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Experimental approaches to a better understanding of mixing performance of microfluidic devices

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Abstract

Two experimental methods are presented that were used to describe the mixing performance of five micromixers differing in mixing principle and internal geometry. The well-known “Villermaux/Dushman method” was adapted to continuous processes and subsequently modified in such a way that the sensitivity of the method can now be adjusted to different flow rates. In addition, a new physical method was developed to investigate mixing performance that is based on the phase transfer of a solvatochromatic dye between two immiscible fluids.

The combination of both methods allows considering very different aspects of mixing performance in both single and multiphase systems. Micromixers can thus be compared qualitatively and quantitatively. In this context the completeness of mixing as well as the influence of pressure drop, hold-up and retention time on the mixing efficiency is discussed.

Keywords: Micromixers; Villermaux/Dushman method; Microfluidic device; Extraction method; Mixing performance

1. Introduction

The rapid development of microreaction technology in recent years has led to a considerable variety of microfluidic devices. In particular, microreactors and micromixers are nowadays commercially available in numerous designs and materials. Since mixing has a decisive impact on the overall performance of microreaction processes, there is an increased desire for measuring and comparing mixing performance.

Therefore, different attempts have been made in the past to describe the efficiency of mixing within microfluidic structures quantitatively. It is expected that such measurements will help in comparing different principles of passive mixing like “multilamination” or “split-and-recombine”. Moreover, both producers and users of commercially available devices ought to be able to identify the appropriate hardware for a specific microreaction process.

Experimental methods to investigate the mixing performance of macroscopic devices (stirred vessels, conventional static mixers) are well known [1–6]. They are based on the spatial and time resolved measurement of temperature or concentration distributions on a typical lengthscale of 10^{-2} to 10^{-3} m. However, these methods are not suitable for the characterisation of mixing within microstructures since good mixedness is inherently provided at such lengthscales. To investigate mixedness on a microscale (10^{-4} to 10^{-7} m) suitable analytical techniques are required which ensure a high spatial resolution. Zech et al., for example, demonstrated the characterisation of gas phase mixing in microstructures by employing spatial resolved mass spectrometry [7]. Comparable investigations in the liquid regime are not known by the authors.

Therefore, alternative methods have been used over the last years to describe the mixing performance of microfluidic devices. Such experiments are based on mixing-sensitive chemical conversions like competing parallel or consecutive reactions. Yields and/or selectivities that are achieved for specific reaction products are used as a measure to quantify the mixing performance. Hessel and coworkers [8], for example, compared the performance of micromixers with that of macroscopic mixing units by using a competing reaction that was originally used by Villermaux and coworkers for the investigation of micromixing phenomena in macroscopic reactors [9–11]. However, transferring these methods to continuously running microfluidic processes requires several modifications of the experimental procedure and set-up, as—for example—suggested by Guichardon and Falk [12].

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In this work, we report on a systematic investigation of two experimental methods with respect to their suitability to quantify mixing performance of micromixers differing in their mixing principle and internal geometry. The experimental procedure for the mixing-sensitive “Dushman reaction” which was applied in the experiments of Villermaux and coworkers [10,11] was modified to achieve an improved reliability of the measured mixing performance. Moreover, we report on a new physical method to quantify mixing performance on basis of the phase transfer of a solvatochromatic dye between two immiscible fluids.

Finally, we show how modifications of the experimental set-up, the stoichiometry and other process parameters may dramatically influence the measured mixing performance. Measured data are also discussed in the context of flow rates, pressure drops, fluid dynamics and the retention time behaviour of the mixers.

2. Method of competing parallel reaction

The determination of mixing performance by the so-called “Villermaux/Dushman method” is based on the competition of two parallel reactions [9–12]. The acid-catalysed reaction of potassium iodide with potassium iodate to elemental iodine competes with the faster neutralisation of the acid by a borate buffer-system (Fig. 1). In the experiments a buffered solution of KI/KIO_3 is mixed with diluted sulphuric acid. In case of ideal mixing the acid is only consumed by the fast neutralisation. However, if mixing is less ideal iodine is formed by the comproportionation reaction and can thus be UV-Vis spectroscopically detected as a triiodide complex which has its characteristic absorption bands centred at 286 and 353 nm. Hence, the more iodine is detected the less ideal is the mixing performance.

2.1. Experimental procedure

The two degased solutions were pumped through the micromixer with identical flow rates by using pulseless syringe pumps (Postnova Analytics, Landsberg/D and ISCO Inc., Lincoln, NE, USA). The triiodide concentration was detected online by a double beam UV-Vis spectrometer (omega 20, Bruins Instruments, Puchheim/D) in a flow-through cuvette which was connected to the outlet of the micromixer via a PTFE capillary of 40 mm length (i.d. 0.8 mm) (Fig. 2). Each recorded spectrum is the mean value of five repeated measurements. Experimental runs at a certain volume flow were repeated up to six times for statistical reasons to ensure a sufficient repeatability of the measured concentrations.

$$H_2BO_3^- + H^+ \rightleftarrows H_3BO_3 \quad \textit{(very fast)}$$

$$5\,I^- + IO_3^- + 6\,H^+ \rightleftarrows 3\,I_2 + 3\,H_2O \quad \textit{(fast)}$$

$$I_2 + I^- \rightleftarrows I_3^- \quad \textit{(detectable by UV/Vis spectroscopy)}$$

Fig. 1. Competing parallel reactions of the “Villermaux/Dushman method”.

