MICROFLUIDIC MIXING TECHNIQUES AND APPLICATIONS

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Abstract:

Microfluidics is a technology that has applications not just in the field of biomedicine but also in other fields. In the realm of medicine, microfluidics has proven to be particularly useful for a wide variety of applications, including single-cell analysis, tissue engineering, capillary electrophoresis, the detection of cancer, and immunoassays. The advancement of microfluidic technology has led to novel research into fuel cells, ink jet printing, microreactors, and electronic component cooling. These developments have benefited a wide variety of industries, including food, pharmaceutics, cosmetics, medicine, and biotechnology. Because laminar flow predominates at most flow regimes in the microscale, achieving thorough mixing is a difficulty in the field of microfluidics. Understanding the flow fields on the micro-scale is therefore essential to the development of ways for successfully applying microfluidic mixing techniques in various applications.

***Keywords:** Microfluidics,Mixing.*

Introduction:

The study of fluids as they pass through channels on a microscale is what we mean when we talk about microfluidics. At this scale, the behavior of fluids deviates from what is "normal" fluid behavior. Things that have minuscule effects on bigger scale systems start to dominate the system when they get a broad enough foothold. Surface tension, the rate at which energy can be dissipated, and the resistance of the fluidic medium all have a significant impact on this system. Microfluidics is the study of how these behaviors interact and interchange in these systems, as well as how they might be worked around or exploited for whole new uses. It can be investigated using CFD (computational fluid dynamics) and experiments. Because it offers a method for carrying out important chemical assessment processes in the biomedical area, this technology has been the subject of a significant amount of research. Microfluidic analyses provide several advantages over the typical bench-top procedures, including the low volume of reagents and buffers that are required for the analysis, as well as the speed with which the analysis is performed. In addition, because of their understanding of the physics and phenomena of micro-scale flow, microfluidic devices can carry out experiments and perform techniques that are not conceivable at the macro-scale. This might potentially pave the way for the development of new functionalities and experimental systems.

Microsystems also have several other benefits, such as the ease with which they may be automated, the fact that they are parallelizable, the fact that they are portable, and the relatively low cost of their materials.

Most microfluidic devices include the movement of sample or reagents through confined microchannels in geometries that are embedded in chips. In addition to doing chemical analysis, microfluidics also provides us with an intriguing set of tools for conducting research in the field of biology. There are numerous biological applications that have been reduced in size and placed on a chip. These applications have been miniaturized into a chip, and they include cell sorting and counting, DNA sequencing, and DNA separation. Other applications include polymerase chain reaction, electrophoresis, and polymerase chain reaction. The sequencing of DNA, the separation of DNA, the polymerase chain reaction (PCR), electrophoresis, and the sorting and counting of cells are some examples of these uses.

Governing Equations:

The equation $Q = P/R$ Q= governs the flow rate Q (m^3s^{-1}) that occurs in microchannels that have been artificially manufactured. Where P represents the pressure drop across the channel and R represents the resistance of the channel. The term "R" takes into consideration changes between channels, such as the surface resistance of the material or the channel geometries. This is done so that the term may be applied consistently. Because of the way that this equation is written, there must be a pressure difference to generate a flow rate. This can be generated in several different ways, however pressure driven flow and electro kinetic flow are two methods that are utilized frequently in mostapplications. Flow that is manufactured using an external pump or a vacuum source is referred to as pressure driven flow. This frequent method creates a flow that has a parabolic velocity profile, which may not be optimal for some applications such tests that call for high-resolution separation. This is one of the reasons why this method is not ideal for some applications. After that, the samples might experience something called axial dispersion, which would lead to a broadening of the felt peak. The electrokinetic flow method is the second approach. Electrokinetic flow is comprised of two distinct processes: electro phoresies and electro osmosis. Electro phoresies is characterized by a uniform plug-like flow of fluid in the channels, whereas electro osmosis results from the accelerating force caused by the charge of a molecule moving through an electric field and is counterbalanced by the force of friction. The machinery that is required to create electrokinetic flow is pricey, but there are a lot of benefits associated with using it. Electrokinetic flow, as opposed to pressure-driven flow, results in flat velocity profiles, which makes it possible for capillary electrophoresis to achieve high resolution separations. The flow may also be readily controlled in electrokinetic flow without the need for valves by simply turning on and off voltages. This is possible since electrokinetic flow does not use valves. One of its drawbacks is that it is incompatible with some buffers. Additionally, this method can only accommodate a limited range of strengths. The pH level and the ionic strength are compatible with one another. A power supply that is external to the microfluidic chip is required, and there is the potential for difficulties to result from unintended heating of the fluid, such as the evaporation of the solvent or the creation of electrolytic bubbles. On the other hand, the huge quantity of surface area in comparison to the volume enables a significant amount of heat to be lost. Other ways of producing flow are now

