

22

Microreactor Applications in the Consumer Goods Industry

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22.1

Introduction

The topic of this chapter is challenging in two ways. The first issue is the term “consumer goods”, which can be used broadly and maybe raises different expectations to this chapter. The second issue is the low level of information available about microreactor applications in the consumer goods industry.

Following the definition of economics, consumer goods are final goods, i.e. goods that are ultimately consumed by consumers rather than used in the production of another good, specifically intended for the mass market [1]. On the one hand, it is clear that this chapter cannot systematically address every type of consumer good. On the other, it is not intended to limit artificially the scope of this chapter by setting definitions in place. The topic of microreactor applications in the consumer goods industry has no clear contours so far because of the small number of reports in this field, and which appear more erratic than regular and systematic. There is furthermore so far no holistic systematic consideration of the potential of microreactor applications in the field of the consumer goods industry. Some areas are covered by first reports, but this does not mean that in other areas there is no potential for microreactor applications. Therefore, it is not the intention here to limit the scope of this chapter solely to the topics addressed so far. The content of this chapter will therefore have no clear cut borders. The opposite: its intention is to stimulate a future broad discussion of this topic. However, to give some orientation, the examples reported in this chapter deal with emulsification, mixing of high-viscosity liquids, customer-based production, vesicle formation processes, detergent production, cream formulation screening, microencapsulation processes, gelation, production of base chemicals, homogenization of dairy products, microfluidic devices for analytical tasks and accessibility of new materials and product properties.

As mentioned above, the low level of available information is the second challenging issue. For example, looking at the series of IMRET conferences (International Conferences on Microreaction Technology), there have been hardly any presentations addressing explicitly the application area of consumer goods. The same is true for microreaction topics during AIChE national meetings. Also taking into account journals in which microreactor applications are normally mentioned fairly frequently (e.g. *Lab on a Chip*, *Chemical Engineering and Technology*, *Chemical Engineering Journal*, *Chemical Engineering Science*, *Organic Process Research and Development*), the picture is the same. The approach followed, therefore, was to pick up the rare examples from these sources, also taking into account examples where only some potential for the consumer goods industry can loosely be assumed. Additionally, some searching has been done on the activities of large consumer goods companies such as Procter & Gamble and Unilever.

The aim of this chapter is to deliver a closed initial overview over the topic. In consequence, there are some overlaps with other chapters in this handbook, where partly similar examples are discussed. Unique to this chapter is nevertheless the permanent orientation towards the application area of the consumer goods industry. The general intention here is to report the existing application examples in the consumer goods industry but also to enable and to stimulate a broader discussion between the microreactor community and the consumer goods industry.

22.2

General Aspects of Microreactor Applications for Emulsification Processes

Emulsions are ubiquitous in consumer applications, including pharmaceuticals, food products, adhesives and personal care products. Product characteristics are influenced both by the chemical formulation and by the processing technology employed. Traditionally, emulsions are formed under high shear conditions using static mixers, ultrasound devices, homogenizers or rotor/stator mixers. Compositions and process conditions are often over-designed to ensure that product requirements are met [2].

The application of microreactors in emulsification processes has been investigated in recent years. A detailed overview on this topic of emulsification in general can be found in Chapters 20 and 21. Here, the focus is only to outline the major traits which might be of interest with regard to the consumer goods industry. Emulsification is certainly currently the application area which shows the largest connection to that industry.

Most of the work done in this area has focused on the exploration of the potential of micromixers, which is seen in attaining narrower size distributions, resolving scale-up problems by a numbering-up approach, better predictability of attainable drop size and a higher energy efficiency of the emulsification process compared with conventional approaches [3]. Exemplary investigations – not necessarily with a background

in the consumer goods industry - illustrating these general advantages are the following:

- *Narrow size distribution.* Kawai *et al.* [4] showed for a dispersion of butyl acetate in water [with 3% poly(vinyl alcohol)] in a microstructured Y-junction (channel width 120 μm , channel depth 48 μm) that a narrower droplet size distribution is obtained compared with the conventional process. The coefficient of variation (CV) is reduced from 36 to 10%.
- *Scale-up by numbering-up.* Kawai *et al.* [4] also validated experimentally an increase in throughput to about 36–378 mL h^{-1} by numbering-up of the Y-junction (with some minor changes in dimensions) by a factor of 300 while keeping the product quality almost constant (CV = 12%).
- *Predictability of drop size.* Another advantage is that in some cases it is possible to predict droplet size by simulation. This was shown by e.g. Hardt *et al.* [5] for droplet formation in a micromixer based on hydrodynamic instability.
- *Higher energy efficiency* by an order of magnitude for a micromixer-based dispersion compared with a batch process was shown by Bayer *et al.* [6] for the system silicone oil (kinematic viscosity $3 \times 10^{-6} \text{ m}^2 \text{ s}^{-1}$)–water (with surfactant). Sugiura *et al.* [7] even estimated for a very specific micromixer a high absolute energy efficiency of 65% compared with 0.1% in a conventional homogenizer.

The above advantages are certainly also relevant for processes in the consumer goods industry. A major point for emulsification processes with throughputs ranging up to the tonnes per hour range is certainly the scale-up issue. Dispersion processes can be very sensitive to variations in scale, i.e. there are issues with up-scalability from the laboratory scale to the plant scale. The hope is to avoid these issues by a scalable design or by numbering-up of parallel units which have been tested and optimized at the laboratory–pilot scale [3]. Furthermore, variations in process conditions affecting product quality should be better controllable in a microreactor plant. Other targets are higher flexibility, improved product quality and a better understanding of the relation between dispersion device properties and performance [3]. Additionally, the customer-based production of emulsions, e.g. cosmetic products, could be of interest (see Section 22.6).

The above examples illustrate the potential of the application of micromixers. It has to be stated, however, that not all this potential can be exploited for given applications at least especially when higher flow rates have to be considered.

Although the above discussion was mainly focused on the application of micromixers in emulsification processes, it should not be forgotten that the application of microreactor technology is not restricted entirely to that area. For example, in addition to the processing parameters mixing time and mixing energy, which are addressed in the application of micromixers, the process parameter thermal history also impacts the final product quality [2]. Therefore, the option of integrating an effective microstructured heat exchanger into an emulsification process could also

be beneficial, e.g. through gentle reagent heating or rapid product cooling [2]. This option could be also seen in a broader sense that microreactor technology allows more precise control over the process conditions and even permits new process conditions and thereby allows, e.g., formulation innovations (see also the corresponding remarks in [2]).

There are additional advantages of microreactor application for emulsification processes that can be imagined, but which are currently lacking detailed publicly available information. Decreased bulk shear rate may allow the use of shear-sensitive ingredients, such as natural oils [2]. Also, the enabling of low capital cost, easy maintenance and cost-effective transport of equipment to new markets because of the compact and possible modular design of microreactors, has been considered [2]. Small equipment size means a small liquid inventory. A low inventory means less off-specification product as the equipment is charged, started and taken down for maintenance and there is a lower solvent requirement during cleaning [2].