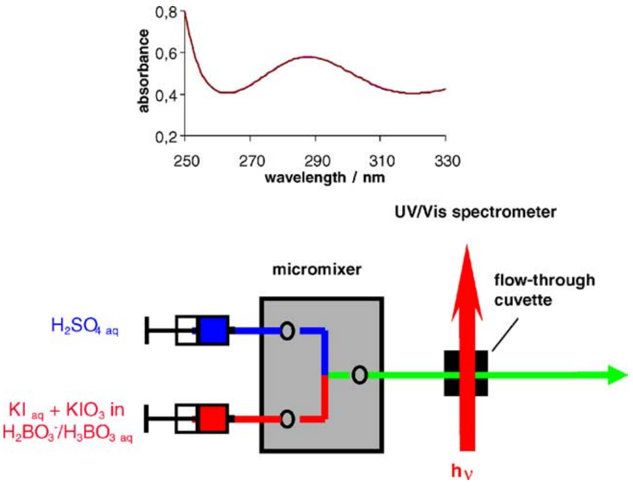


Fig. 2. Scheme of experimental set-up for the “Villermaux/Dushman method”.

The mixing performance of each micromixer was measured for at least four different volume flows in the range of 0.1 up to 40 mL/min. All experiments were conducted at room temperature.

2.2. Investigated micromixers

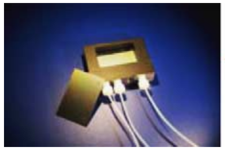
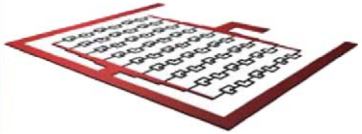
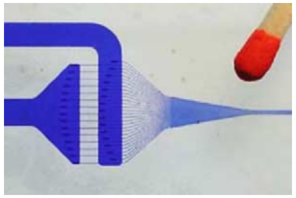
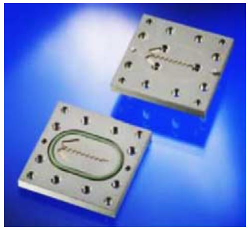
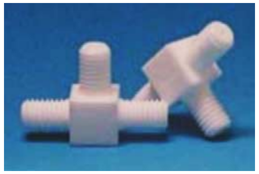
A miniaturised T-shaped mixer (i.d. 0.8 mm; PTFE) and four commercially available micromixers were investigated in the mixing experiments (Table 1). It is not the intention of this work to assess the performance of purchasable microfluidic devices. They were rather randomly selected to test and optimise the experimental methods for different mixing principles and microchannel geometries.

2.3. Influence of reactant concentrations

To transfer the mixing experiments that Villermaux et al. conducted in macroscopic batch processes to a continuous microreaction process several modifications of the experimental procedure are required. In particular, the concentration of the acid has to be adapted to the conditions of continuous mixing with 1:1 volume flows, as it was already discussed by Guichardon and Falk [12]. For example, Hessel and coworkers used in their work a relatively high acid concentration (c_{HCl}: 0.1374 mol/L [8]) which gives a final pH value of the reaction mixture of 5.7. At such low pH values iodine is continuously formed although mixing is already completed. Therefore, the final pH value has to be in the basic range (>7) to ensure that the measured concentration of iodine is only a result of imperfect mixing due to momentary local excess of the acid, and not an effect of consecutive reactions.

To illustrate the pH dependence of the measured mixing performance we varied systematically the concentration of

Table 1

Investigated micromixers	Mixing principle and typical channel dimensions	Supplier
MM 1: accoMix micromixer  	Split-and-recombine G-shaped microchannels: approx. 250 μm × 250 μm	Accoris GmbH, Ilmenau, Germany
MM 2: standard slit interdigital micromixer  	Multilamination Meander-shaped microchannels: 40 μm width, 300 μm height	Institut für Mikrotechnik, Mainz GmbH, Mainz, Germany
MM 3: triangular interdigital micromixer 	Multilamination Fluid feed channels: 50 μm width, 150 μm height	mgt mikroglas technik AG, Mainz, Germany
MM 4: caterpillar micromixer 	Split-and-recombine Size of structured single channel: 1200 μm × 1200 μm	Institut für Mikrotechnik, Mainz GmbH, Mainz, Germany
MM 5: T-Mixer 	T-mixing Internal diameter of fluid channels: approx. 800 μm	Bohlender GmbH, Grünsfeld, Germany

sulphuric acid and that of the borate buffer. In preliminary tests a KI concentration of $c_{\mathrm{KI}} = 0.0319\,\mathrm{mol/L}$ and a KIO_3 concentration of $c_{\mathrm{KIO_3}} = 0.00635\,\mathrm{mol/L}$ according to [8] turned out to be suitable in combination with the buffer system $H_2BO_3^-/H_3BO_3$ used in [9]. Three different acid concentrations ($c_{\mathrm{H_2SO_4}} = 0.015$, 0.020, and 0.030 mol/L) and two different buffer concentrations ($c_{\mathrm{H_2BO_3^-}} = 0.0454$ and 0.0898 mol/L) were investigated. The latter correspond to mixtures of sodium hydroxide and orthoboric acid in a molar ratio of 1:2 and 1:1, respectively.

Fig. 3 shows the strong dependency of measured iodine concentrations on the pH value of the reaction mixture adjusted by different acid and buffer concentrations (here shown for micromixer MM 1 at different flow rates). Similar dependencies were observed for all other micromixers. The data confirm that already under neutral and in particular under acid conditions high concentrations of iodine are detected without any changes over the entire volume flow range. Such acid/buffer concentrations are thus not suitable to observe any mixing effects arising from the microfluidic structure. At higher pH values the measured iodine concentrations show a clear influence of the mixing performance at different flow rates. Hence, the sensitivity of the measuring method can be adjusted for individual flow rates by varying the acid resp. buffer concentration. In the following experiments we kept the buffer concentration constant (molar ratio of $NaOH:H_3BO_3 = 1:1$) and varied only the acid concentration to achieve a specific sensitivity. However, to be able to compare measured mixing performances of different micromixers all applied experimental conditions must be specified accurately.

