On mechanisms of mixing by forced and natural convection in microfluidic devices

Dmitry Bratsun¹, Alexey Mizev², Elena Mosheva², Len Pismen³, Ramil Siraev¹ and Andrey Shmyrov²

¹Department of Applied Physics, Perm National Research Polytechnic University, 614990, Perm, Russia
²Hydrodynamic Stability Laboratory, Institute of Continuous Media Mechanics, 614013, Perm, Russia
³Department of Chemical Engineering, Technion-Israel Institute of Technology, 32000, Haifa, Israel

E-mail: DABracun@pstu.ru, alex_mizev@icmm.ru

Abstract. Continuous-flow microfluidic devices are applied in the study of microorganisms, in genetic research, production of pharmaceutical substances, lab-on-a-chip technology, biomedicine etc. Some applications require continuous mixing of the solutions that flow through the devices. However, straight-line mechanical mixing methods cannot be used due to the small size of the channels. In this paper, we discuss from a theoretical and experimental point of view the prospects of using various mechanisms of natural or forced convection for efficient mixing of solutions entering a microfluidic chip. Different designs of micromixers operating on gravity-dependent instabilities of the Rayleigh-Taylor type, double diffusion convection, and surface-dependent Marangoni instability are considered. Micromixers, in which the fluid flow is controlled by an electro-osmotic mechanism and directional deformations of the channel walls, are considered as examples of forced convection. For each case, we will provide the assessment of the range of chip sizes in which this mixing mechanism works effectively. The examples of experimental implementation of different mixing principles are given.

1. Introduction

Microfluidic devices are one of the most promising applications of classical fluid mechanics, which has accumulated vast experience in studying the behavior of fluids on different spatial scales over more than 150 years of its development. These devices have developed a fairly wide range of applications [1], which include solving problems of synthetic biology and gene regulation, studying the physiology of microorganisms, producing valuable pharmaceutical substances and new materials, synthesizing cellular structures and whole organs, solving problems of micro-robotic technology and controlling microsystems. The miniaturization of continuous-flow devices is due to the requirement for the industry to be more flexible in the ability to change the nomenclature of the final product. Changes in chemical technology are
an illustrative example. Significant changes in this area occurred in the early 2000s when the new technologies penetrated an organic synthesis. Since the pharmaceutical production needs more flexibility in reconfiguring the synthesis system rather than large product volume, the process has been developing towards the design of increasingly miniature reactors or microreactors [2]. It is necessary to note that the traditional chemical production, as a rule, is carried out in the discontinuous stirred reactor (or batch reactor, BR). In industry, discontinuous operations are well suited for rather complex reactions and allow driving the process by controlling the temperature [3]. In contrast to the BR, the continuous operations traditionally were typical for large productions (for example, in the oil and gas industry) based on more simple chemistry [3,4]. The advantages of the new reactor type, the continuous-flow microreactor (hereinafter, CFMR) against the BR are

- high productivity due to the elimination of the loading-unloading stage;
- the stable consumption of reagents and energy due to the small reactor zone;
- the replication of the production line to increase product yield.

As a result, multiple studies have been published in recent years detailing the valuable outcome of continuous-flow technology applied to single or multi-step syntheses of target composites on various reaction schemes and spatial scales [5,6]. At the moment, the revolution in this technology has led to the CFMR with a characteristic size comparable to microfluidic devices (100-1000 µm). In microfluidics, it is traditionally believed that, due to the laminar nature of flows in microreactors, diffusion is the main mixing mechanism for the reactants initially separated in the flow. This paper presents an overview of research results demonstrating the fallacy of this point of view. The problem is that the practical mixing of the reactants due to diffusion needs a decrease in the channel section, which, in turn, grows the cost of pumping the liquid. In this Communication, we show that various mechanisms of natural and forced convection can be effectively used for mixing liquids in microchannels.