Some additional and more specific aspects of microreactor applications for emulsification are addressed in the following sections.

22.3

Comparison of Micromixers with Regard to Performance in Liquid–Liquid Dispersions

As stated above, the focus of recent investigations of microreactor applications in the field of emulsification was on the use of micromixers, and different types of micromixers have been employed. However, it is difficult to compare them with regard to liquid–liquid dispersion performance since the mixers are most often investigated for different specific applications. However, a suitable comparison is the basis for future targeted equipment selection. Furthermore, micromixers are in competition with conventional and other innovative equipment such as static mixers, membranes and homogenizers. Therefore, benchmarking with such equipment is also required.

In this context, the work of Löb *et al.* [3] is considered below since it describes a first comparison of different micromixers based on a common model system. The micromixers investigated cover three different functional principles and also different characteristic internal dimensions. Albeit the work is not final and cannot be regarded as comprehensive, it points out some of the major issues to be considered when comparing micromixers with regard to liquid–liquid dispersion performance.

Performance was determined using heptane–water [sodium dodecyl sulfate (SDS), 0.01 M] as a model system at a constant volumetric flow ratio of 1 : 5 for different total flow rates. Exemplary results are given in Figure 22.1. As expected, the mean droplet size generally decreases with increase in total flow rate since it is associated with an increase in energy input. The micromixer SIMM-V2-Ag40 with the smallest internal dimensions (40 μm feeding channels) leads at a given flow rate to the smallest droplets. In the class of so-called caterpillar micromixers (CPMM), which represent split-and-recombine mixers, a smaller internal cross-section of the mixing channel leads to smaller droplets at a given flow rate (compare the CPMM-V1.2-R600/8 with a

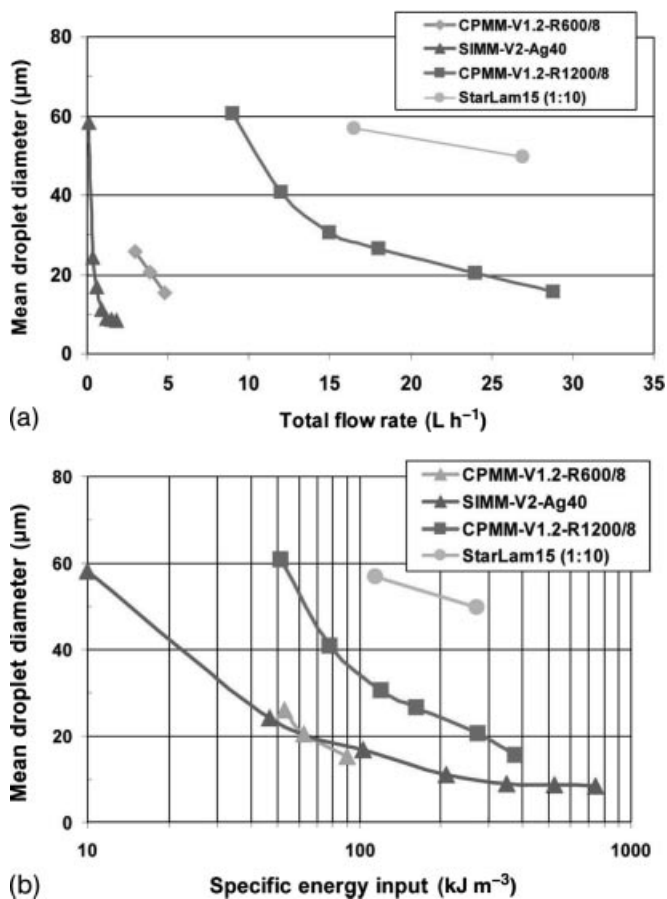


Figure 22.1 Comparison of different micromixer performances with regard to liquid–liquid dispersion. The scope of the investigations was IMM’s SIMM-V2-Ag40, CPMM-V1.2-R600/8, CPMM-V1.2-R1200/8 and StarLam15. The model system was heptane–water (SDS, 0.01 M) with a volumetric flow ratio of 1 : 5 (1 : 10 in the case of the StarLam15). The mean droplet diameter of the volumetric size distribution is plotted as a function of the total flow rate (a) and of the specific energy input (b) [3].

600 × 600 µm cross-section with the CPMM-V1.2-R1200/8 with a 1200 × 1200 µm cross-section in Figure 22.1a). The StarLam15 consists of a stack of thin and structured plates with a central mixing chamber formed by a hole in the middle of each of the plates. The velocity of injection of the two phases into the mixing chamber is low because of the large number of feeding structures. It was necessary to change the flow ratio for the StarLam15 mixer to 1 : 10 to achieve, for the investigated total flow rate range, droplet sizes comparable to those with the other mixers. Better performance is expected for significantly higher flow rates. The diagram showing the dependency of mean droplet size on total flow rate is a first aid in selecting a suitable micromixer based on total flow rate requirements. Another basis for comparison is

the specific energy input given in the case of static mixers by the pressure drop over the mixer (see Figure 22.1b).

The width of the size distribution has also been determined but there is no significant difference between the different mixer types [3]. This might be a consequence of the fact that in the selected model system the viscosities of the two phases are comparable. It is assumed that experiments with model systems with other viscosity ratios could reveal the impact of mixer type here [3]. On one hand micromixer geometry should influence the ratio between elongational forces and shear forces and on the other hand the importance of these forces with regard to droplet decay depends on the viscosity ratio [8].

22.4 Dispersion and Mixing of High-viscosity Liquids

A large range of micromixers have been described both for use in mixing mixable liquids and also for liquid–liquid dispersions. However, the topic of handling high-viscosity liquids is hardly explicitly described, although this is a specific point of interest with regard to consumer goods since many products are of high viscosity or processing requires handling of high-viscosity media (e.g. toothpaste, highly viscous silicone oils in cosmetic cream formulations).

A rare example in the literature dealing with the topic of dispersing high-viscosity liquids in microreactors is the work of Seemann *et al.* [9]. Micromixer-based emulsion formation processing liquids of high viscosity can lead to problems such as a high pressure drop and blocking of the microchannels. To overcome such problems, Seemann *et al.* [9] suggested a microdispenser where a raw dispersion is led through a single channel having a defined diameter. In the middle of this channel a pressure impulse is applied on this fluid by a nozzle introducing a micro liquid jet of the continuous phase (Figure 22.2). The nozzle is linked to a membrane. The pressure drop over the channel can be adjusted through the channel size according to the viscosity of the fluids. The microdispenser was designed to handle liquid–liquid dispersions up to 200 mPa s. Prototypes were tested using gear oil–water and silicone oil–water. The tests confirmed the principal feasibility. More details were not given.