being investigated as potential options. Chou et al. developed a pneumatically actuated pump that could mix fluids coming from several different inlets.

Principles and Terminology of Fluid Mixing:

There are several terms that, when used interchangeably, can convey the same sense as mixing without causing substantial difficulties or confusion. These include things like stirring, combining, agitating, and kneading, amongst others. It is not our intention to make a detailed distinction between the two at this time; however, it is important that we highlight the plausible definition offered by

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With relation to the distinction between mixing and stirring because the distinction lies in the process that is actually taking place during mixing. In other words, when we talk about mixing, we are referring to a physical process in which both stirring, and diffusion are happening at the same time. When applied in this context, the term stirring refers to the advection of material blobs that are mixed without the effect of diffusion. In other words, we can say that the process of effectively mixing materials with low diffusivity takes place in two stages: the first stage involves stirring, and the second stage involves diffusion. Imagine for a moment that we have two distinct types of liquids near one another, and that our primary objective is to combine the liquids (see Figure 1 for an illustration of this). Even if random motion of the molecules in the liquid occurs everywhere, it does not produce any noticeable change in the bulk of each liquid far from the interface. This is because all the molecules in each distinct liquid have the same characteristics. However, in the region close to the interface, molecules on both sides have distinct characteristics; as a result, random motion of molecules causes molecules to pass through from one side to the other. This process is known as permeation. The term "diffusion" refers to this type of apparent penetration. Because there has been no permeation yet, the interface is initially quite acute; nevertheless, as the diffusion process continues, it gradually causes the liquid species to distribute themselves across the contact. The gradual spread of the substance results in a slower progression of the diffusion process. It is known as Fick's law that the flux of one species over the interface is proportional to the gradient of the concentration of the species, and the constant that defines the proportional relationship is known as the molecular diffusivity.

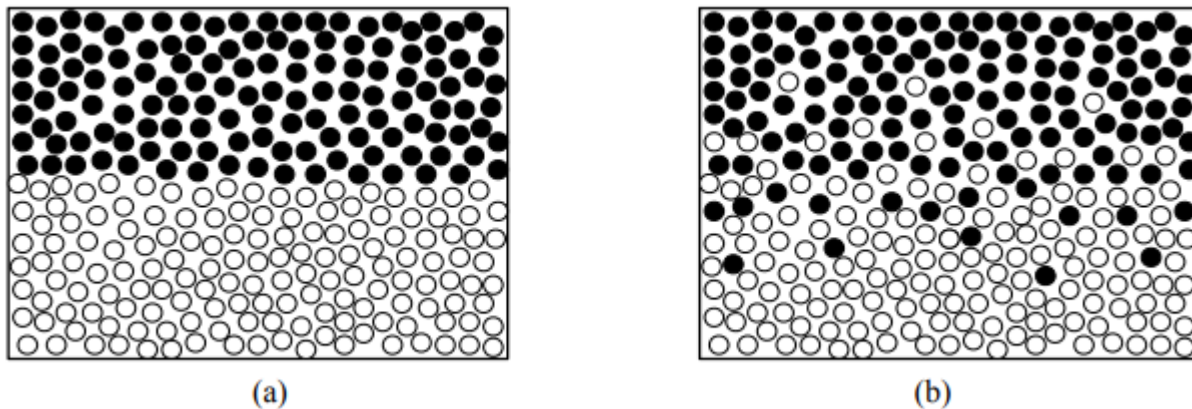(a)   (b)