2.4. Influence of distance between mixing and spectroscopic measurement

Besides of reactant concentrations further experimental variables were investigated that might have an impact on the measured iodine concentration and thus on the measured mixing performance. For this reason the potential influence of the PTFE capillary that connects the micromixer to the flow-through cuvette was proven. In particular, the length of the capillary representing additional retention time was considered. Fig. 4 shows, as an example, iodine concentrations measured under identical experimental conditions but conducted with PTFE capillaries of different lengths (here shown for micromixer MM 3). Although the distance between mixer outlet and point of spectroscopic measurement was varied between 4 and 200 cm no significant influence was observed. Under the chosen experimental conditions with $c_{\mathrm{H_2SO_4}} = 0.015\,\mathrm{mol/L}$ no additional iodine is formed along the capillary due to complete consumption of the acid within the micromixer.

From the practical point of view this is a convenient fact because it allows setting up the entire experiment more flexible according to individual needs.

2.5. Pressure drop

When studying mixing performance in micromixers or static mixers in general, pressure drop is one of the key parameters. Pressure drop is directly related to the energy input that is expended for the mixing process. Hence, better mixing performance can be generally achieved by applying higher pressure drops. However, the highest mixing efficiency is achieved with such types of static mixers that provide a certain mixing performance with the slightest pressure drop.

Therefore, mixing performances of micromixers measured in terms of iodine concentrations have to be discussed always in the context of their specific pressure drops. Fig. 5 shows the pressure drops of the five investigated micromixers at volume flows between 0.1 and 20 mL/min. The T-Mixer (MM 5) and the two “split-and-recombine” mixers (MM 1 and MM 4) show almost similar pressure drops within the considered flow range whereas the two

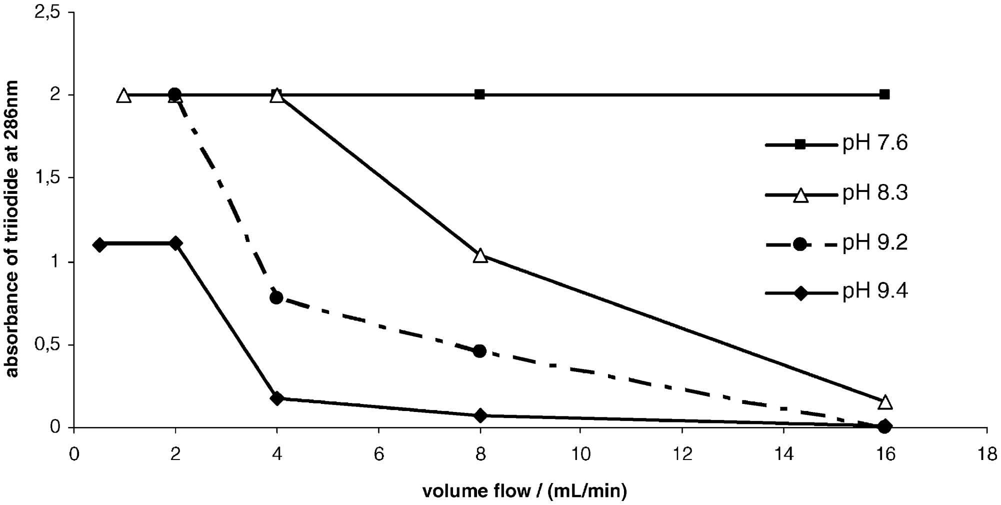


Fig. 3. Dependency of measured mixing performance on the pH value of the reaction mixture (here: micromixer MM 1).

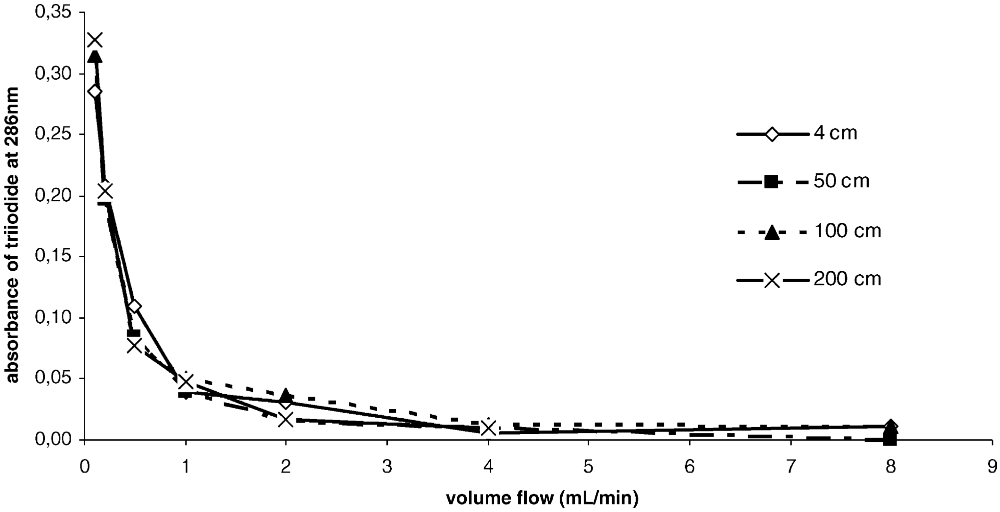


Fig. 4. Dependency of measured mixing performance on the distance between micromixer and optical cuvette (here: micromixer MM 3, $c_{H_2SO_4} = 0.015$ mol/L).