Concerning mixing of highly viscous media, it may worth mentioning the type of split-and-recombine micromixers exemplified on the so-called Caterpillar Micro

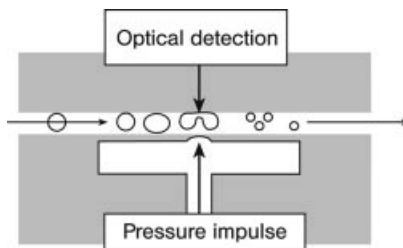


Figure 22.2 Principle of the microdispenser [9].

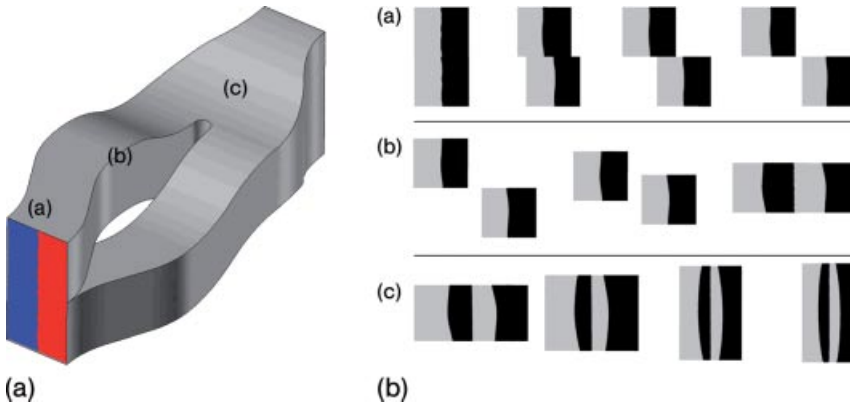


Figure 22.3 Functional principle of the split-and-recombine micromixer CPMM-V2 (IMM). (a) Representation of one mixing step; the colors blue and red represent two liquids entering the mixing step; the complete mixer is made up by a sequence of such mixing steps. (b) Simulated flow pattern at different cross-section points over the length of the first mixing step. Source: Institut für Mikrotechnik Mainz GmbH.

Mixer Version 2 (Institut für Mikrotechnik Mainz, Mainz, Germany; CPMM-V2 [10, 11]). The advantage with regard to mixing of high-viscosity media is that through the repeated splitting and recombination of flows finally very thin fluid lamellae in an alternating configuration are achieved while the mixer structures themselves are fairly large. Thereby, the risk of clogging and a too high pressure drop can be minimized or avoided. The basic principle of one mixing step of the CPMM-V2 is shown in Figure 22.3. The flow pattern was visualized in a set of experiments using a transparent version with cross-section 2×4 mm and eight mixing steps [10, 12]

In the visualization experiments, two glycerol solutions (85 wt% in water) were used. Figure 22.4 shows the flow pattern in each mixing step and illustrates nicely the

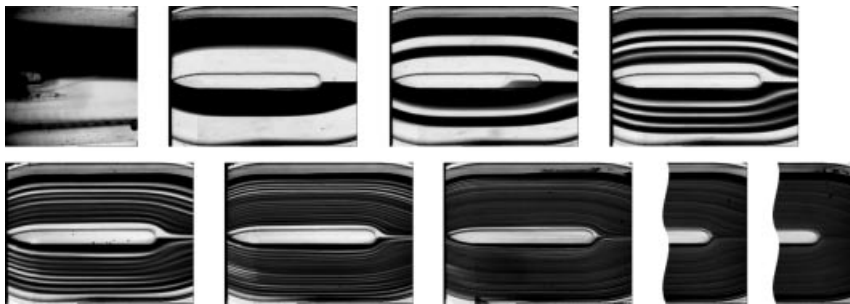


Figure 22.4 Flow pattern in the inlet region of CPMM-V2-R2000/8-PMMA and in the following eight mixing steps (aqueous glycerol 85 wt%, flow ratio 1 : 1; one phase is colored with water blue) [11].

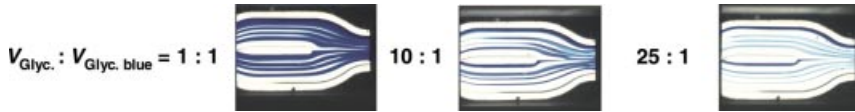


Figure 22.5 Flow pattern in the third mixing step of CPMM-V2-R2000/8-PMMA for different flow ratios of 1 : 1, 10 : 1 and 25 : 1 (aqueous glycerol 85 wt%, one phase is colored with water blue; total flow rate 200 mLh^{-1}). Source: Institut für Mikrotechnik Mainz GmbH.

increase in the number of alternating liquid lamellae from step to step by a factor of two and connected thereby with the decrease in lamella width. The decrease in lamella width is aimed finally to achieve fast mixing by pure diffusion. It is also possible to mix the two liquids in different ratios (see Figure 22.5) [12]. It is also in principle feasible to mix liquids of different viscosity and also more than two components [13]. Naturally, certain parameter ranges have to be respected for proper operation.

The topic of handling liquids of different viscosities for dispersion processes in microfluidic networks with two microreactors (“droplet emitters”) is addressed by Unilever R&D (Vlaardingen, The Netherlands) in a patent [14, 15]. The patent deals with the flow distribution in a microfluidic network on the background of dispersion processes with two supply sources for the two phases, which supply via upstream channel systems two microfluidic reactors called “drop emitters” (Figure 22.6). The dispersion leaves the microreactors via downstream channels. The major point of the patent is that the flow distribution is controlled by a design which creates a high pressure drop in the upstream channels. The pressure drop in the downstream

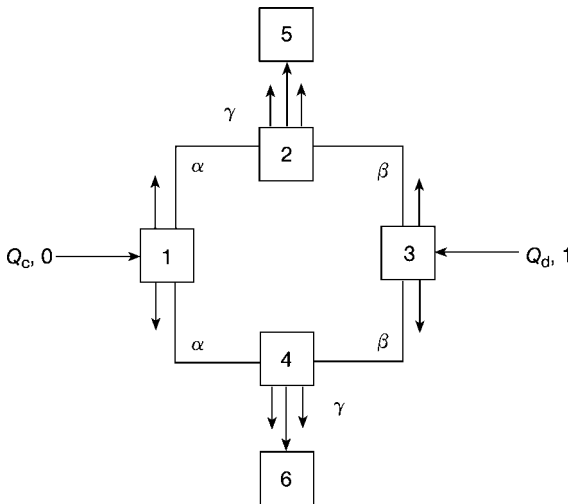


Figure 22.6 Microfluidic network to supply two microreactors for dispersion as outlined in a patent from Unilever R&D (Vlaardingen, The Netherlands) [14].

channels is lower. As application areas of such a microfluidic network, food and personal care applications are mentioned.