Figure 1 is a cartoon that illustrates the exchange of molecules across an interface between two different fluids, which is activated by the molecules' random motion; (a) before commencing the exchange, and (b) the instantaneous state while the exchange is taking place.

There are several terms that, when used interchangeably, can convey the same sense as mixing without causing substantial difficulties or confusion. These include things like stirring, combining, agitating, and kneading, amongst others. It is not our intention to make a detailed distinction between the two at this time; however, it is important that we highlight the plausible definition offered byThere are several terms that, when used interchangeably, can convey the same sense as mixing without causing substantial difficulties or confusion. These include things like stirring, combining, agitating, and kneading, amongst others. illustrates a typical microchannel that does not have any mixing elements or structures; it is not our intention to make a distinction between the two in this context, but we do feel the need to emphasize the realistic definition offered by Figure 2. Because of the way in which two distinct fluids coming from separate reservoirs run parallel to one another, there is no stirring that occurs, and the mixing that does take place is entirely diffusive. We will refer to the proportion (also known as the concentration) of fluid A that is present in an unspecified volume that is occupied by a combination of fluids A and B with the symbol c. Then, the bottom half region will be given $c = 0$ while the upper half will be given $c = 1$ at the entry of the channel (also known as P0 in Figure 2), which is where the two different types of fluids begin to encounter one another. As can be seen in Figure 2, the gradient of the concentration distribution flattens out as one moves further downstream from the point of origin (P0). The maximum values of the concentration, however, are still present.

Remain the same at $c = 1$ and $c = 0$ all the way down to point P1. After passing this point, farther downstream, the maximum and lowest values of c will begin to decline and grow, respectively, until they ultimately approach the ultimate value of c, which is equal to 0.5.
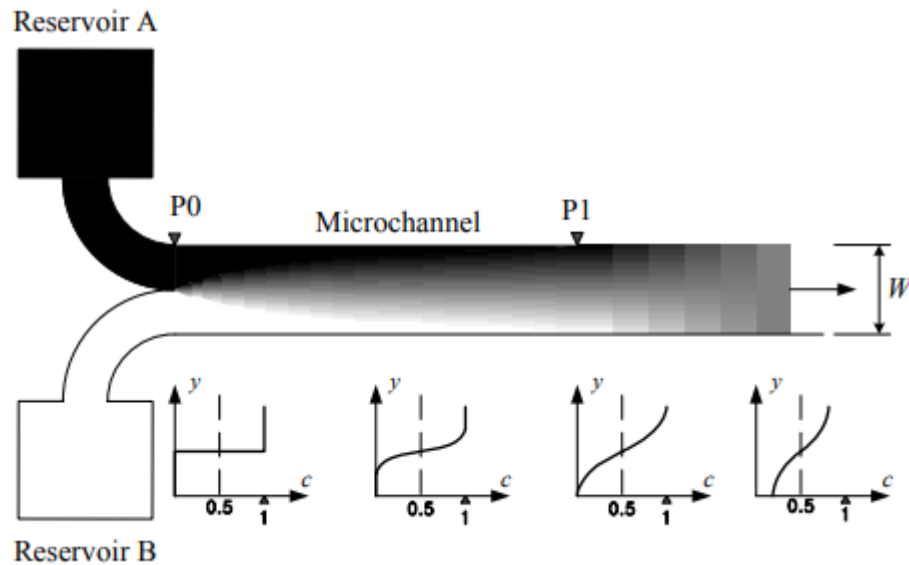
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Figure2 A schematic representation of a typical concentration distribution (at the grey level) inside of a microchannel that does not contain a particular mixing element. The concentration distribution at several different channel sections is depicted in the following graphs as a function of the coordinate that is normal to the channel wall (y).