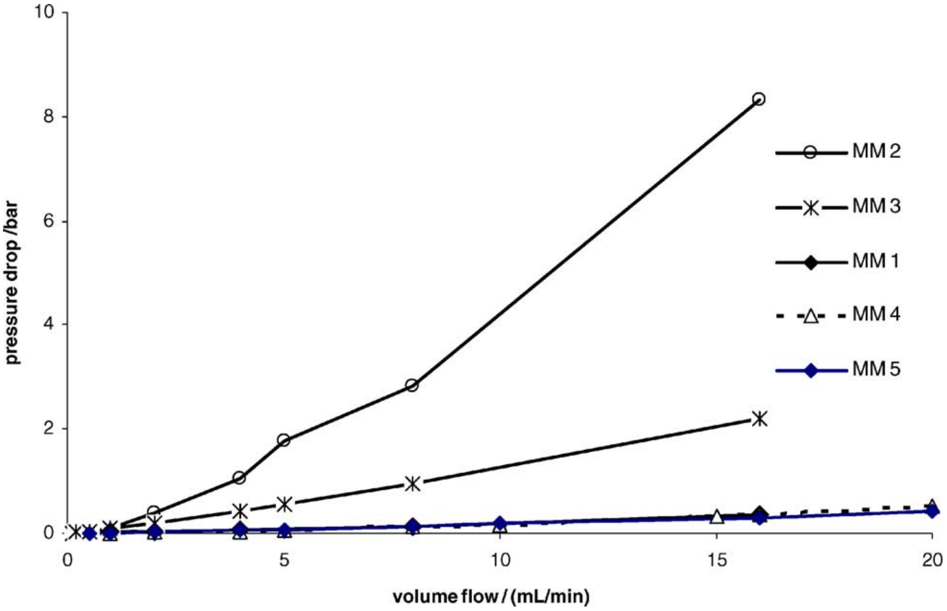


Fig. 5. Pressure drops of investigated micromixers.

multilamination mixers (MM 2 and MM 3) exhibit significant higher pressure drops.

2.6. Comparison of micromixers

The five micromixers were systematically investigated under equal experimental conditions. Only the acid concentration was varied (0.015, 0.020, 0.030, and 0.040 mol/L) to adjust the sensitivity of the experimental method to different volume flows, but also to avoid absorbance values of >1.2. The mixers were dismounted after each experimental run and measured six times in alternating sequences.

Figs. 6 and 7 show the iodine concentrations that were measured for the five micromixers with H_2SO_4 concentrations of 0.015 and 0.030 mol/L, respectively. Under both stoichiometric conditions iodine concentrations decreases significantly with increasing volume flow which makes it difficult to distinguish between individual micromixers at higher volume flows. Under these conditions mixing is increasingly governed by pressure drop effects and fluid dynamic phenomena than by particular contributions of the specific microfluidic design. Moreover, by applying different acid concentrations one has to ensure that the detection of less iodine at higher volume flows is a result of improved mixing and not a result of insufficient hold-up

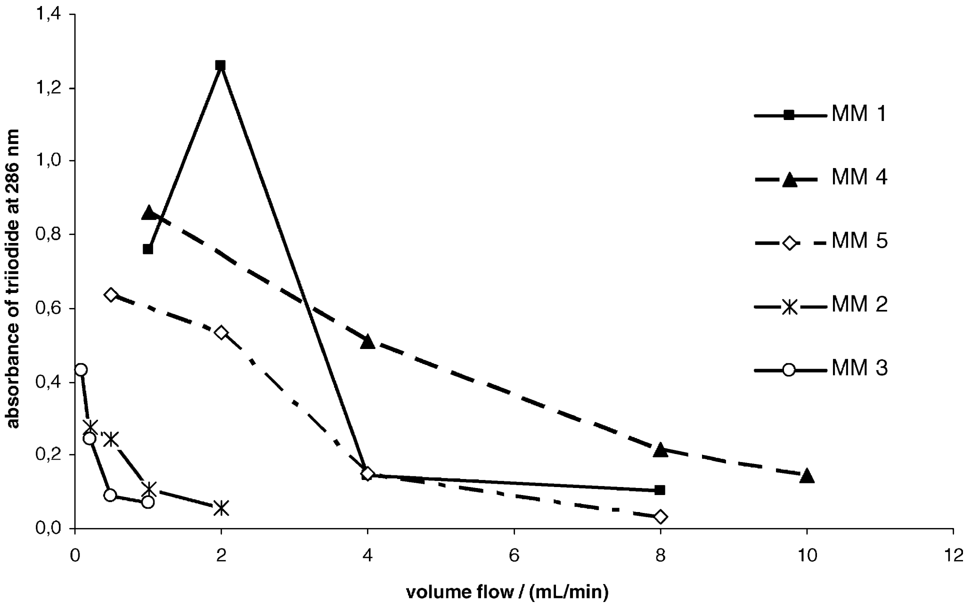


Fig. 6. Mixing performance of micromixers MM 1–MM 5 measured at $c_{H_2SO_4} = 0.015\,mol/L$.