22.5

Cream Formation in Micromixers Targeting a Reduction in Emulsifiers and Preservatives

The micromixer-based continuous formation of a hydrophilic cream for dermal application was studied by Schiewe *et al.* [16]. In addition to showing the feasibility and exploring the advantages compared with a conventional laboratory shaker, the investigations also targeted lowering the amount of emulsifiers and preservatives required since they can be the source of allergic reactions.

The composition of the hydrophilic cream formulation was chosen according to pharmaceutical recommendations. The oily phase consisted of sorbitan monostearate, macrogol-9-stearate, medium chain length triglycerides and retinol palmitate. Sorbitan monostearate and macrogol-9-stearate are emulsifiers often used for pharmaceutical applications to guarantee stability of the cream over a period of several years. The aqueous phase contained glycerol and citric acid and sodium benzoate acting as preservatives. An interdigital micromixer was used (SSIMM with 25 and 40 μm inlays, Institut für Mikrotechnik Mainz GmbH [17]). The mixer to form an oil-in-water emulsion was operated at 60–80 °C. The emulsion cools after leaving the mixer to yield a thixotropic cream at room temperature. The flow ratio of oil phase to water phase was set to 1 : 10.

Depending on the operating conditions, mean droplet sizes of 0.8–2.5 μm with standard deviations ranging from 0.4 to 1.3 μm were measured. As expected, the mean droplet size decreased with increase in total flow rate. For instance, on increasing the flow rate from 0.3 to 0.9 L h^{-1} , the droplet diameter decreased by a factor of almost two.

No temperature dependence was found. Furthermore, in the investigated range an influence of the mixer dimensions on the mean droplet diameter was not observed.

Compared with a laboratory shaker (8 μm mean droplet size and 5 μm standard deviation of the size distribution), clear advantages of the micromixer-based cream formation were revealed, i.e. smaller droplets and a narrower size distribution (Figure 22.7).

Further investigations were performed with a gradually decreasing content of emulsifiers. The amount was reduced from initially 5% to 3, 1 and 0.5%. Homogeneous cream formulations were obtained even with only 1% emulsifier. A lower content of 0.5% no longer stabilizes the formation of an emulsion and leads to phase separation within minutes. Figure 22.8 shows cream samples obtained having different emulsifier contents. The cream formulations with 1% emulsifier can be stored at 8 °C over a period of at least 7 days without a decrease in quality. No phase separation was observed. Furthermore, the mean droplet diameter was found to be almost constant and also the deviation of the size distribution did not increase with time, indicating good short-term stability.

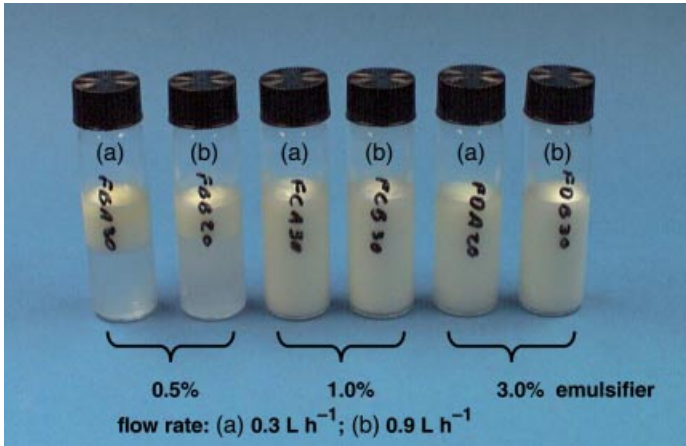


Figure 22.7 Microscopic images (500-fold magnification) of cream samples generated using either (a) a micromixer at 60 °C and 0.6 L h⁻¹ or (b) a laboratory shaker at 60 °C. Source: Institut für Mikrotechnik Mainz GmbH, Mainz, Germany.

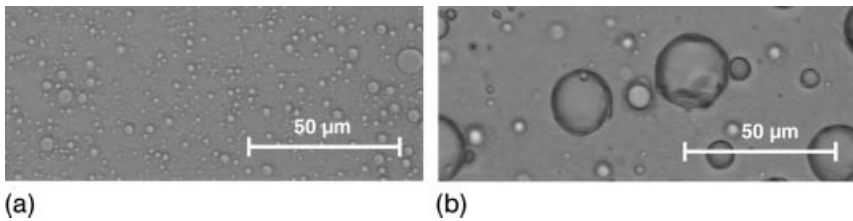


Figure 22.8 Photograph of cream samples generated at two different flow rates and varying content of emulsifiers (60 °C). Source: Institut für Mikrotechnik Mainz GmbH, Mainz, Germany.

Summarizing, the investigations have shown the feasibility of producing temporary stable creams (weeks to months) with low contents of emulsifiers and preservatives in a continuous flow setup using a micromixer.

Mae *et al.* [18] performed experiments with micromixers with regard to a soap-free emulsion using salad oil and water as the test system. Special attention was also given to the influence of the material of the micromixers on the emulsification process. They found that the proper choice of micromixer material supports the formation of emulsions (Figure 22.9).

22.6 Customer-based Production of Emulsions and More

In many emulsions, stabilizers are added to assure long-term stability of the emulsions produced. In the case of emulsion-based cosmetic products, it is obvious

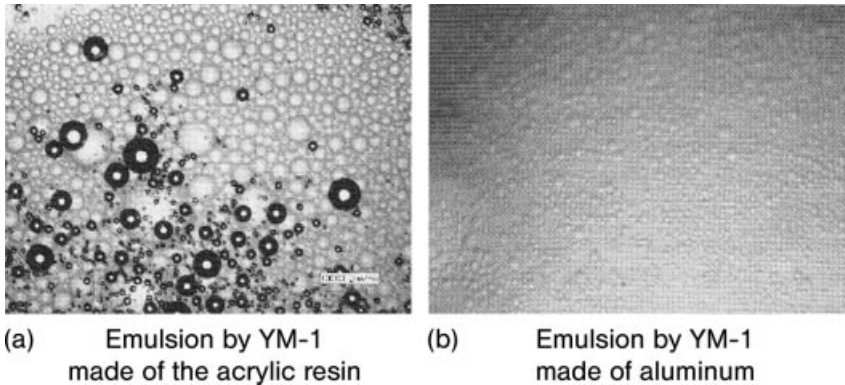


Figure 22.9 Comparison of emulsions formed in YM-1 split-and-recombine micromixers of the same design but using different mixer materials: (a) acrylic resin mixer; (b) aluminum mixer [18].

that the stabilizers could also have a negative influence. Skin products such as creams often contain stabilizers at levels up to 90%. Unfortunately, these stabilizers could produce unwanted allergic reactions. Therefore, the cosmetics industry is interested in a reduction in the amount of stabilizers while maintaining the quality of their products. Furthermore, the production of emulsions on demand to prevent decomposing and aging effects is of interest. In the following, a specific study is described based on the specific background outlined above. Thereafter, the topic is broadened further by taking into account a patent [19] filed by Wella (Darmstadt, Germany) which now belongs to Procter & Gamble.