2. Natural convection

The differences in the physical properties of miscible media can be used to develop one of the convective instabilities. Let us, first, consider the case of natural convection, defined as a type of flow, in which some parts of the fluid being heavier than surrounding fluid cause the fluid motion. The driving force for natural convection is gravity. For example, a significant difference in the diffusion coefficients of the reactants makes it possible to trigger the development of either double-diffusive instability of diffusive layer convection. The difference in the densities of the reactants can be used to generate the Rayleigh-Taylor instability.
Figure 1. Experimental interferograms showing the process of mixing two solutions, which are pumped through a Y-shaped microfluidic device in the case of (a) only diffusion processes (water versus 0.5 mol/L aqueous solution of KCl); (b) double-diffusive instability (0.45 mol/L aqueous solution of CuSO\textsubscript{4} versus 1.9 mol/L aqueous solution of KCl); (c) diffusive layer convection (1 mol/L aqueous solution of CuCl\textsubscript{2} versus 2.5 mol/L aqueous solution of KCl); (d) Rayleigh-Taylor instability (0.5 mol/L aqueous solution of KCl versus water). The gravity is directed from top to bottom. Channel height is 5×10\textsuperscript{-4} m.

Recently, we experimentally investigated the mixing efficiency of various instabilities of natural convection using a Y-shaped microfluidic chip as an example. Figure 1 shows the interferograms of the mixing zone in a Y-shaped microfluidic device, in which two converging solutions are mixed using one of the gravity-dependent types of instability. We have chosen model liquids that mimic reaction compositions formed by aqueous solutions of various salts of inorganic acids. The fluids are brought into contact in a Y-shaped micromixer and then they propagate along a channel with a height of \( h = 0.5 \) mm and a thickness of 0.1 mm in the form of a two-layer system being under the influence of gravity. We used glass side borders, which allow visualization of the distribution of substances by optical methods. Figure 1a shows the Fizeau interferogram illustrating mixing due to only the diffusion mechanism. In this case, the two-layer system is statically stable at the very beginning (heavy solution in the lower layer), and the dissolved component exists in only one of the layers. One can see that mixing proceeds slowly, and the significant concentration gradient is still evident in the system at a distance of 15\( h \) from the place of the first contact of solutions. The total mixing length, in this case, exceeds the downstream distance equal to 50\( h \) (Fig. 1a).

If the solutes in a two-layer system have different diffusion coefficients, this can lead to the excitation of the diffusive instability. Depending on the layer, which contains a solute with a higher diffusion coefficient, two types of instability can occur. If the fast component dissolves in the lower layer, then double-diffusive instability arises. In the opposite case, there is diffusive layer convection. In the former case, the fluid instability develops as fingers propagating vertically in two opposite directions (Fig. 1b). In this case, one can see an almost homogeneous medium at a distance of 15\( h \) from the point of the first contact of mixtures. In the latter case, the instability develops on both sides of the statically stable diffusive layer separating domains of fluid flows. The diffusion of both solutes leads to the formation of symmetric convective motion in two unstable layers above and below the stable diffusive layer (Fig. 1c). One can see that a stable diffusive zone with significant concentration gradients exists up to the channel end indicating that low efficiency of this type of convective flow for the mixing process. Finally,
Figure 1d shows an interferogram for the case when a two-layer system is unstable from the very beginning of evolution, i.e. a heavier liquid is supplied through the upper channel of the Y-shaped microfluidic device. In this case, the Rayleigh-Taylor instability develops. One can see that this type of convective flow evidently demonstrates the highest mixing efficiency: the total mixing length does not exceed $3h$. We should note that the Rayleigh-Taylor instability is sensitive to the condition of two-dimensionality of the flow: if the channel’s height is comparable to its depth, then the ascending flow of a light fluid prefers to diverge from the descending flow of a heavy liquid in the third dimension. In this case, the real mixing of the solutions does not occur; rather, they simply change places.

