# Intensified Liquid/Liquid Mass Transfer in Corning® Advanced-Flow™ Reactors

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Corning® Advanced-Flow™ reactors are continuous flow reactors with hydraulic diameters in the range of 0.3 up to few millimetres. These devices make possible the switch of chemical reactions from batch mode to continuous processing through more efficient, more economical and safer processes. In addition, they provide a platform for developing innovative chemistries that have never been considered industrially practical, either for high exothermicity, hazard or yield reasons.

Corning proprietary apparatuses are compact, adaptable and scalable, optimizing the overall production cost and quality of high-value specialty, fine, and pharmaceutical chemicals.

This paper presents the mixing of immiscible liquids in fluidic modules devoted to low flow applications in laboratory studies. The degree of mixing is quantified through extraction efficiency measurements at organic/aqueous phase ratios of 0.25. The satisfactory high extraction efficiency, which was superior to 0.8, indicates Corning®-Advanced Flow Reactors™ as efficient tools, providing good characteristics for multiphase applications.

## 1. Introduction

Small-scale channel reactors have emerged as a technology offering advantages over classical approaches due to miniaturization, such as faster mixing, better heat and mass transfer. The large surface-to-volume ratios of the small channels improve heat transfer for exothermic reactions, thus preventing thermal degradation or explosive evolution (Mae, 2007; Watts and Wiles, 2007; Hessel et al., 2008). It allows the control of reactions that need very short residence time and/or fast mixing and enables performing greener, more economical and safer processes.

The economic production of large numbers of flow reactors enables the shift from the present production paradigm of batch process and "scaling up" to a new paradigm of continuous process and "numbering up", i.e., running a reasonable number of reactors in parallel for mass production (Lavric and Woehl, 2009).

Corning developed continuous flow reactors that are easily scalable and can be customized to specific needs, enabling a cost-effective solution for a single reaction or a wide portfolio of reactions. The key component of the system is a specialty glass fluidic module having hydraulic diameters in the range of 0.3 up to few millimetres. The

module's structure, design and surface technology enable controlled, continuous and efficient streaming together of chemicals, resulting in excellent mixing quality and heat exchange performance. These devices are devoted to both laboratory studies and production, and have internal volumes from 0.5 to about 100 ml. Designs with various footprints and / or channel heights are produced, allowing higher throughput for a given residence time and pressure drop.

Immiscible liquid-liquid is an important system occurring in numerous liquid reactions and phase transfer processes such as nitration of organics (Burns and Ramshaw, 2002; Ducry L. and Roberge, 2005; Shen et al., 2009; Kashid and Kiwi-Minsker, 2009), oxidations with liquid oxidation agents (Ferstl et al., 2008), diazo-reaction (Salimi et al., 1997), isomerization of allylic alcohols (Hessel and Löwe, 2005), nanoparticles synthesis (Ying et al., 2008), extraction (TeGrotenhuis et al., 1999; Dehkordi, 2001; Su et al., 2009; Kashid et al., 2010) etc.

In classical devices, high shear stresses or emulsifiers are used in liquid/liquid phase transfer processes. In microreaction technology either emulsification or laminar flow in microcontactors can be applied. In most cases, the phases must be separated after the processes. Therefore, the application of emulsifier is avoided in order to ease the phase separation; in consequence, such emulsions are stable only for a limited time. Under reduced shear stress, the emulsified liquid droplets coalesce quickly. The efficiency of emulsion formation and the size distribution are important for the efficiency of the whole extraction process under these conditions (Sprogies et al., 2008).

Today's microreactor standard setups consist of a system with two or more feeds that pass a mixing zone followed by (a) residence time channel(s). These setups have some limitations when it comes to immiscible liquids; the mixing zone creates an emulsion, but this emulsion is not maintained and phase separation is observed. This might be slowed down by using small channel diameters, higher flow rates or chemical additives. Corning developed a family of designs able to provide efficient mixing for homogeneous systems, and also fine and stable dispersions in the case of heterogeneous ones, with no need for emulsifiers, high energy or high pressure drop devices (e.g. porous membranes) to create and maintain the quality of emulsions.