Mahe *et al.* [20] of the LVMH Group, Christian Dior, reported a microstructured device for the production of emulsions on demand. The basic design criterion was that the microstructured device is hand operated, i.e. emulsification has to be achieved with relatively low external forces and internal pressures. Assuming the thumb as most powerful digit, required forces for operation higher than 20 N cannot be accepted.

An initial test using an existing split-and-recombine micromixer based on fork-shaped channel units showed that this requirement was not met because a too high pressure drop was required for producing fine emulsions. A new design was derived in which a continuous flow in a meander main channel is permanently influenced by partial flows stemming from the former slope of the main channel transferred via sideways channels. This *in silico* realized micromixer has dimensions of $5 \times 28 \times 1.6$ mm. The mixer was tested using standardized flacons for cosmetic solutions. These flacons consisted of two glass bottles fixed together with a cap on their top. Two small spray pumps were arranged in the cap supplying the liquids from the bottles underneath by pressing the cap down. The outlet of the pumps was directly connected to the micromixer. For the tests an aqueous phase with a viscosity of 1.2 mPa s and an oily phase with a viscosity of 4.0 mPa s were used. Due to the same

specifications of the pumps, no differences in the flow rates of the two phases were found. It was possible to produce emulsions by pressing the cap downwards with an acceptable force of a fingertip (less than 10 N). Typical total flow rates amounted to up to $250 \mu\text{L s}^{-1}$. The emulsions obtained were very stable over a long period. The pressure required to form the emulsion was about 0.08 MPa, significantly lower than in the case of the initial micromixer (up to 1.0 MPa). According to the authors, especially this property of the new mixer increases the probability of producing emulsions without stabilizers and on demand. Furthermore, it makes the application of microstructured components in the hands of the end users useful and possible.

After this specific example, which has already demonstrated some potential advantages of applying microreactors for customer-based production of emulsions, the topic can be broadened as mentioned at the beginning on the basis of a patent [19] filed by Wella (Darmstadt, Germany).

The patent deals with a package system including a static micromixer for the production of formulations consisting at least of two components directly prior to its application. Figure 22.10 illustrates exemplarily such a package system containing two supply containers (18a, 18b) and a specific static micromixer (1) made up of a stack of specially designed plates.

The background and motivation for this package system are outlined in the patent as follows. In application formulations consisting of several components, there is

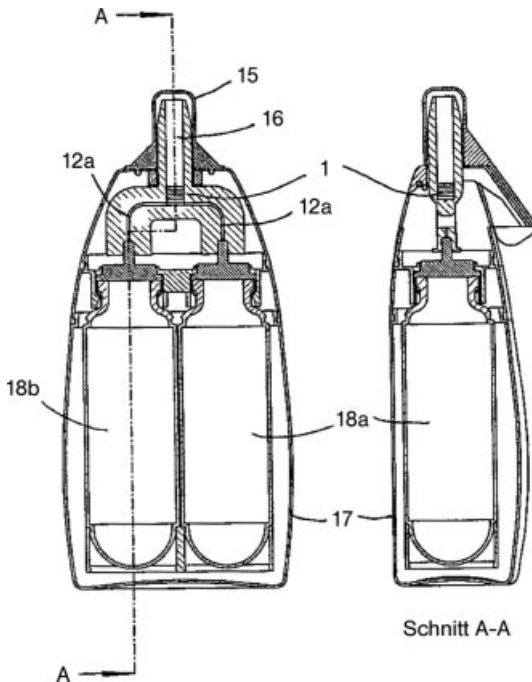


Figure 22.10 Package system with static micromixer for the production of formulations directly prior to application as outlined in the patent filed by Wella (Darmstadt, Germany) [19].

often the danger that the product is not stable over a longer time, since ingredients can react in an undesirable manner. Therefore, additives are often necessary. Disadvantages of the additives are that they increase costs or they can influence the product properties in an undesirable way; especially they can lead to unwanted adverse reactions. To avoid these problems, the product can be delivered in the form of separated components which are mixed directly prior to the application. The separated components contain the later active ingredients as a pre-step or in a modified version. Only after mixing the separated components are the final active ingredients formed. Examples are the retarded release or formation of pharmaceutical or cosmetic active ingredients, the formation of oxidation hair color from dye pre-steps and an oxidizing agent or the formation of retarded hardening of glues after adding suitable hardeners. A way to do this is to integrate the separated components into one package equipped with a suitable pump system, a mixer and a common outlet. The disadvantage of conventional systems is that the quality, consistency and activity of the mixture often are not satisfactory. In the case of viscous systems, inhomogeneities can occur, and in the case of liquid, non-viscous fluids the formation of fine dispersed mixtures is often not feasible. The use of a suitable static micromixer should overcome these problems. The patent is not limited to liquid-liquid dispersions, it also includes mixing, liquid-liquid, gas-liquid and solid-liquid dispersions. Additionally, it is aimed that there should be no remaining mixture in the package system after the application which could spoil the following steps in the package system. It is also aimed to be able to contact components of different viscosities.

As potential application areas the following are mentioned:

In the field of cosmetics:

- *in situ* production of shampoos, deep conditioners, hair or skin milk;
- mixing of dye precursors and oxidizing agents for hair colors;
- mixing of reactive solutions with thickeners, especially viscous preparations with oxidizing agents and thickeners for hair bleaching or the fixation of permanent waves;
- formation of foams by chemical release of gases;
- foams for hair or skin treatment from a liquid surfactant containing and gaseous component;
- mixing of special final products to achieve special effects such as a color change caused by a time-retarded chemical reaction with special adaptation to the aimed for application (e.g. hair deep conditioners);
- formation of gels starting from low-viscosity components.

In the field of pharmaceuticals:

- mixing of water-sensitive formulations at the moment of application from a waterless and a water-containing phase;
- ointments, emulsions, milks, etc., at the moment of application with avoidance or reduction of normally needed stabilizer additives which could also lead to a decrease in adverse reactions.

In the field of adhesive technology:

- formation of multicomponent formulations at the moment of application.

In the field of foods:

- formation of mayonnaise, mustard, etc., at the moment of use;
- homogenization of milk, milk products, etc.;
- formation of cream without mechanical whipping.

22.7

Vesicle Formation in Microfluidic Structures

In the sections above, the focus has been on liquid–liquid dispersions and the topic of vesicular dispersions has not been addressed, at least not specifically. Studies have been reported in the area of nanobiotechnology aiming at encapsulation of beads, proteins and cells inside vesicles, using microfluidic devices for this process. This might be of interest in the future for application also in the context of consumer goods. Jahn *et al.* [21] reported the formation of vesicles made up of phospholipids in a microfluidic device in the context of single molecule encapsulation. Thereby the microstructure and the operating conditions allow the control of vesicle size and uniformity. In the following, some details from this work are given to illustrate the possibilities of microfluidic structures to influence the vesicle formation process.