We can construct an approximate formula for time that is required for the diffusive mixing if we assume that the concentration distribution is in a steady state and that the flow fluid velocity is uniform along the channel, u = U, v = 0. With these two assumptions, we can calculate the amount of time that is required for the mixing to occur. The equation for transport for c looks like this:

$$U\frac{\partial c}{\partial x} = D\frac{\partial^2 c}{\partial y^2} \tag{1}$$

Where there is a disregard for diffusion in the direction of the mainstream. To obtain the result, we need to use the Lagrangian's coordinate = x/U.

$$\frac{\partial c}{\partial \tau} = D\frac{\partial^2 c}{\partial y^2}. \tag{2}$$

The coordinates y and, also known as Lagrangian's coordinates, are currently being used to measure, respectively, the space and time that follows the fluid substance. The second equation is referred to as the heat equation, and the precise the solution is common knowledge. Nevertheless, it depends on the error function; hence, its evaluation calls for an additional calculation to be performed. As a result, in this work, we make use of an integral method to make the analysis more straightforward. We assume that the answer lies in the transient process that occurs during the first stage (i.e., between P0 and P1 in Figure3

$$c = \begin{cases} 1 - \dfrac{1}{2}\exp[-\eta/\delta(\tau)] & \text{for } \eta \geq 0 \\ \dfrac{1}{2}\exp[\eta/\delta(\tau)] & \text{for } \eta < 0 \end{cases} \qquad (3)$$

where $\eta = y - W/2$ and $\delta(\tau)$ represents the thickness of the interface between the high concentration in the upper region and the low concentration in the lower part,when we plug three into two and integrate

$$\delta = \sqrt{2D\tau}$$

the resulting function across the whole range of, we get the following:

As the solution for the second-stage's diffusion process, the concentration profile can be approximated as.

$$c = \frac{1}{2} + \frac{1}{2}\exp\left[-\pi^2 D(\tau - \tau_1)/W^2\right]\sin(\pi\eta/W) \qquad (4)$$

where τ_1 is the time needed for the first stage's process, which can be given from the requirement.

$$\left[\int_0^\infty (1-c)d\eta\right]_{1st} = \left[\int_0^W (1-c)d\eta\right]_{2nd}$$

Then, we obtain.

$$\tau_1 = \frac{(1-2/\pi)^2 W^2}{8D}$$

The time needed for the second stage, τ_2, depends on the requirement for the smallness of $\varepsilon \equiv 2|c-1/2|_{max}$, e.g., $\varepsilon = 0.01$. Then we derive

$$\tau_2 = \frac{(-\ln\varepsilon)W^2}{\pi^2 D}$$

The total time $\tau_{tot} \equiv \tau_1 + \tau_2$ is then

$$\tau_{tot} = \left[\frac{(1-2/\pi)^2}{8} - \frac{\ln\varepsilon}{\pi^2}\right]\frac{W^2}{D} \qquad (5)$$

For the case of D = 1011 m^2/s and W = 200m, we get τ1 = 66s and τ2= 1,870 s, both of which are significantly longer than what is required for the applications in the real world. As a result, the development of an extra device to expedite the mixing process is required. The notion of a typical configuration of the hydrodynamic focusing method that was designed to hasten the mixing is depicted

in figure 3, which provides an illustration of the concept. Both the upper and lower fluids are directed into the channel in such a way that the contact area is greatly enlarged because of the process. Again, there is no stirring that can be detected, but the interfacial area is much enhanced in comparison to what was seen in Figure 2. It is possible to demonstrate that the amount of time required to complete the first stage and the second stage of the concentration diffusion are, respectively, given from.