![Interferogram](image)

Figure 2. (a) Schematic representation of a micromixer based on the Marangoni effect: an inlet for air to produce the bubble 1; plastic insert to hold the bubble 2; inlets for the solutions 3 and 4; outlets for the mixed flow 5 and 6. Arrows indicate the direction of observation with the Fizeau interferometer. The characteristic bubble size $2$ is $10^{-3}$ m. The acceleration due to gravity is directed from top to bottom. Typical experimental interferograms showing the process of mixing two solutions, which are pumped through an X-shaped microfluidic device in the case of (b) pure diffusion mechanism; (c) the solutal Marangoni convection arising near the air bubble in the center of the cavity when 15% isopropyl alcohol solution supplied for the above inlet. Inflow velocities from both inlets are $V = 0.02$ mm/s.

For example, for the double-diffusive instability to develop, the following condition for the solutal Rayleigh number $Ra_C$ must be satisfied [7]

$$Ra_C = \frac{g\beta_C \Delta Ch^3}{\nu D} > \frac{1}{2} \pi^4,$$

where $\nu$ is the kinematic viscosity, $D$ is the coefficient of diffusion, $\beta_C$ is the solutal coefficient of the volume expansion, and $\Delta C$ stands for the characteristic concentration difference. The condition (1) allows obtaining the following estimate for the minimum height of the microfluidic channel: $h > 100 \mu m$.

In the recent work [8], we proposed a micro-mixer design in the form of an X-shaped microfluidic chip operating on the Marangoni effect. Fig. 2 shows a microfluidic chip designed to excite a solutary capillary Marangoni flow for mixing two liquid flows. A rounded cuvette with dimensions 15x10x2 mm has two channels at the top and bottom through which two miscible mixtures seep with the same flow rate (Figure 1a). We made a series of experiments using non-reactive liquids: water (coming from below) and an aqueous solution of isopropyl alcohol (coming from above). The latter solute played the role of a
surfactant. On the lateral boundaries of the chip, there are two channels for removing the resulting mixture. In the center of the cuvette, we inserted a thin plastic ring with a diameter of 3 mm with two slots 1 mm wide and an angular size of 150 degrees. If the volume inside is filled with air, there exist two liquid-gas interfaces. Figure 2b shows the photograph obtained with a Fizeau interferometer characterizing the concentration distribution in the quasi-two-dimensional chip. One can see that, in this case, the mixing occurs in a narrow zone due to the diffusion mechanism. The interface dramatically changes the situation (Figure 2c). The presence of a surface tension gradient along the surface results in the development of an intense convective Marangoni flow quickly stirring liquids within the mixing zone.

There are two important points to note. First, the force of gravity also plays an important role in the design of the micromixer since the inhomogeneous surfactant field occurs due to the acceleration of gravity. Secondly, the device does not consume additional external energy but works due to the repeated consumption and regeneration of the driving concentration gradients. Thus, the micromixer automatically adapts to the conditions in the reactor zone. If the concentration field becomes sufficiently uniform, the oscillations stop. When the concentration inhomogeneities reappear, the system indicates that the reactants in the reactor zone still are not mixed, and the convection is excited again. We can estimate the minimum size of a microfluidic device that could operate on the Marangoni effect. The solutal Marangoni number must satisfy the following condition

$$Ma_c = \frac{h^2 \frac{\partial \sigma}{\partial C}}{\eta D \Delta C} > 10^7,$$

where the typical critical value for the onset of Marangoni convection in an aqueous solution of isopropyl alcohol is indicated on the right. In (2), \(\eta\) is the dynamic viscosity, \(\sigma\) is the surface tension. Based on the research (2) and taking into account the realistic concentration gradients that can be achieved experimentally, we can estimate the size of the device as \(h > 50 \mu m\).