The ability of these fluidic modules in creating fine and stable emulsions was evaluated using the efficiency of extraction. This physical method was developed and applied to investigate mixing performance by Panić et al. (2004), who used the phase transfer of a solvatochromatic dye between two immiscible liquids. 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 (Panić et al., 2004). Later on, Sprogies et al. (2008) quantified the mixing efficiency of different static micromixers by the characterization of the extraction efficiency of iodine from water using n-hexane.

## 2. Device

The analyzed device is composed of chain of identical cells having variable cross sections and internal elements whose presence on one hand determines the formation of a jet and on the other hand forces the liquid to split and then recombine (Figure 1). The

result is an efficient and continuous mixing along the dwell time path, even at low flow rates, without the need of additives (Chevalier et al., 2008; Lavric and Woehl, 2009). The devices incorporate an injector (a) or an injector and a mixer (b), enabling feeding and mixing of two fluids, but can also be used as dwell only (c). For these flow fluidic modules, having about 0.5 ml internal volume, the recommended operating flow rate is in the range of 2 to 15 g/min (with a nominal value of 5 g/min) for water-like fluids.
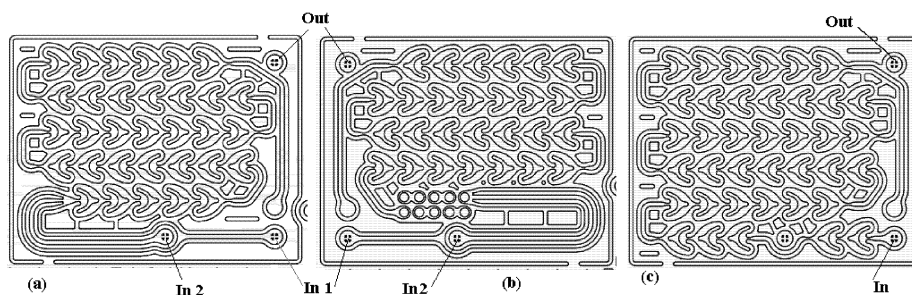


*Figure 1: Mixing and dwell time fluidic module for low flow multi-phase applications*

## 3. Experimental

The degree of mixing of immiscible liquids was quantified through the extraction efficiency of one species from aqueous liquid to heptane. Iodine ($I_2$) as a "trace" species has much higher solubility in organic phase (n-heptane) than in water; therefore, when the aqueous phase (water with iodine) is mixed with the organic phase (n-heptane), the large solubility difference drives the trace-iodine being transferred from water phase to n-heptane phase.

Figure 2 shows the diagram of the experimental setup, which consists of two liquid supply systems (liquid tanks, pumps and mass-flow meters) and the mixing section (which is either a small batch or the studied fluidic module). The mixed liquids are collected and then separated for measuring the residual concentration of iodine in water phase using UV-VIS.

## 4. Results and Discussion

The iodine extraction efficiency ($\eta$) (proportional with the mass-transfer rate of iodine) is correlated with the level of the mixing of these two immiscible liquids and the residence time given for extraction to take place.

By measuring the residual concentration ($C_r$) of $I_2$ in aqueous phase after the two liquids have been mixed and then separated, the extraction efficiency, $\eta$, can be calculated as:

$$\eta = \frac{C_0 - C_r}{C_0} \tag{1}$$

where $C_0$ is the iodine concentration in water before mixing, $C_r$ is the iodine residual concentration after mixing.
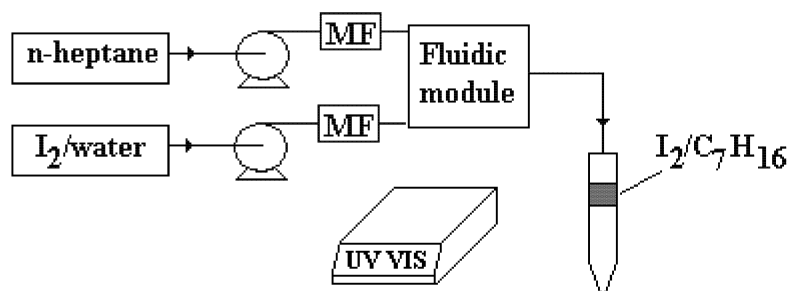


*Figure 2. Experimental set-up*

Before applying the method to the fluidic modules, it was tested and validated in a batch flask system with water-heptane. Five different speed rates of the magnetic stirrer were used. The extraction correlated well with the agitation speeds.