$$\tau_1 = \frac{(1-2/\pi)^2 (W/n)^2}{8D}$$

$$\tau_2 = \frac{(-\ln \varepsilon)(W/n)^2}{\pi^2 D}$$

n is the number of fluid segments, hence the total time is calculated as τtot = n + 2, where n represents the number of fluid segments. For example, in Figure 3, n equals 6. As an illustration, where D is equal to 1011 m 2 /s, W is equal to 200 m, we have 1 = 0.66 s and τ2 = 18.70 s, both of which are within a suitable range. However, if we use a diffusivity that is ten times smaller than this one, we get τtot= 194 s, which is once again an unacceptable value. If this is the case, we could have to increase the number of fluid segments that have been separated or employ another strategy to improve the mixing, such as chaotic advection. Figure 3 is an illustration of the usual growth of concentration along the cross-section of the channel that occurs during the hydrodynamic focusing method.

Figure 3 The dashed, dash-dot, and dash-dot-dot lines illustrate the first stage, while the solid line is for the second stage in this schematic of the two-stage evolution of concentration distribution over the cross-section of the channel in the one-dimensional diffusion model for the hydrodynamic focusing method. Figure 4 shows a schematic representation of the two-stage development of concentration distribution along the cross-section of the channel in the one-dimensional diffusion model for the hydrodynamic focusing method. The dashed, dash-dot, and dash-dot-dot lines represent the first stage, while the solid line represents the second stage.
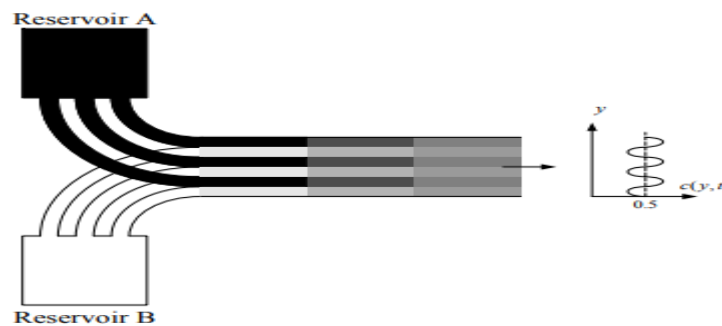
Figure 3The diagram shows a schematic of the two-stage evolution of concentration distribution over the cross-section of the channel in the one-dimensional diffusion model for the hydrodynamic focusing method. The dashed, dash-dot, and dash-dot-dot lines indicate the first stage, while the solid line is for the second stage.
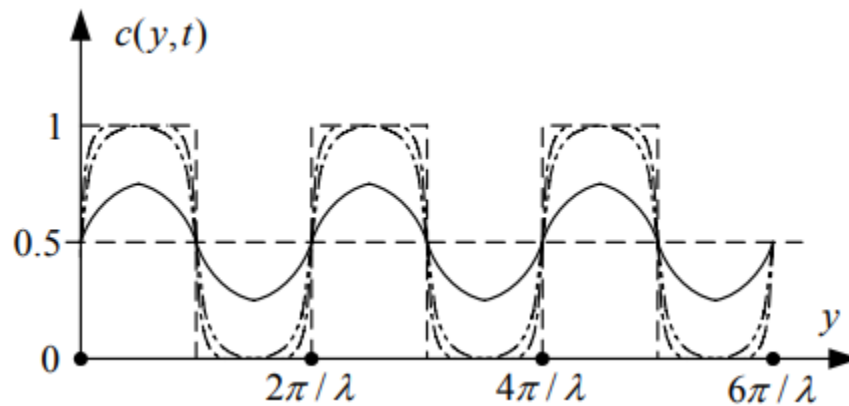
Figure 4 depicts the usual development of the striation pattern and the concentration distribution that is generated by chaotic mixing to be realized from a one-dimensional model.