3. Forced convection
The use of natural convection to control the transfer processes in microdevices is beneficial in that the energy of the system itself is consumed. However, forced convection, which we can define as a mechanism or a type of transport in which fluid motion is generated by an external source (such as a pump, moving wall, fan, suction device, etc.), is a more suitable tool. In the recent work [9], we theoretically studied the influence of the shape of the microreactor walls on the mass transfer processes inside it. The device can be made in the form of the Hele-Shaw cell, which is externally controlled by the system of actuators enabling the variation of the width of the cell gap in both time and space. Such control can be organized in various ways. For instance, the intensity of an undesirable flow can be significantly reduced by setting a narrower gap between the side walls of the reactor, i.e., by reducing the local permeability of the medium (Fig. 3a). In the opposite case, the flow can be supported by expanding locally the gap in the area where this flow is present (Fig. 3b). To apply active control, the walls of the microreactor must be deformable. Then one has to establish real-time feedback between the actuators and sensors, signaling the mass transfer processes inside the reactor. If the product yield is considered as a control parameter, then the controller could be programmed so that it would stimulate useful convective structure in real-time. This method to control the microreactor has not yet been discussed in the literature, since, until the invention of 3D-printing, the fabrication of microcells with slightly non-planar walls was not a trivial task. To implement it, the walls of the microreactor must be made of a deformable, chemically inert, and resistant material. If this condition is met, then it is possible to design a device that would change the local permeability of the quasi-planar microreactor in real-time. It opens up broad possibilities for controlling the processes in the microdevices.
Nevertheless, a decrease in the size of the channel forces to search for new non-mechanical mechanisms for mixing the initial solutions. This problem is relevant both for slow reactions, in which diffusion processes, are unable to mix the reagent at reasonable distances from the entrance to the system and for quick reactions, which occur in a frontal manner. Natural convection as a mixing mechanism also has its drawbacks. It requires special conditions. For example, the reactor zone should be of an appropriate size and special orientation for convection. If these requirements are not met, then no mixing occurs. Besides, these mechanisms are not flexible enough: they do not encourage the flows with random topology and configuration. These drawbacks are not typical for the electrokinetic mixing mechanisms, including the electroosmosis driven mechanisms [10].

![Image](image.png)

**Figure 3.** Salt concentration field in a continuous-flow reactor, which is controlled by the deviations of microchip's wide walls from the perfectly planar form [9]. Transfer processes are under the control of the concentration-dependent diffusion instability introduced in [11]. The corresponding wall deformations are shown in Insets. (a) – the stimulation of convection in the reactor using the expanded walls of the microchip; (b) – the suppression of convection in the reactor using the concave walls of the microchip. All parameter values and conditions for reaction-diffusion-convection processes are the same in both cases.

Electro-osmotic flow (EoF) occurs when a diffusive ion cloud near the charged surface moves electrolyte solution under the applied electric field. One expects that electrokinetic phenomena near heterogeneous (texturized) surfaces will solve the problem of liquid mixing in the microchannels, which could be the basis for the micromixers with flow anisotropy or heterogeneity of the surface charge [12]. Periodic or impulse changes of zeta potential cause vortex hydrodynamic change in the flow, which triggers the mixing. As it is shown in the work [10], to apply the Helmholtz - Smoluchowski equation to the liquid-solid body borders, the electric field should at least be quasistatic to neglect the transition effects. In other words, the scale of the non-stationary electric field should be larger than the one of the transition flow. Recently, we have studied the efficiency of mixing the reactants induced by electro-osmotic flow in a Hele-Shaw configuration with non-uniform zeta potential distribution. We consider the neutralization reaction, which has simple but non-linear kinetics, as a test reaction [11]. The reaction takes place between two miscible solutions, which are initially separated in space and come into contact after passing through the Y-shaped microfluidic device. The reaction proceeds frontally, which prevents the
efficient mixing of the reactants just due to diffusion. We have shown numerically that the mixing of solutions can be effectively controlled by specifying special forms of the zeta potential, which make it possible to lengthen the reaction front by an order of magnitude and increase the yield of the reaction product by several times.