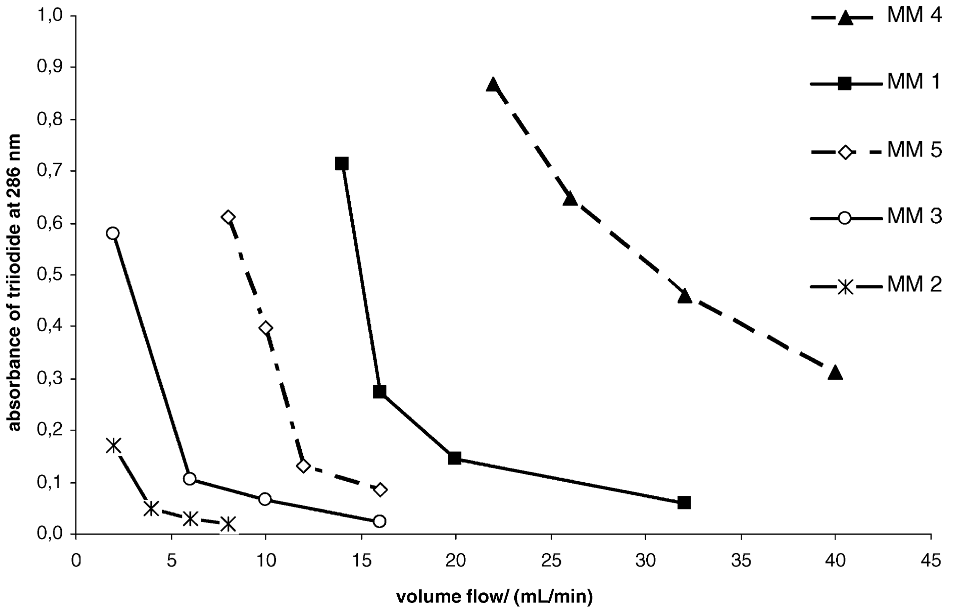


Fig. 7. Mixing performance of micromixers MM 1–MM 5 measured at $c_{H_2SO_4} = 0.030\,mol/L$.

resp. retention time. Therefore, comparison of micromixers must always be conducted in a confined volume flow range and by applying appropriate concentrations of the reactants.

By comparing the results shown in Figs. 6 and 7 it is obvious that the performance ranking of the five micromixers remains constant. The differences between the individual mixers can be observed more clearly if the higher acid concentration and thus the higher sensitivity is applied (see Fig. 7). Moreover, also the difference between MM 4 and the other four micromixers is more conspicuous. MM 4 is explicitly constructed for high flow rates up to 100 L/h [13] and will thus provide best mixing performance at $\gg$40 mL/min as it was confirmed by the measurements (see Fig. 7).

In Figs. 8 and 9 the mixing efficiencies of MM 1 to MM 5 are shown by considering the pressure drops of the individual mixers (see Fig. 5). As expected, the data confirm that differences in mixing efficiency are most obvious at low pressure drops. However, the relative ranking of the five micromixers is almost the same.

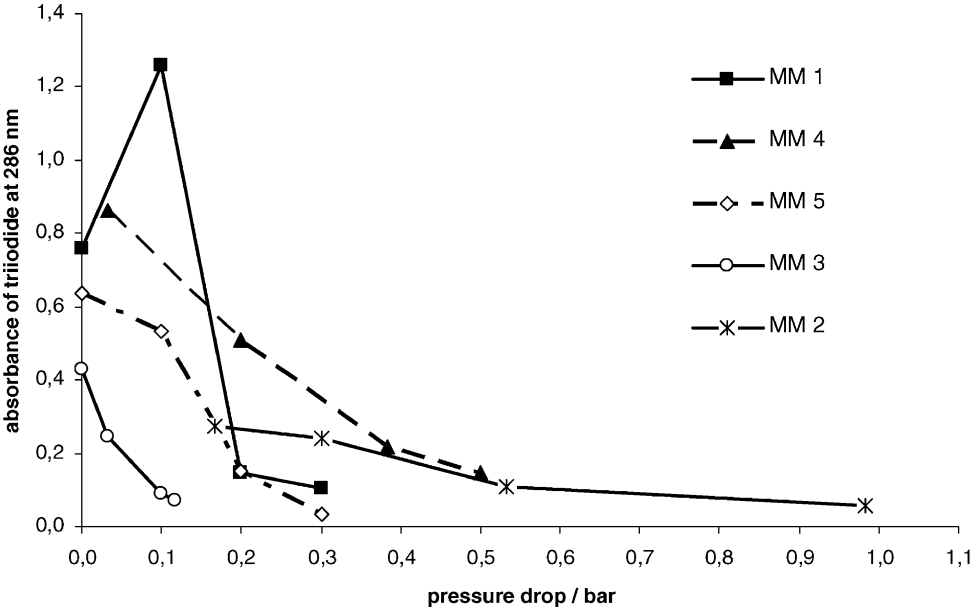


Fig. 8. Mixing efficiency of micromixers MM 1–MM 5 measured at $c_{H_2SO_4} = 0.015$ mol/L.