It is now generally acknowledged as a rule that the chaotic mixing mechanism is superior to other mixing mechanisms when it comes to microscale mixing. Both patterns are a result of the chaotic mixing process. In this animation, we detect two distinct mechanisms that take place at the same time. The first mechanism is the stretching and folding of fluid blobs, which results in the exponential decrease of the striation thickness. The second mechanism is the diffusion of the concentration across the striation. Both mechanisms are occurring concurrently. Aref was the first person to describe the former process, which is known as chaotic advection or chaotic stirring the final procedure to obtain a uniform distribution of the concentration, which is the symptom of the completion of mixing, is brought about by molecular diffusion, which is the second mechanism. This is the case because molecular diffusion is the mechanism that allows molecules to move from one location to another. However, without the assistance of the chaotic advection, it is not possible to have the fine structure in the striation pattern that is necessary for rapid diffusion. This is a precondition for the process.Figure 5. The chaotic advection (on the left) and the molecular diffusion (on the right) of the chaotic mixing mechanism are responsible for the typical development of the striation pattern (on the right) and the concentration distribution (on the left). The chaotic advection has been enhanced, but the profiles in (a) to (c) should also look smooth like in (d) and (e)
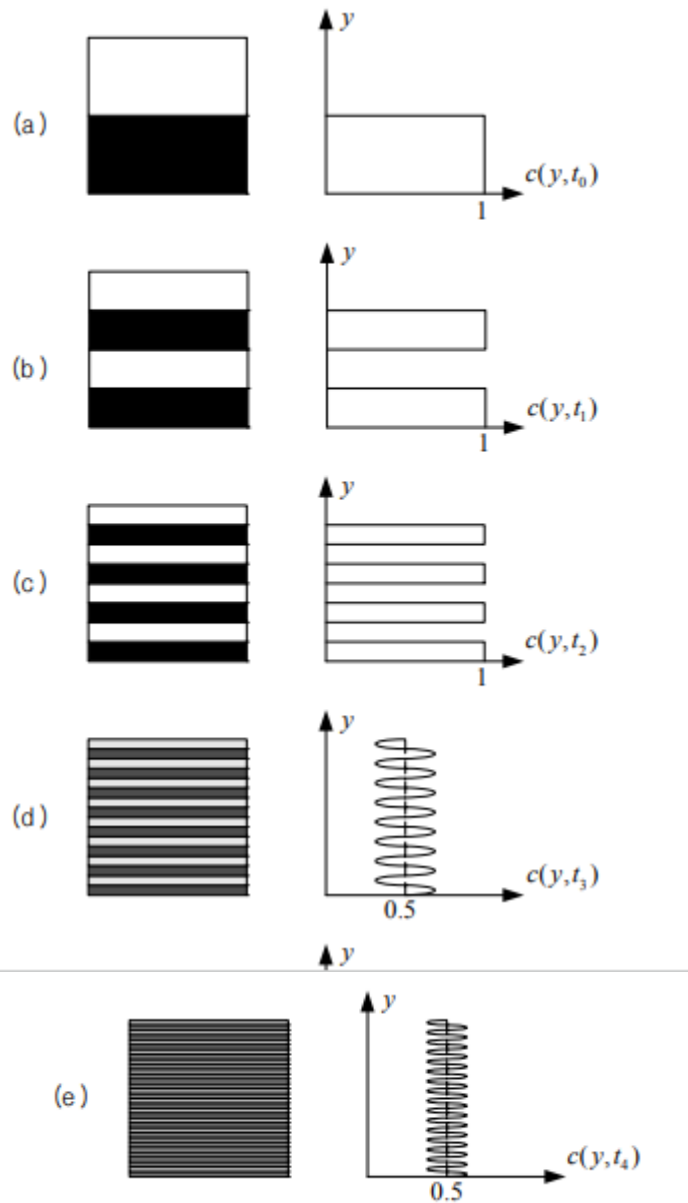
Figure 5 occurs regularly in time with the period T; more specifically, we will say that the striation is cut in half after each time T.