Due to their amphiphilic nature, phospholipid molecules, when dispersed in water, self-assemble into bilayer membranes to form structures called liposomes that are often spherical and encapsulate an aqueous internal volume. Liposomes made using bulk techniques range in size from 50 nm to tens of micrometers. Water-soluble molecules can be incorporated into the liposomes upon formation. The final goal of the work of Jahn *et al.* [21] was to use liposomes as discrete packages to sequester very small amounts of reagents in order to control their reaction finely. For this purpose, two characteristics of the liposome population are critical – the liposome size and the number of encapsulated molecules contained inside each liposome. However, liposomes prepared using bulk techniques generally exhibit very high polydispersity with either uncontrolled or unpredictable encapsulation efficiency. To improve this, a microfluidic system was applied by Jahn *et al.* A stream of a lipid solution is hydrodynamically focused at a microchannel cross-junction between two aqueous buffer streams. The lipids, dissolved in isopropyl alcohol, flow through the center inlet channel and an aqueous buffered solution flows through the two side inlet channels. When the two liquid phases come into contact, the isopropyl alcohol rapidly diffuses into the aqueous phase and *vice versa*. At a critical point, the lipids are no longer soluble and self-assembly of the lipids starts. The flow rates of the alcohol and buffer can be adjusted to control the degree of hydrodynamic focusing influencing both the dilution rate and the shear stress at the fluid/fluid interface. Jahn *et al.* determined that changing this parameter allows one to maintain

unprecedented control over the liposome size and homogeneity. The number of encapsulated molecules can be manipulated by the starting concentration in the buffer solution.

This example represents a good starting point for re-thinking processes for producing vesicular dispersions taking into account microreactors. The following section deals with surfactant dispersion in the context of large-scale liquid detergent production, which also leads to vesicular dispersion and thereby extends the topic discussed in this chapter.

22.8 Liquid Detergent Production by Surfactant Dispersion

Within the public funded EU project IMPULSE [22], the applicability of microreactor-based continuous processing for liquid detergent production is currently being checked, where the application example stems from the industrial partner P&G [3]. The work performed was outlined by Löb *et al.* [3] without disclosing the precise formulation. A molten surfactant has to be dispersed in a dilute aqueous electrolyte at about 80 °C. The weight content of the surfactant is thereby in the region of about 10%. The process leads to the formation of a colloidal dispersion consisting of vesicles formed by assembly of the surfactant molecules with water also included inside the vesicles. On the one hand it is aimed to increase the surfactant content limited by a maximum viscosity and on the other hand to influence the viscosity at the same time by vesicle size distribution. Here the motivation for the use micromixers is the pragmatic assumption that there are more uniform process conditions in micromixers (and microreactor setup) leading to a better controllable vesicle formation process and thereby to more defined and uniform vesicle size distributions (see the discussion in Section 22.7). The vesicle formation process described in Section 22.7 is different to surfactant dispersion since vesicle formation is induced there by a change in solubility by polarity changes of the solvent. In general, dispersion processes can be very sensitive to variations in scale. Therefore, another driving force for microreactor application is the hope of avoiding these issues by a scalable design or by numbering-up of parallel units, tested and optimized on the laboratory–pilot scale. Also, greater flexibility of the production process could be of advantage. So far, microreactor setups for laboratory-scale investigations have been realized and first experiments have been performed.

The Forschungszentrum Karlsruhe (Karlsruhe, Germany) (FZK) and the Institut für Mikrotechnik Mainz GmbH (Mainz, Germany) (IMM) have realized experimental continuously operated setups including microstructured components to investigate the surfactant dispersion process [3]. Figure 22.11 shows the flow chart of the FZK setup. The molten surfactant is fed by a pump over pipes heated by electric heating strips to the heated micromixer. The aqueous phase is fed at room temperature via a pump and heated by a micro heat exchanger. Via a T-junction, a concentrated electrolyte is dosed to the aqueous feed stream before entering the micromixer. The product is cooled to room temperature in a second micro heat

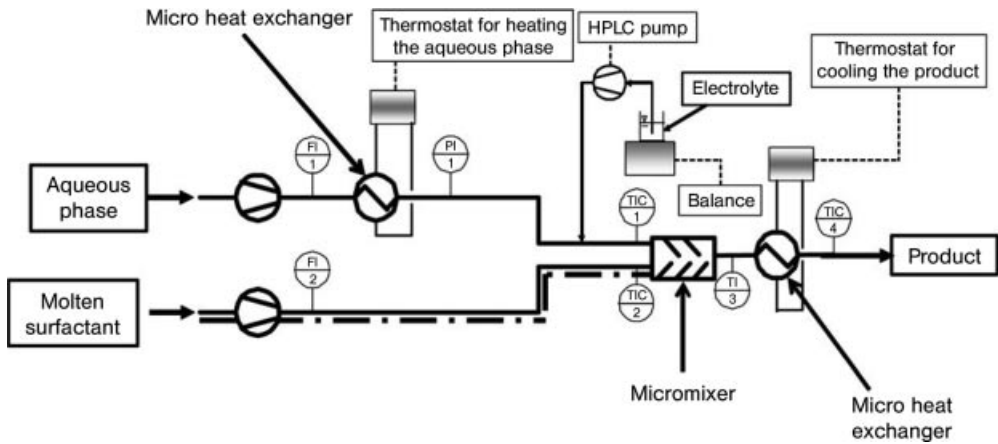


Figure 22.11 Flow chart of the experimental set-up at FZK for surfactant dispersion. Shown is the version with electrolyte dosing in front of the micromixer [3].

exchanger. In principle, the IMM set-up follows the same flow chart. The major difference is that apart from the supply vessel of the surfactant, the whole fluidic part of the set-up is embedded in a thermostated bath (Figure 22.12). In the case of the FZK set-up, a parallel multilamination mixer and in the IMM set-up a split-and-recombine micromixer are employed, giving the possibility of studying the impact of

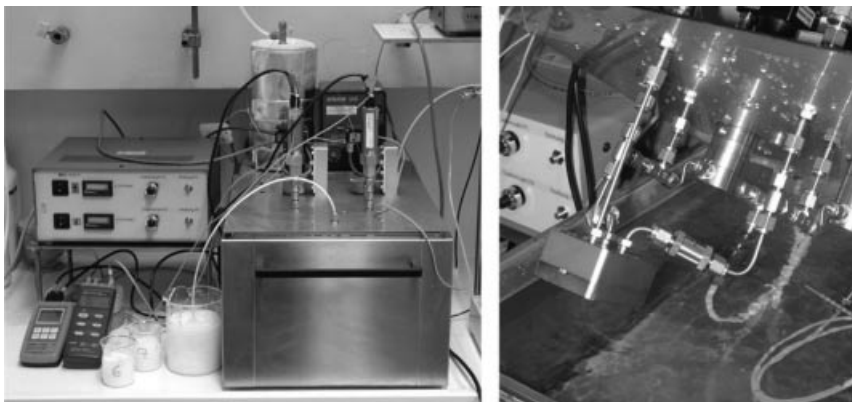


Figure 22.12 Experimental set-up at IMM for surfactant dispersion. All heated parts beside the supply vessel are embedded in a thermostated bath. (a) Complete view of the setup with control units at the left side and the thermostat at the right side with heating jacket for the supply vessel and pumps. (b) View inside the thermostatic bath. Visible is especially the caterpillar micromixer and the pump heads [3].