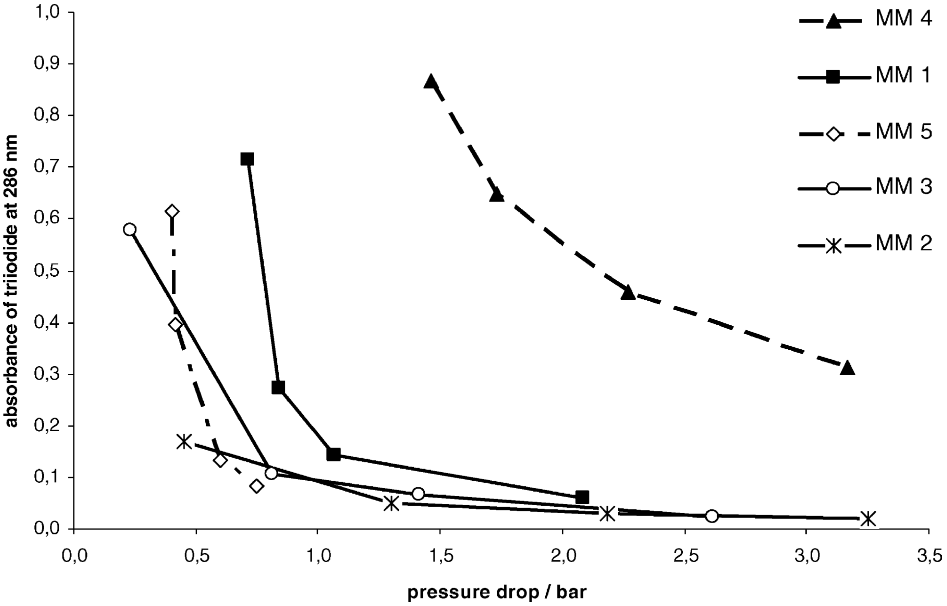


Fig. 9. Mixing efficiency of micromixers MM 1–MM 5 measured at $c_{H_2SO_4} = 0.030$ mol/L.

Finally, two additional surprising results were obtained by comparing the different micromixers. One is that the miniaturised T-Mixer provides an unexpected good mixing performance contrary to widespread opinion. The second surprising observation is that micromixer MM 1 exhibits a sudden decrease in mixing performance at a volume flow of 2.0 mL/min. No satisfactory explanation could be found so far for this effect. Since this behaviour is highly repeatable it seems to be caused by the specific microfluidic “split-and-recombine” structure.

3. Dye extraction method

Since the “Villermaux/Dushman method” describes mixing performance in a single-phase system the relevance of the measured data for multiphase mixing is uncertain. Therefore, we developed an additional physical method to quantify mixing performance on basis of a reference process that incorporates two immiscible fluids.

This new method is based on the phase transfer of the solvatochromatic dye Nile Red from a water/methanol phase to

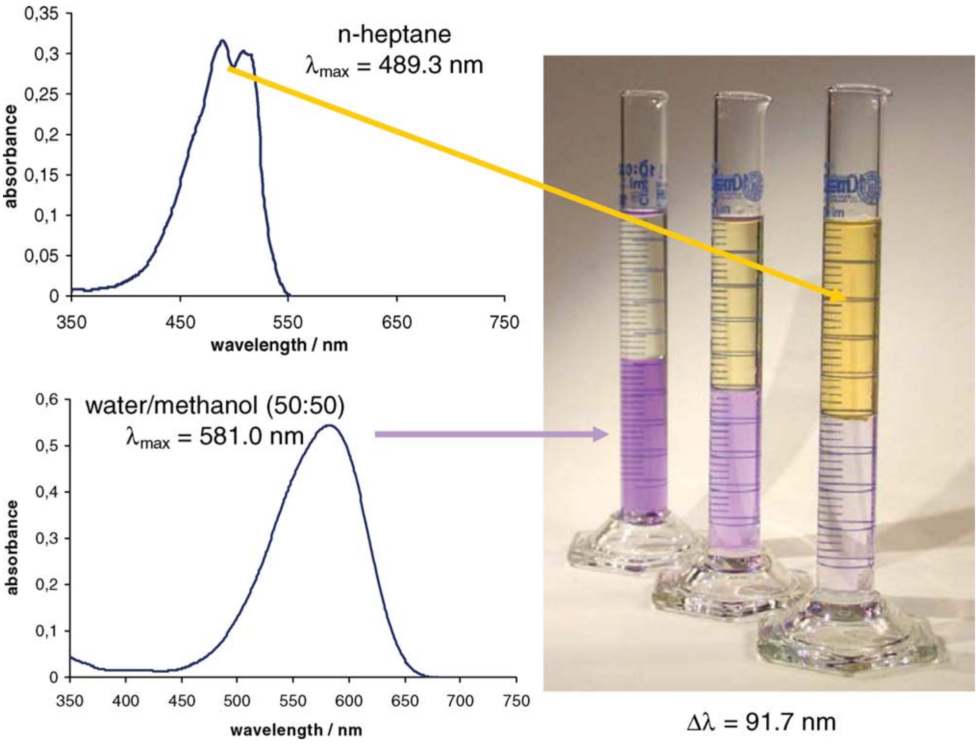


Fig. 10. The solvatochromic behaviour of Nile Red.

an *n*-heptane phase. Hence, an extraction process within a two-phase system is considered to describe the mixing performance of micromixers resp. microreactors. Microstructures which provide large interfaces between the two fluids enhance the extraction process and thus improve the mixing performance. The quantity of the extracted dye is measured UV-Vis spectroscopically at the outlet of a micromixer and is taken as a measure for mixing performance. Due to the solvatochromic behaviour of Nile Red (absorption maximum in methanol/water: 581 nm, in *n*-heptane: 489 nm; Fig. 10) we were able to provide evidence that only the pure dye is extracted into the *n*-heptane phase. We could rule out that small droplets of Nile Red dissolved in water/methanol are physically distributed within the organic phase. Such water or methanol shells in the cybotactic region of the Nile Red molecules can be spectroscopically detected by a significant bathochromic shift of the Nile Red absorption band to >489 nm [14]. However, a bathochromic shift was not observed what substantiates that pure Nile Red is extracted into the *n*-heptane phase.

3.1. Experimental procedure

Nile Red (Aldrich) was dissolved in a water/methanol mixture of 50:50 vol.%. The absorbance of the 0.01 mmol/L dye solution was adjusted to a value of 0.536 ± 0.008, if necessary by adding a few drops of the methanol/water mixture or of the Nile Red stock solution. The stock solution was prepared immediately before conducting mixing experiments to avoid ageing.

