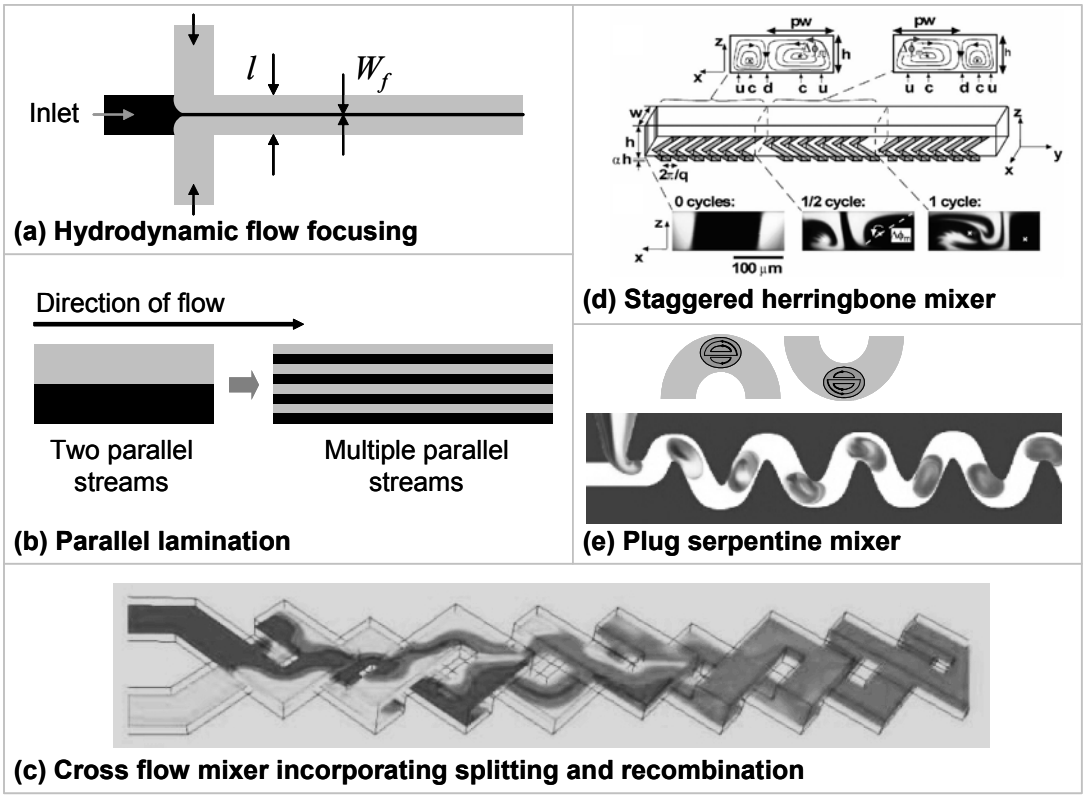

Figure 3. (a) Hydrodynamic flow focusing mixer. (b) Concept of parallel lamination. Rapid mixing is achieved by splitting two streams to be mixed into multiple parallel streams, thereby decreasing the striation length. (c) A passive chaotic advection mixer employing splitting and recombination. Reproduced from Xia with permission of RSC Publishing. (d) Staggered herringbone mixer uses grooves on channel walls to drive chaotic advection in microchannels. Alternating groove patterns result in asymmetric circulating flows similar to blinking flows. Reproduced from Stroock et al. [7] with permission of the American Association for the Advancement of Science. (e) Plug serpentine mixer uses a curved microchannel to induce chaotic advection inside plugs (droplets). Inset cartoon depicts alternating flow patterns inside individual plugs as they traverse through the channel. Reproduced from Song et al. [8] with permission of Wiley Interscience.