If the mixing is chaotic, we try to estimate how long it will take. To do this, we will assume that the stretching-folding process in When we consider the stretching mechanism, we are able to write the following one-dimensional governing equation for the growth of the concentration.

$$\frac{\partial c}{\partial \tau} + v \frac{\partial c}{\partial y} = D \frac{\partial^2 c}{\partial y^2} \tag{6}$$

Take note that the second term on the left-hand side of the preceding equation represents the material's stretching effect, and that v is not the velocity of the fluid but rather the squeezing velocity of the striation; the fluid material is 'stretched' along the longitudinal direction of the striation, but it can also be said to be 'compressed' across the striation pattern. By introducing the coordinate and placing its origin at the location where the concentration is guaranteed to always remain at c = 0.5, we can put = in a local context. In addition to this, we will use the integral approach, and we will assume the form. Then, we are given.

$$\delta = \left\{ \frac{DT}{\ln 2} [1 - \exp(-2\tau / T \ln 2)] \right\}^{1/2}$$

where the relation αT = ln2 has been used to eliminate α. After a sufficiently long time, δ reaches the limit value $\delta_\infty = \sqrt{DT / \ln 2}$. The number of periods k_c needed for the first stage is then given by equating $l_k = W / 2^k$ and δ_∞;

$$k_c = \frac{1}{\ln 2} \ln \left(\frac{W}{2\sqrt{DT / \ln 2}} \right)$$

The time needed for the first stage is then given by τ1 = kcT. Next, we introduce the Lyapunov exponent Λ related to T as ΛT = ln2. Then we have

$$\tau_1 = \frac{1}{\Lambda} \ln \left(\frac{W}{2\sqrt{D / \Lambda}} \right)$$

Finally, we arrive at the value 2, which represents the amount of time necessary for the second stage of mixing. The analysis is performed in the same manner as it was before, and the conclusion that we

$$k_d = \frac{1}{2 \ln 2} \ln \left[4^{k_c} - \frac{3(W / \pi)^2}{DT} \ln \varepsilon \right]$$

reach is that τ2 = (k_d − k_c) T, where dk is derived from.
The total time for the mixing is then obtained from,

$$\tau_{tot} = \tau_1 + \tau_2 = k_d T \qquad\qquad (7)$$

As an example, for D = 10 -11 m ^{2} /s, W = 200 μm, ε = 0.01 and T = 3 s, we get τ1 = 11.8 s, τ2 = 4.76 s and τtot = 16.6 s, which is again in the acceptable range. Even for diffusivity 10-times smaller than this, we get τtot = 38.4 s, This is barely one sixth of the value that was produced when hydrodynamic focusing was performed. The straightforward analysis that has been presented up to this point could be sufficient to demonstrate how significant the role of stirring is throughout the whole mixing process. Due to the enormous molecular sizes of the materials, the samples that need to be mixed in many

different applications have a very low diffusivity. One example of this would be for a chemical reaction. Therefore, the function of stirring should be prominent in the mixing process, and it is known that chaotic advection, which can also be described as stirring, is the only mechanism that can cause the exponential stretching of material blobs that is necessary for the optimal mixing.

Review on Various Mixer Designs for Microfluidic Applications:

Now we will go over the many different concepts of microfluidic mixers that have been described since 2005. In our review of the published research, we discovered that most studies focus on flows with a moderate or high Reynolds number. On the other hand, we chose not to include these articles in this analysis since flows with such a moderate or high Reynolds number are only occasionally observed in microfluidic applications. In addition, using these types of flows, it may be simple to create unstable complex flows, which, by their very nature, contribute greatly to the mixing of the fluid. There are several different ways in which the microfluidic mixers might be categorized. For classification in this article, we make use of the physical mechanism, specifically, hydrodynamic focusing, alternative injection, geometry effect, electrokinetic method, droplet mixing, and stirring by particles.