The degassed Nile Red stock solution and *n*-heptane (99% synthesis grade) were pumped through the micromixers (MM 1–MM 5) at identical volume flows by applying pulseless syringe pumps (Fig. 11). The mixture was collected in a macroscopic 10 ml glass cylinder which was connected to the outlet of the micromixer via a 60 mm PTFE capillary.

After fast phase separation a sample of the upper *n*-heptane phase was transferred into a 10 mm optical cuvette and subsequently measured in the above described UV-Vis spectrometer. The Nile Red absorption measured at 489 nm was corrected by the baseline absorption at 600 nm.

Preliminary tests confirmed that the time required for the macroscopic phase separation within the glass cylinder has no measurable influence on the Nile Red concentration in the *n*-heptane phase measured later on. Since the interface between the two fluids decreases dramatically after leaving the micromixer additional phase transfer of the

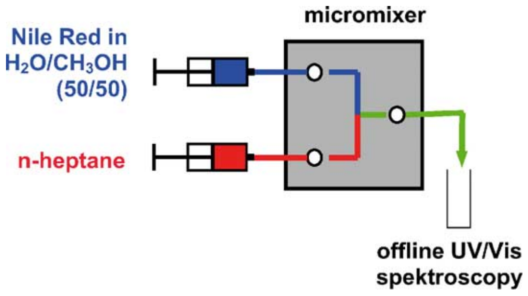


Fig. 11. Scheme of experimental set-up for the “dye extraction method”.

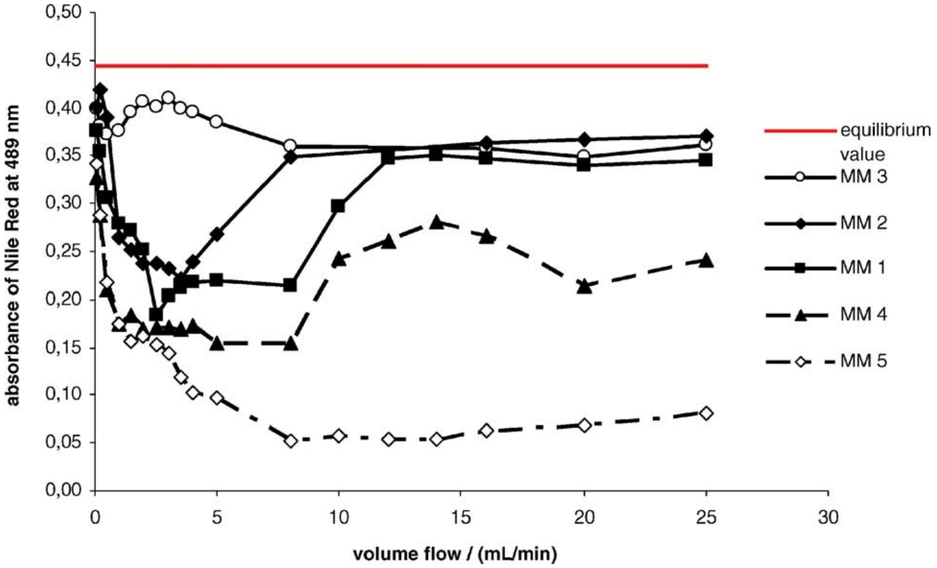


Fig. 12. Mixing performance of micromixers MM 1–MM 5 measured by the “dye extraction method”.

dye in the glass cylinder can be neglected. Mixing experiments were conducted at different volume flows and were repeated at least five times for statistical reasons. To suppress systematic errors micromixers were dismounted after each experimental run and measured again in alternating sequences.

3.2. Results and discussion

Fig. 12 shows the absorbance of Nile Red measured in the *n*-heptane phase after mixing at different volume flows. In contrast to the “Villermaux/Dushman method” high absorbances represent good mixing performances. The maximum absorbance of 0.445 ± 0.023 is achieved for an equilibrium distribution of the dye under the chosen experimental conditions.

Apart from the T-Mixer (MM 5) all micromixers show a characteristic curve progression over the entire volume flow range. At low volume flows mixing performance decreases, passes a minimum and increases again while volume flow is also increased.

To explain this behaviour two physical effects have to be considered: the energy input and the residence time. The diffusion of the dye from the water/methanol phase to the heptane phase is an entropy controlled process that can be accelerated by introducing energy, i.e. by increasing the impulse of the impinging fluids. However, by increasing volume flow not only energy is introduced but also the residence time is reduced. Hence, in the lower volume flow range the energy input caused by a slightly increased volume flow is not sufficient to compensate the effect of reduced residence times. As a result less dye is transferred to the heptane phase and thus the mixing performance is reduced. However, if the volume flow is increased beyond a certain point (minima in Fig. 12) the impulse of the impinging fluids is sufficiently high to accelerate the diffusion of the dye, in spite of shorter retention times. Of course, the position of the minimum along the volume flow axis depends on the individual microfluidic structure of the investigated mixers.

Therefore, this experimental method shows that good mixing performance can be achieved either by intensive and rapid mixing (main focus on introduced energy) or by less intensive but longer mixing (main focus on residence time).

Best mixing performance was achieved with the Triangular Interdigital Micromixer (MM 3), in particular at lower volume flows. The combination of multilamination and subsequent constriction of the microchannel leads to high pressure drops (see Fig. 5) and thus to a significant energy input. The second multilamination mixer (MM 2) investigated in this work shows also a good mixing performance but only at volume flows >7 mL/min. Higher pressure drops are required compared to MM 3 to compensate the small hold-up resp. low retention time. Hence, the mixing performance is high, but the mixing efficiency is low.