Focusing/Injection Mixers

Focusing or injection mixers are not true mixers; rather, they are very efficient at diluting one stream in another. In the hydrodynamic focusing mixer, three streams converge and flow into one microfluidic channel. Figure 2a shows a cartoon of the hydrodynamic focusing mixer reported by Knight et al. [5]. The inlet stream can be focused into a very thin stream by the adjoining side streams, either by controlling pressures of the three

streams or by controlling the flow rates of each stream using a syringe pump. Sub-micron focusing of the inlet stream enables species from the side streams to rapidly diffuse into the focused stream. Homogeneity of concentration is achieved as far as species in the adjoining streams are concerned. However, species in the focused stream take much longer to distribute uniformly across the channel cross section. Mixing time in this mixer depends only upon the width (w_f) of the central focused stream, which defines the striation length in this case:

$$t_{mix} \sim \frac{w_f^2}{D} = \left(\frac{w_f}{l}\right)^2 \tau_{conv} Pe \qquad (7)$$

It is seen that mixing time scales linearly with the Peclet number. However, the mixing time is decreased dramatically since $w_f << l$. For $D = 10^{-9}$ m^2/s (typical of small molecules or ions) and $w_f = 100$ nm, the mixing time is only 10 μs. This mixer is a very effective tool for rapidly changing the chemical environment of species in the central focused stream, at the same time consuming a smaller sample due to the low flow rate of the inlet stream. Hydrodynamic focusing mixers find applications in the study of fast kinetics such as protein folding.

Injection mixers are similar to flow focusing mixers in that they also dilute one stream into another stream; however they differ from focusing mixers in that a small aperture is used to inject a thin stream into another stream. These mixers enable multiple flow streams to be injected, and may be more desirable when flow rates or pressures cannot be controlled. Mixing time depends on the method of injection and device geometry. However, construction of small apertures or the use of a membrane with apertures is required, making injection mixers harder to fabricate compared with focusing mixers.

Lamination mixers

Lamination mixers employ parallel lamina across which diffusion can take place. The simplest mixer is the classic T-mixer that brings together two fluid streams and allows diffusive mixing as they flow parallel in a channel. In the absence of turbulence, the effective striation length is of the order of the channel size. Therefore, the mixing time in this case is given by

$$t_{mix} \sim \frac{l^2}{D} = \tau_{conv} Pe \qquad (8)$$

Mixing time scales linearly with the Peclet number, and mixing time is equal to the characteristic time for diffusion across the channel cross-section. This mixer requires long mixing times, but is very simple to implement and hence becomes a practical multi-purpose mixer in cases where there are no severe demands on mixing time and channel length. An improvement over the T-mixer is the parallel lamination mixer (Figure 2b). This mixer splits the streams to be mixed into multiple streams, which are interdigitated and recombined. If each stream is split into N streams, the striation length is decreased by a factor of N and mixing time is consequently decreased by a factor of N^2.

$$t_{mix} \sim \frac{(l/N)^2}{D} = \frac{\tau_{conv} Pe}{N^2} \qquad (9)$$

For example, with D = 10^{-9} m^2/s, l = 100 μm, and N = 10, the mixing time decreases from approximately 10 seconds to just 100 ms, and the channel length required for mixing also decreases by two orders of magnitude. This mixer is therefore more effective than the T-mixer, even though mixing time scales linearly with the Peclet number. However, interdigitation involves crossing over of channels, requiring a two-level fluidic architecture that is harder to fabricate than the single-level fluidic architecture of the T-mixer.

Passive chaotic advection mixers

Proper design of mixers incorporating the principles of chaotic advection can result in striation lengths that exponentially decrease in time. Since steady two-dimensional flows cannot exhibit chaotic advection [1], passive chaotic advection mixers need either three-dimensional geometries or use of weak inertial effects in order to achieve chaotic advection. Alternatively, flow in the third dimension can be imparted using two-phase flows in channels with two-dimensional geometries (i.e. obtained by extrusion of a two-dimensional pattern). Continuous flow chaotic advection mixers usually consist of repeating units that perform stretching and folding or breakup and rejoining operations in each unit. After each unit, the striation length decreases by a constant factor (e.g. by a factor of 2), and exponential decrease in the striation length is achieved as the fluid stream traverses multiple units. The mixing length scales only as the logarithm of the Peclet number, making chaotic advection mixers highly effective in mixing at high Peclet numbers (low diffusivity or high velocity). For example, consider a mixer in which the striation length decreases by a factor of two after every unit. If τ_{conv} is the time required to traverse one unit of the mixer,

$$l_{st} = l2^{-t/\tau_{conv}} \tag{10}$$

Mixing may be said to be complete when the time required for diffusion across the striation length equals the time required to traverse one unit of the mixer [6].