The experiments were performed using a total mixture volume of 50 ml n-heptane and water, in mass ratios of organic liquid/water in a range of 0.25 to 4.0. After stirring at a certain rate for 30 seconds, the mixture was allowed to separate in a funnel. The aqueous phase containing residual iodine was then collected for analysis in a UV spectrometer, at a wavelength range from 454.5 to 455.5 nm. The absorption data was recorded with a frequency of 2 seconds, and then averaged over a 2 minute interval.

The extraction efficiency is affected by both the organic phase/aqueous phase ratio and the stirring speed (Figure 3). For a given mixing rate, the extraction efficiency increases as the ratio of organic/aqueous phase does, due to the high solubility of iodine in organic phase. The extraction efficiency tends to approach a plateau at high organic/aqueous ratio; the individual values of this plateau depend on the agitation speed.

For a given organic/water-iodine ratio, the iodine extraction efficiency increases with an increase in the stirring speed. This mixing impact becomes pronounced at a low ratio of organic/aqueous, such as 0.25. In this condition, the organic phase is dispersed as droplets which extract iodine from a continuous aqueous phase. Due to the good sensitivity of extraction efficiency with respect to the degree of mixing, this phase ratio of 0.25 was selected for this study.

The sensitivity of the method to the initial concentration of iodine was considered. No measureable impact of the initial iodine concentration in the aqueous phase was observed (not shown); this finding significantly simplifies the testing procedure.

The reproducibility of the method was examined both in batch systems and in continuously operated fluidic modules. The average variation of extraction efficiency, slightly higher for batch systems, is less than about 2% (not shown).
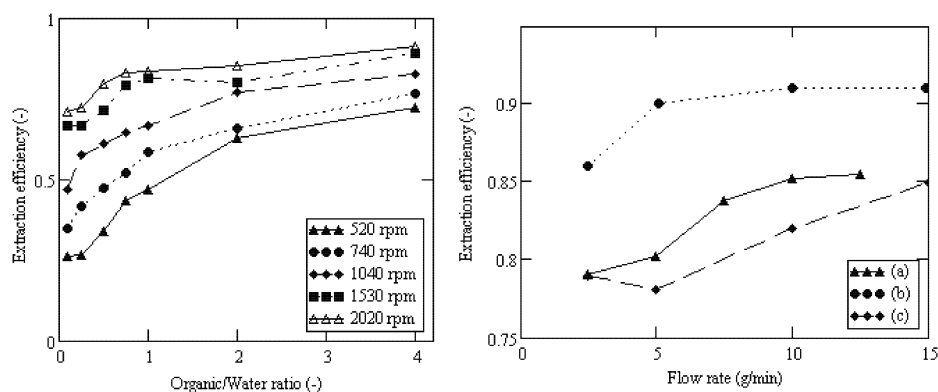
*Figure 3. Extraction efficiency: influence of liquid/liquid phase ratio and agitation speed for batch experiments (left); influence of flow rate and design (right). The symbols in Figure 3 right refer to the designs presented in Figure 1.*

The method was applied to the HEART cells-based fluidic modules using a ratio of organic/aqueous of 0.25. The extraction efficiency varies between 0.79 and 0.9, slightly higher for the fluidic modules having a mixer (Figure 3 centre). The results show that residence time modules (c) are effective in maintaining the dispersions already created in the devices (a) and (b).

## 5. Conclusions

The mixing of immiscible liquids in fluidic modules devoted to low flow applications in laboratory studies was quantified through extraction efficiency measurements. Extraction efficiency correlates well with the degree of mixing and is more sensitive to the mixing at low ratios of organic/aqueous phases (0.2-0.5) where organic droplets act as a discrete phase distributed in a continuous aqueous phase.