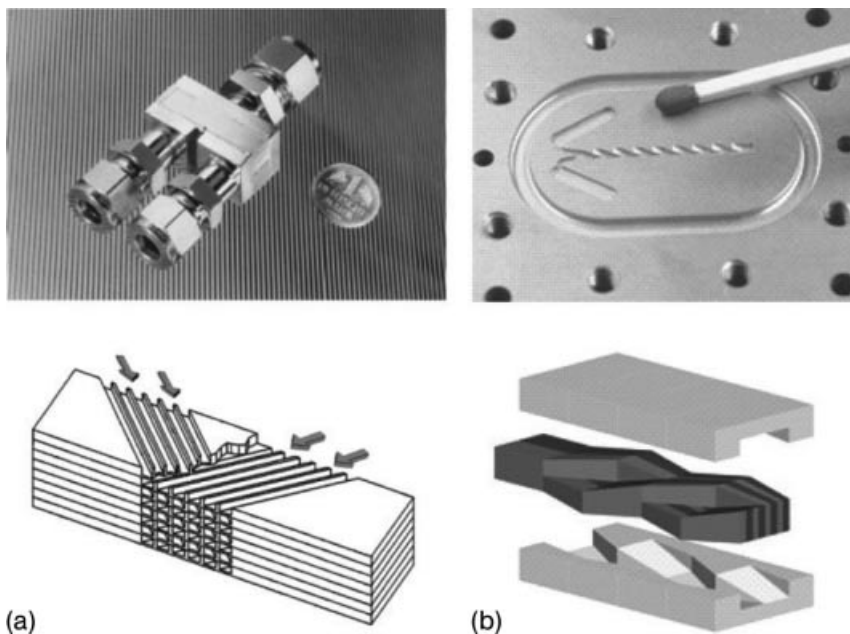


Figure 22.13 Micromixers employed in the experimental setups for surfactant dispersion. The V-type mixer of FZK (a) is a parallel multilamination micromixer whereas the caterpillar mixer of IMM (b) is a split-and-recombine micromixer (serial multilamination) [3].

different mixer principles on the vesicle formation process (Figure 22.13). Both setups have been operated successfully for total flow rates up to 10 kg h^{-1} .

First results of the experiments performed are given in Figure 22.14, showing the dependence of the vesicle size distribution on the total flow rate obtained with the IMM setup, i.e. employing the caterpillar micromixer. The total flow rate was varied from 4.3 up to 12.7 kg h^{-1} while keeping the surfactant content almost constant at about 10 wt\% and working at a temperature of about $80 \text{ }^\circ\text{C}$. The results indicate the formation of nanosized vesicles. Furthermore, analogous to the case of the liquid–liquid dispersion, a decrease in vesicle size with increase in total flow rate is observed. Currently, there are not enough data to identify differences between the performance of the V-type mixer and the caterpillar mixer.

Since only first experimental results are given, it is too early to make concluding remarks. Nevertheless, the setups have proven to be versatile tools for laboratory-scale investigations. Due to its modular setup, it is possible to make adjustments fairly easily. Thus it is possible, e.g., to change the position of the dosing of the concentrated electrolyte via a T-junction from before the mixer to after the mixer. The location of electrolyte dosing could be a parameter influencing product quality. Also, the mixers are exchangeable. Temperature, flow rates and flow rate ratios can be varied easily and quickly. Furthermore, a first relationship between process

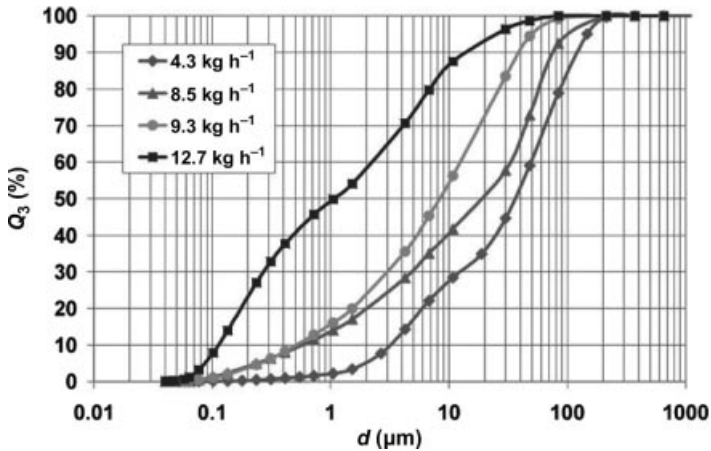


Figure 22.14 Sum curve of the volumetric vesicle size distribution (Q_3) for different total flow rates obtained with the IMM setup at about 80°C and at an almost constant surfactant content of 10 wt% [3].

conditions (total flow rate) and mixer performance with regard to vesicular dispersion formation has been found.

22.9 Screening of Cream Formulations

A general application area of microreactors is screening. Screening applications have been described, for example, for catalyst search in the area of heterogeneously catalyzed gas-phase reactions [23] and homogeneously catalyzed gas-liquid reactions and for parameter screenings in process development.

Correspondingly, there might also be screening applications in the consumer goods industry which could profit from the use of microreactors.

As an example, the screening of different cream formulations can be mentioned. This forms the background of a setup offered by IMM [17] (Figure 22.15). The basic idea behind the setup is to create continuously formulation samples made up of up to eight components mixed in a multicomponent static micromixer. The micromixer and parts of the feed system are embedded in a thermostated bath, allowing the temperature to be set during the process but also allowing the handling of molten components, as is often required for creams. By varying the feed flow rates, different compositions can be realized. Due to the small inner volume of the setup, the amounts of formulation needed are small and, furthermore, changing rapidly to new formulation compositions is possible. According to a press release [24], such a system was presented by IMM in 2005 to Shanghai Jahwa, the largest domestically owned Chinese cosmetic company.