$$\frac{l_{st}^2}{D} \sim \tau_{conv} \tag{11}$$

The mixing time and mixing length are then given as follows:

$$\begin{aligned} &\frac{l_{st}^2}{D} \sim \tau_{conv} \\ &t_{mix} \sim \tau_{conv} \log Pe \\ &l_{mix} \sim l \log Pe \end{aligned} \tag{12}$$

It is thus seen that mixing time now scales logarithmically with the Peclet number instead of linearly as in the case of the T-mixer or flow focusing mixer.

Low Reynolds number chaotic advection mixers

Microfluidic mixers can be designed to mix using the principles of chaotic advection even in the purely viscous flow regime. Xia et al. [7] reported a mixer that splits, reorients and recombines flows using crossing channels (Figure 3c). While several mixers with three-dimensional geometries mix flows at intermediate Reynolds numbers, this mixer is one of the few mixers that can mix in the regime of purely viscous flow. The three-dimensional architecture is essential for reorienting the fluid elements before recombination. The mixer was fabricated using two-level microchannels using PDMS, a silicone polymer commonly used for fabrication of microfluidic devices. Good mixing was possible at very small Reynolds numbers down to 0.01.

Stroock et al. [8] reported a staggered herringbone mixer that uses grooves on channel walls to drive transverse flows. An asymmetric herringbone groove structure results in two asymmetric circulating flows in the channel. Circulating flows that alternate periodically along the channel

are established by alternating the herringbone pattern (Figure 3d). Effectively, it results in a time-dependent two-dimensional blinking flow with intersecting streamlines, resulting in chaotic advection. In this mixer, the mixing length was shown to scale logarithmically with Peclet number over a range of 6 orders of magnitude of the Peclet number. Unlike other chaotic advection mixers that require a two-level fluid architecture, this mixer only requires grooves on the substrate, greatly simplifying the fabrication process. This mixer has therefore found wide application in microfluidics.

Two-phase flow mixers

Three-dimensional geometries are inherently more difficult to fabricate than two-dimensional channel geometries. However, steady two-dimensional viscous flows are inherently integrable, and chaotic advection is not possible. Two-phase flows overcome this obstacle by introducing circulating flows inside fluid segments or droplets, which can be used to convert the inherently two-dimensional flows to three-dimensional chaotic flows under suitable conditions. The serpentine mixer reported by Song et al. [9] is the most prominent mixer in this category (Figure 3e). This mixer consists of a wiggly serpentine channel in which droplets of one phase (usually aqueous) flow in another continuous phase (usually oil). When the droplets occupy nearly the entire channel cross-section, they are termed as plugs. As a plug traverses a serpentine channel, the flow inside each plug alternates between two flow patterns with crossing streamlines. This flow pattern results in chaotic advection and rapid mixing. The same principle can be applied to mix liquid segments separated by gas bubbles. Millisecond mixing timescales are possible with this mixer, and sub-millisecond timescale kinetics can be probed, making the it one of the fastest mixers for mixing fluid streams in any given flow ratio. While increasing flow speed can decrease mixing time, this mixer is limited by break-up of the plugs/fluid segments that occurs at high flow speeds. In order to sustain plug flows without breakup of the plug or bubble, surface tension (γ) must be sufficiently large compared to shear forces. This phenomenon is characterized by the Capillary number:

$$Ca = \frac{\eta l U}{\gamma} \tag{13}$$

For Ca>1, plugs may be sheared into smaller droplets that destroy proper flow in the mixer. Two-phase mixers are well-suited for studying reaction kinetics because each plug or fluid segment acts as an individual reactor, and there is no dispersion along the flow direction. With increasing use of two-phase systems, this mixer has found wide application in areas ranging from chemical synthesis to biochemistry.