Figure 4 shows the effect of the EoF on the reaction-diffusion processes in a Hele-Shaw microreactor. The initial state includes two converging streams of reactant solutions (acid at $z > 0$ and base at $z < 0$) that move from left to right. In the absence of external influence, the contact zone between the solutions remains narrow and flat since the neutralization reaction proceeds rapidly. When we impose the zeta potential in form $\zeta = \sin 4\pi(vt - x)$, which excites perturbations directed across the direction of the base flow, the reaction zone becomes unstable with respect to a zigzag instability. The elongation of the reaction front, which follows, leads to a sharp intensification of the reaction rate. Figure 4c demonstrates that on the right border of the cuvette, the salt concentration field is already practically uniform at any point in the cross-section.

![Figure 4](image)

**Figure 4.** Instant concentration fields of acid (a), base (b), and salt (c) for non-stationary EoF shown at $t = 10$. The zeta potential in the form $\zeta = \sin 4\pi(vt - x)$ is applied to the Hele-Shaw microreactor. The initial state is a laminar flow of aqueous solutions of acid ($z > 0$) and base ($z < 0$). The velocity of the base flow $v = 5/7$.

4. Conclusion

The mechanisms of either natural or forced convection, which are currently underestimated in microfluidics, can be successfully used for mixing flows in microfluidic devices. We found that in the case of natural convection, the best result is obtained in the case of the Marangoni instability due to the surface activity of dissolved species, or the Rayleigh-Taylor instability arising in the presence of the density difference.

We demonstrated that convection can reduce the mixing length by an order of magnitude in comparison with mixing using a pure diffusion mechanism. In the case of forced convection, we have considered two fundamentally different flow control mechanisms, which could be applied in a microfluidic channel. The first mechanism is supposed to manipulate the channel permeability by changing the shape of its walls. This method is very efficient but hard to implement. The second mechanism is based on the use of the electro-osmotic flow and is currently considered to be the most
promising for microfluidic devices. The EoF is simple enough for experimental implementation and is most suitable for small devices since the zeta potential is usually small.

Acknowledgments
This study was funded by the Government of the Perm Region within the research project No. C-26/174.2. A.M. and E.M. gratefully acknowledge financial support provided by the Ministry of Science and High Education of Russia (theme No. AAAA-A18-118020590106-3).

References
1. Herold K E and Rasooly A 2009 Lab-on-a-Chip Technology: Fabrication and Microfluidics (Caister Academic Press) 410 p
2. Jensen K F 2001 Chem. Eng. Sci. 56 293–303
3. Levenspiel O 1999 Chemical Reaction Engineering (Wiley, New York, USA) 578 p
4. Levich V G, Brodskii A M and Pismen L. M. 1967 Dokl. Akad. Nauk SSSR 176 371–373
5. Reschetilowski W 2013 Microreactors in Preparative Chemistry (Wiley-VCH, Weinheim, Germany) 352 p
6. Baumann M and Baxendale I R 2015 Beilstein J. Org. Chem. 52 1194–1219
7. Gershuni G Z and Zhukovitsky E M 1963 J. Appl. Math. Mech. 27(2) 301–308
8. Bratsun D, Kostarev K, Mizev A, Aland S, Mokbel M, Schwarzenberger K and Eckert K 2018 Micromachines 9(11) 600
9. Bratsun D and Siraev R 2020 Int. Commun. Heat Mass Transf. 113 104522
10. Boyko E, Rubin S, Gat A D and Bercovici M 2015 Phys. Fluids 27 102001
11. Bratsun D, Kostarev K, Mizev A and Mosheva E 2015 Physical Review E 92 011003
12. Stroock A D, Dertinger S K W, Ajdari A, Mezic I, Stone H A and Whitesides G M 2002 Science 295 647–651