The investigation shows that the analyzed devices give good extraction efficiency without the need for emulsifiers. The satisfactory high extraction efficiency indicates Corning®-Advanced Flow Reactors™ as efficient tools, providing good characteristics for multiphase applications.

## References

Burns J.R. and Ramshaw C., 2002, A microreactor for the nitration of benzene and toluene, Chemical Engineering Communications, 189, 1611–1628.

Chevalier B., Lavric E.D., Cerato-Noyerie C., Horn C. and Woehl P., 2008, Microreactors for industrial multi-phase applications. Test reactions to develop innovative glass microstructure design, Chemistry Today, 26, 1-4.

Dehkordi A.M., 2001, Novel Type of Impinging Streams Contactor for Liquid-Liquid Extraction, Industrial & Engineering Chemistry Research, 40, 681-688.

Ducry L. and Roberge D.M., 2005, Controlled Autocatalytic Nitration of Phenol in a Microreactor, Angewandte Chemie International Edition, 44, 7972–7975.

Ferstl W., Schwarzer M., Loebbecke S., Langhals E.F. and Stohrer J., 2008, Process optimization of a catalyzed bleach oxidation for the production of functionalized aldehydes using microreaction technology, Chemical Engineering Journal, 135S, S292–S297.

Hessel V. and Löwe H., 2005, Organic Synthesis with microstructured reactors, Chemical Engineering & Technology, 28, 267-284.

Hessell V., Knobloch Ch. and Löwe, H., 2008, Review on Patents in Microreactor and Micro Process Engineering, Recent Patents on Chemical Engineering 1, 1-16.

Kashid M.N.and Kiwi-Minsker L., 2009, Microstructured reactors for multiphase reactions: state of the art, Industrial & Engineering Chemistry Research, 48, 6465–6485.

Kashid M.N., Gupta A., Renken A. and Kiwi-Minsker L., 2010, Numbering-up and mass transfer studies of liquid-liquid two phase microstructured reactors, Chemical Engineering Journal, 158, 233–240.

Lavric E.D. and Woehl P., 2009, Advanced-Flow$^{TM}$ glass reactors for seamless scale-up, Chemistry Today, 27, 45-48.

Mae K., 2007, Advanced chemical processing using microspace, Chemical Engineering Science, 62, 4842-4851.

Panić S., Loebbecke S., Tuercke T., Antes J. and Bošković D., 2004, Experimental approaches  to a better understanding of mixing performance of microfluidic devices, Chemical Engineering Journal, 101, 409-419.

Salimi-Moosavi H., Tang T. and Harrison D.J., 1997, Electroosmotic pumping of organic solvents and reagents in microfabricated reactor chips, Journal of American Chemical Society, 119, 8716-8717.

Shen J., Zhao Y., Chen G. and Yuan Q., 2009, Investigation of nitration process of iso-octanol with mixed acid in a microreactor, Chinese Journal of Chemical Engineering, 17, 412-418.

Sprogies T., Köhler J.M. and Groß G.A., 2008, Evaluation of static micromixers for flow-through extraction by emulsification, Chemical Engineering Journal, 135S, S199–S202.

Su Y., Chen G., Zhao Y. and Yuan Q., 2009, Intensification of Liquid–Liquid Two-Phase Mass Transfer by Gas Agitation in a Microchannel, AIChE Journal, 55, 1948-1958.

TeGrotenhuis W.E., Cameron R.J., Butcher M.G., Martin P.M. and Wegeng R.S., 1999, Microchannel devices for efficient contacting of liquids in solvent extraction, Separation Science and Technology, 34, 951–974.

Watts P. and Wiles C., 2007, Recent advances in synthetic micro reaction technology, Chemical Communications, 5, 443-467.

Ying Y., Chen G.W., Zhao Y.C., Li S.L. and Yuan Q., 2009, A high throughput methodology for continuous preparation of monodispersed nanocrystals in microfluidic reactors, Chemical Engineering Journal, 135, 209–215.