Intermediate Reynolds number mixers based on weak inertial effects

While turbulence sets in at Reynolds numbers greater than about 2300, even at low Reynolds numbers inertial effects can induce transverse flows that impart three-dimensionality to a flow that is otherwise two-dimensional at lower Reynolds numbers. At still higher Reynolds numbers, inertial effects can produce flow separation, vortex formation, and vortex shedding. These effects can be harnessed for mixing, and proper design can even lead to chaotic advection at intermediate Reynolds numbers. The simplest mixer in this category is the serpentine mixer that consists of a zigzag channel. Sharp bends in the mixer create cross-flows that enhance mixing. Mixing is due to diffusion alone at Reynolds numbers below about 80, and it improves at higher Reynolds numbers [5]. Another class of mixers based on Tesla structures employ in-plane splitting and recombination of streams and can mix at Re>5 [5]. Liu et al. [5] reported a three-dimensional serpentine mixer that uses C-shaped segments. The device has two fluidic layers, and was fabricated in silicon and glass. Chaotic advection was found to occur at Reynolds numbers higher than 20. Mixers operating at intermediate to high Reynolds numbers are especially useful when comparatively high flow rates are required, such

as in chemical synthesis. However, these mixers are typically not used for biological applications, where the samples are usually smaller and more expensive.

Mixers based on other instabilities

Mixing in turbulent flows that occur at high Reynolds numbers is an illustration of mixing due to instability induced in the flow by inertial effects. Similarly, other phenomena may lead to instabilities in microfluidic flows and may be harnessed for mixing. The only known examples of mixing using other instabilities are the electrokinetic instability mixer and the viscoelastic instability mixer [6]. The electrokinetic instability mixer uses instabilities induced in the charged region at the junction of two fluid streams with differing ionic compositions when an electric field is applied parallel to the junction. The viscoelastic intability mixer exploits non-Newtonian fluid properties in order to achieve mixing.

Active Mixers

In addition to pressure gradients and inertial effects, several other mechanisms can be used to drive fluid flow for mixing. These mechanisms can range from simple pressure disturbances to more complicated systems utilizing miniature actuators.