The “split-and-recombine” mixer MM 1 requires also higher volumes flows (>10 mL/min) to achieve a mixing performance comparable with that of the two multilamination mixers. Micromixer MM 4 shows only a moderate mixing performance but is actually designed for higher flow rates which are far beyond the range that was investigated in Fig. 12.

In contrast to the single phase experiments the T-Mixer exhibits an insufficient mixing performance for multiphase systems. A neglectable pressure drop combined with the absence of internal passive mixing elements makes this mixer unsuitable for contacting immiscible fluids.

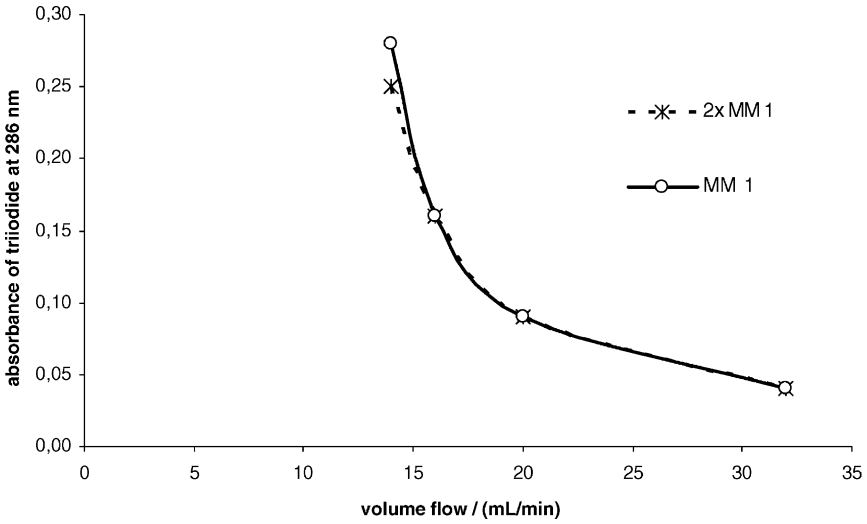


Fig. 13. Mixing performance of one and two connected micromixers MM 1 measured by the "Villermaux/Dushman method" ($c_{H_2SO_4} = 0.030$ mol/L).

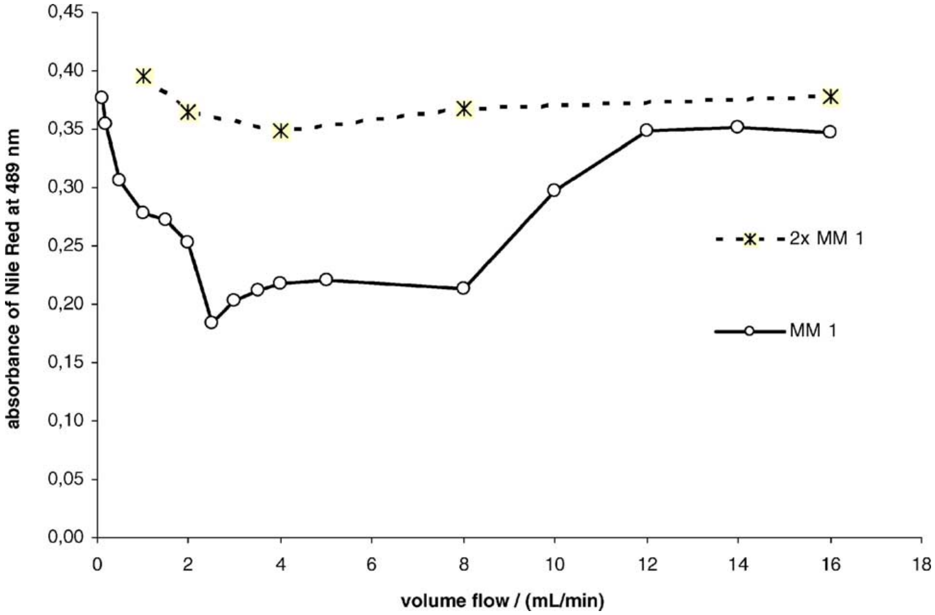


Fig. 14. Mixing performance of one and two connected micromixers MM 1 measured by the "dye extraction method".

4. Conclusions

Two different experimental methods have been discussed in this work to describe and compare the mixing performance of micromixers.

The so-called "Villermaux/Dushman method" was modified in order to adjust the sensitivity of the method to different volume flows by varying the acid concentration. The acid concentration has a significant influence on the measured mixing performance and must kept constant for a direct comparison of different micromixers. Since the method is based on competing parallel reactions under stoichiometric conditions it describes in particular molecular interactions at the beginning of mixing. Fig. 13 shows the example of two micromixers (here: MM 1) that were connected in series and were investigated in comparison to a single MM 1 mixer. Obviously no differences in mixing performance are observed due to complete consumption of the acid within the first mixing device. In addition to the "Villermaux/Dushman method" a second method was developed to describe and compare the mixing performance of micromixers for multiphase systems. Since the method is based on the phase transfer of a specific dye between two immiscible fluids no consumption takes place and mixing performance can be evaluated over the entire mixing set-up. Hence, the investigation of two connected MM 1 mixers show an improved mixing performance in contrast to the "Villermaux/Dushman method" (Fig. 14).

However, both experimental approaches are complementary because they allow considering very different aspects of mixing performance:

- mixing in single or multiphase systems;
- the extent of initial mixing;
- the completeness of mixing, and
- the influence of pressure drop, hold-up and retention time on the mixing efficiency.

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