The fundamental mechanism underlying the hydrodynamic focusing was discussed in Section 2, as was previously mentioned. constructed a silicon microchannel with ten entry points for the purpose of mixing acidic and basic liquids (Figure 6). A comparison between the analytical solution and the experimental measurement of the diffusion of samples in a hydrodynamic focusing means was presented. Both sets of results showed a good level of agreement in terms of the residence time presented. Their experimental measurement for the mixing performance was compared with the results of computational fluid dynamics (CFD). They were successful in focusing by utilizing a pair of entrance channels in their system. To expedite the reaction, the authors of this study made use of a technique known as "pulsed addition of solute to the channel." Two piezo discs are used to control the valves that are located at the air intakes in this configuration. According to the implication of this work, the Taylor dispersion has the potential to significantly improve mixing. to combine the contents of two different fluid samples, so-called multilaminate/elongational micromixers were introduced. Their architecture is made up of a multitude of mixing structures that have been meticulously positioned on the channel floor of the mixing device and blocks that have been arranged in a staggered manner at the inlets. It has been demonstrated that their method of fluid multilaminate and elongation is quite effective in increasing the amount of mass that is transferred. The checkerboard mixer is the name given to the 3D micromixer that was proposed This mixer combines the functions of focusing and split-and-recombination (SAR). The employment of sheath flows resulting from hydrodynamic focusing was proved to be an efficient technique for controlling the reactivity of samples at a flow rate of 12.7 L/min, and it was found that 90% of the mixing takes place exclusively inside the length of this method. They created a total of five inlet channels: one in the center for a solution containing an analyte; two on each side for solution B; and two on the diagonals for solution A. They were able to avoid the unintended mixing of the solutions this manner, which allowed them to finish focusing on the problem without delay. By imitating the geometrical qualities of a vascular system, the researchers created a branched

channel and quantitatively studied the mixing performance. They paid particular attention to the effect that the number of branches had on the mixing performance.
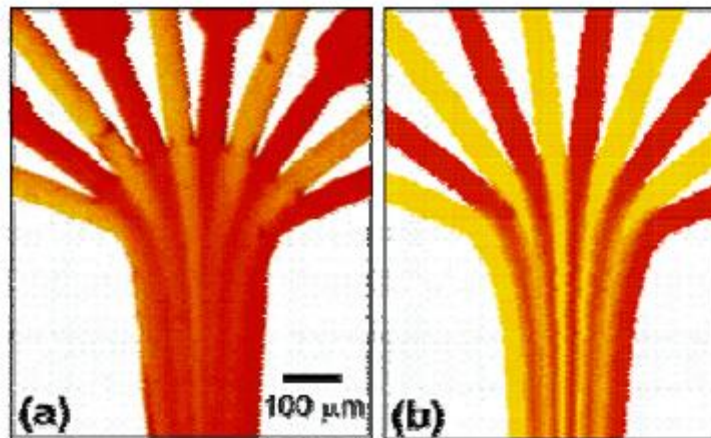

Figure 6. (a) Experimental and (b) numerical visualizations of fluid mixing in hydrodynamic focusing channels.

Conclusions

In this review, a variety of methods and mechanisms have been provided that can be utilized in microfluidics to accomplish mixing. There is an implication that every design comes with its own set of benefits and drawbacks, and that the method of mixing that is chosen should be optimized in accordance with the requirements of the application in question. According to what is said research, "there is no single mixing concept fulfilling all the requirements set by the application envisaged." On the other hand, when viewed from a more macro perspective, in terms of the mixing performance as well as the fabrication cost, etc., we cansummarize the essential aspects of each mixing concept as When evaluated based on these four criteria, droplet mixing came out on top as the method that offered the best mixing performance at the lowest possible cost to fabricate. A way of making the channel geometry complicated would, of course, be favored over droplet mixing if a low-price design is achievable that exhibits chaotic advection over the entire range of the channel section. This would be the case if the channel section could be designed to exhibit chaotic advection.

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