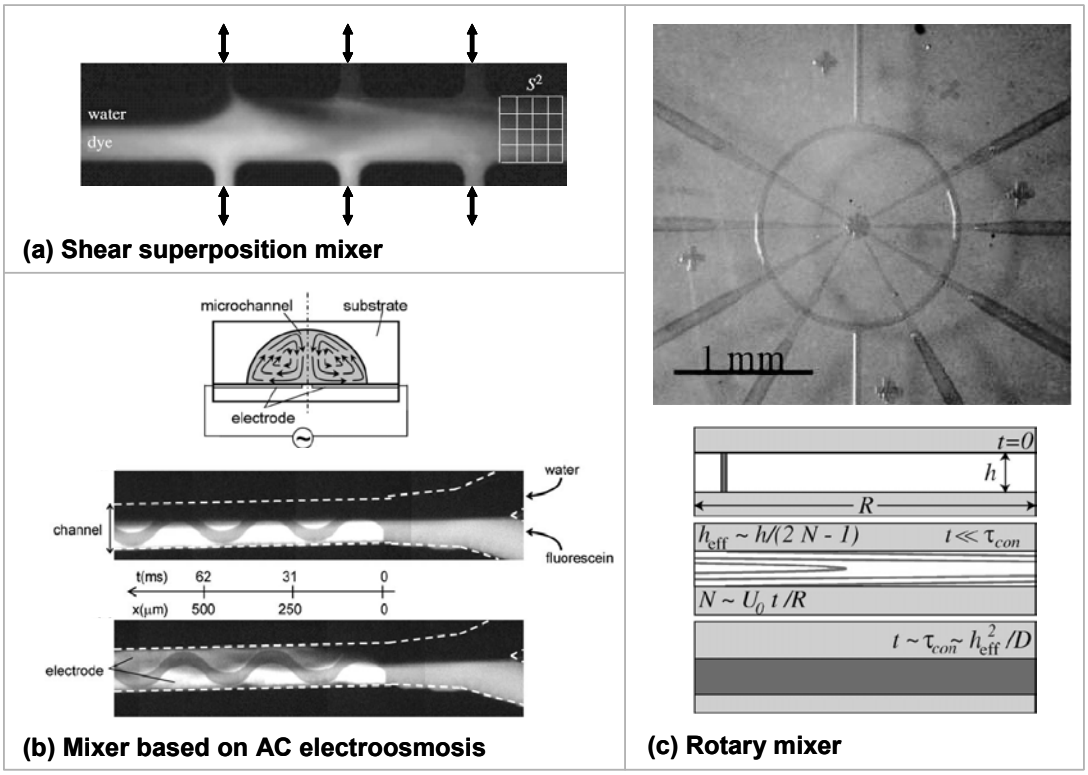

Figure 4. (a) The shear superposition mixer employs side channels to drive oscillating flow and induce chaotic advection in the main channel. The micrograph depicts six side channels mixing a stream of water and dye solutions in the main microchannel. The grid shown is used for computing mixing using the mixing variance coefficient (MVC). Reproduced from Bottausci et al. [4] with permission of Royal Society Publishing. (b) A mixer based on AC electroosmosis to mix by driving asymmetric circulating flows inside a microchannel. Cartoon depicts circulating flow; water and dye streams are shown in the absence and presence of AC electroosmosis. Reproduced from Sasaki et al. [10] with permission of RSC Publishing. (c) A rotary mixer uses pumps to drive flow in a circular microchannel. Algebraic stretching of the fluid results in a rapid decrease in the striation length (h_{eff}) and thus enables mixing. Reproduced from Squires et al. [9] with permission of the American Physical Society.

Pressure/velocity field disturbance mixers

These mixers rely on external pressure or velocity disturbances to change the flow pattern inside the channel and thereby enable faster mixing. Bottausci et al. [4] reported a shear superposition mixer that employs actuating side channels that are perpendicular to the main channel (Figure 4a). An oscillating pressure or velocity disturbance in these channels affects flow in the main channel and causes mixing. With the correct choice of driving frequencies and amplitudes in the side channels, it is possible to induce chaotic advection and rapid mixing. Another simple design is a modification of the T-mixer. Instead of a steady flow in the two input channels, the driving pressure or flow rates are oscillated so that the mixing channel receives alternating longitudinal bands of fluid from each input channel. The parabolic flow then stretches these bands, algebraically decreasing the striation length and enabling faster mixing.

Rotary mixer

Rotary mixers [6] are very useful in integrated microfluidics, pioneered by the group of Stephen Quake. This microfluidic architecture uses a control layer of fluidic channels that can squeeze an underlying layer of channels, just as stepping on a garden hose clamps it shut. The operation of such elements requires a flexible material such as PDMS for device fabrication. A single element can function as a valve, and three elements operating together can function as a pump. With this basic design of externally actuated valves and pumps, it is possible to perform complex multiplexed fluidic manipulation. The mixer works by driving fluid flow in a circular microchannel using a pump. Fluid volumes to be mixed are first metered into the circular channel, forming bands shaped like arcs in the circular microchannel. Driving fluid flow around the circular channel results in linear stretching of the fluid inside the channel and the striation length decreases algebraically with time. Complete mixing can be achieved within one second. Rotary mixers are useful in such architectures for mixing metered volumes of fluid in a serial fashion or for continuous stirring in confined volumes, and have found applications in chemical synthesis and combinatorial screening.

Induced field electroosmosis mixers

Induced field electroosmosis (sometimes known as AC electroosmosis) is electroosmotic flow generated under AC excitation in an electrolyte solution due to tangential migration of induced charges at the electrode-solution interface. This method is relatively simple for driving fluid flow because it does not involve any moving parts and planar electrodes can be easily fabricated using conventional lithographic techniques. Sasaki et al. [10] demonstrated one such mixer that involves asymmetric patterned electrodes inside a mixing microchannel. AC electroosmosis drives asymmetric circulating flow that results in rapid mixing. Mixing was observed to occur in 0.18 s, approximately independent of the flow velocity and 20 times faster than that in the absence of AC electroosmosis. While this mixer was not designed for chaotic advection, induced field electroosmosis offers a wide variety of design possibilities by changing the device geometry. The main drawback of induced field electroosmosis is that it is sensitive to the presence of buffers and biomolecules in the solution.

Other types of mixers

Apart from the methods described above, there are several different ways in which microfluidic flows can be driven [5]. Several of these methods have been used for microfluidic mixing including dielectrophoresis (migration of polarizable particles under an electric field gradient), electrokinetics (fluid flow driven by migration of charges at microchannel surfaces under an electric field along the channel), acoustic actuation, thermally generated bubbles, magnetohydrodynamics (flow in a current-carrying fluid in a magnetic field induced by

Lorentz forces) among others. Most of these mixers are highly specialized and do not find broad applications.

Future Directions for Research

Recent years have seen rapid progress in application of the theory of mixing as well as in the innovative design of new microfluidic mixers. The design space available for innovation in this field is vast, and new mixers are constantly being developed. The mathematical foundations of mixing are being used to optimize the design of mixers. Theorists have developed models and guidelines for mixer design that can be easily adapted by researchers who use microfluidic mixers, but are typically not involved in the theory of mixing. In the future, we may see innovative mixer designs that are effective yet easy to implement, and rest on the mathematical foundations of mixing.

Cross-references

Active Mixing
Browning Motion and Diffusion
Chaotic Flow
Chaotic Mixing Based on Viscoelasticity
Compute Mixing Efficiency
Curved Microchannel Flow
Droplet Based Lab-on-chip Devices
Passive Mixing

Further Reading

1. Wiggins S, Ottino JM Foundations of chaotic mixing (2004) Philosophical Transactions of the Royal Society of London Series A-Mathematical Physical and Engineering Sciences 362(1818): 937-970
2. Ottino JM (1997) The kinematics of mixing: stretching, chaos and transport. Cambridge University Press, Cambridge, UK
3. Aref H Stirring by Chaotic Advection (1984) Journal of Fluid Mechanics 143(Jun): 1-21
4. Bottausci F, Mezic I, Meinhart CD, Cardonne C (2004) Mixing in the shear superposition micromixer: three-dimensional analysis. Philosophical Transactions of the Royal Society of London Series A-Mathematical Physical and Engineering Sciences 362(1818): 1001-1018
5. Nguyen NT, Wu ZG (2005) Micromixers - a review. Journal of Micromechanics and Microengineering 15(2): R1-R16
6. Squires TM, Quake SR (2005) Microfluidics: Fluid physics at the nanoliter scale. Reviews of Modern Physics 77(3): 977-1026
7. Xia HM, Wan SYM, Shu C, Chew YT (2005) Chaotic micromixers using two-layer crossing channels to exhibit fast mixing at low Reynolds numbers. Lab on a Chip 5(7): 748-755
8. Stroock AD, Dertinger SKW, Ajdari A, Mezic I, Stone HA, Whitesides GM (2002) Chaotic mixer for microchannels. Science 295(5555): 647-651
9. Song H, Tice JD, Ismagilov RF (2003) A microfluidic system for controlling reaction networks in time. Angewandte Chemie-International Edition 42(7): 768-772
10. Sasaki N, Kitamori T, Kim HB (2006) AC electroosmotic micromixer for chemical processing in a microchannel. Lab on a Chip 6(4): 550-554

2.674 / 2.675 Micro/Nano Engineering Laboratory

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