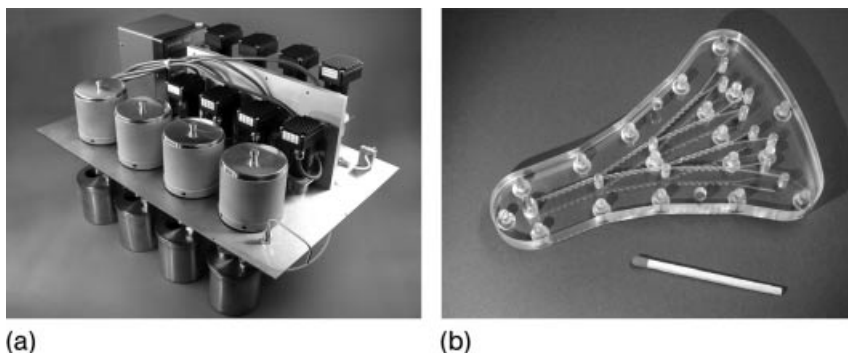


Figure 22.15 Parts of a cream plant offered by IMM [17]. (a) On a plate a thermostat inset, eight feed pumps and four supply vessels are fixed. The shown part will be set on/in a thermostat bath. Parts of the feed vessels and also the pump heads are inside the thermostated bath, allowing handling of molten formulation components. (b) PMMA version of a multicomponent caterpillar micromixer of IMM allowing mixing of up to eight different components. Source: Institut für Mikrotechnik Mainz GmbH.

22.10 Microencapsulation Processes

Microcapsules are small particles that contain an active agent or core material surrounded by a coating or shell [25]. Although there is no universally accepted size range, often particles in the range 1–1000 μm are classified as microcapsules [25]. Most capsule shell materials are organic polymers [25]. A wide range of core materials have been encapsulated, including adhesives, agrochemicals, live cells, active enzymes, flavors, fragrances, pharmaceuticals and inks [25]. Microcapsules are used in a wide range of commercial products including consumer goods. The size range of microcapsules is in the range addressed by microreactors. This raises the question of whether encapsulation processes can be done and improved by microreactor processing.

There are different types of encapsulation processes [25], for example complex coacervation, polymer–polymer incompatibility, interfacial polymerization and *in situ* polymerization, and each certainly has its different process challenges which might need to be addressed. The following discussion focuses on the topic of interfacial polymerization.

Floyd [26] investigated the application of a microreactor for encapsulation by interfacial polymerization. In an interfacial polymerization, in a first step a dispersion is formed and then in a second step polymerization is initiated at the interface of the two phases. Floyd [26] used a system of toluene with a dissolved diisocyanate and water with a dissolved diamine (Figure 22.16). Interfacial polymerization is caused by the reaction of the diamine with the diisocyanate, forming a polyurea shell. The focus of this work was to influence the size of the droplets formed during the dispersion step, which was performed in a focusing interdigital micromixer. The second step

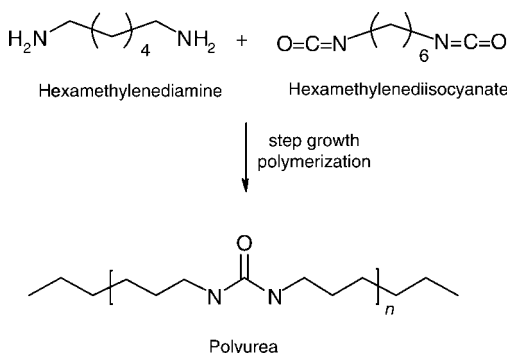


Figure 22.16 Encapsulation chemistry used in the investigations of Floyd [26] and Hollomatz [27].

was separated from the first by using for the first step pure water, i.e. excluding the shell forming interfacial polymerization. This was done by dropping the formed toluene-in-water dispersion into a vial containing the aqueous diamine. By varying the operating parameters total flow rate and flow rate ratio, it was possible to influence the droplet size.

Influenced by this work, Hollomatz [27] investigated the process further towards transferring the process into a complete continuous microreactor-based process, i.e. he also included the second step. Like Floyd, he performed the first step using a micromixer for the controlled dispersion without reaction but using a different mixer. But then the process is modified. The dispersion is transferred into a second micromixer where aqueous phase containing the diamine is added to the continuous phase (pure water) of the dispersion. Thereby, interfacial polymerization is initiated. The decisive point here is that the second micromixer should just add the reactant without changing the originally formed dispersion, i.e. in the second micromixer no dispersion should occur. The approach followed was that the second micromixer has larger internal dimensions, which should prevent the energy input being lower than required for drop breakup.

By this method, it was feasible to produce polyurea microcapsules continuously. Due to measuring problems concerning drop size and capsule size, it was not possible to show without doubt that the second micromixer does not change the dispersion. At present, it can only be stated that the impact is small.

Albeit no ingredient was encapsulated during these investigations, in principle they show the potential for applying microreactors for encapsulation processes. The investigations directly address the aim of having control over drop size and size distribution (and more defined product characteristics stemming therefrom) and to achieve continuous processing. More complex setups allowing tempering of the fluids, temperature ramps during the process and residence time sections of defined length to control shell growth and so on are also possibilities. Hence it is obvious that at least the potential exists that by applying microreactors, good or better control over encapsulation processes can be achieved, maybe resulting in better or new products.

22.11

Alginate Gelation in Microfluidic Channels

Amici *et al.* [28] of Unilever Corporate Research (Bedford, UK) investigated alginate gelation in microfluidic channels. Alginates are extremely versatile biopolymers used in a variety of technical applications, including as viscosifiers, stabilizers and gelling agents in the food and pet food industries. Furthermore, they are increasingly studied for biotechnical and biomedical applications. A focus is the production of microspheres, usually with the aim of encapsulation of bioactive or cellular material. This area forms the background of the work reported by Amici *et al.*

Amici *et al.* used a microstructured modified T-junction realized in polydimethylsiloxane (PDMS). At the T-junction of two channels, an additional third channel joins the junction forming a 45° angle with the other channels (Figure 22.17).

In this device, sunflower oil (SFO) flows along the main channel as the continuous phase. An aqueous solution of the acid D-gluconic- δ -lactone (GDL) is introduced into the main channel via the channel forming a right-angle with the main channel. The alginate stock solution containing also calcium carbonate introduced via the third (smallest) channel merges with the acid stream at the time of entering the main channel. The aqueous phase represents the disperse phase. Under suitable parameter settings, drop formation occurs at the T-junction (Figure 22.18). The calcium released by the GDL induces chain aggregation and the formation of viscoelastic gels. By varying the concentrations of calcium and alginate, it is possible to influence the gelation kinetics. The investigations revealed that it is necessary for a controlled drop production to find a balance between the drop formation time and the alginate gelation kinetics. If the drop formation time is shorter than the structuring time, regular drop formation occurs, otherwise an alginate structured solution obstructs the channels.

The investigations prove that monodisperse alginate drops can be produced in the manner described above. Nevertheless, modifications are required to the device

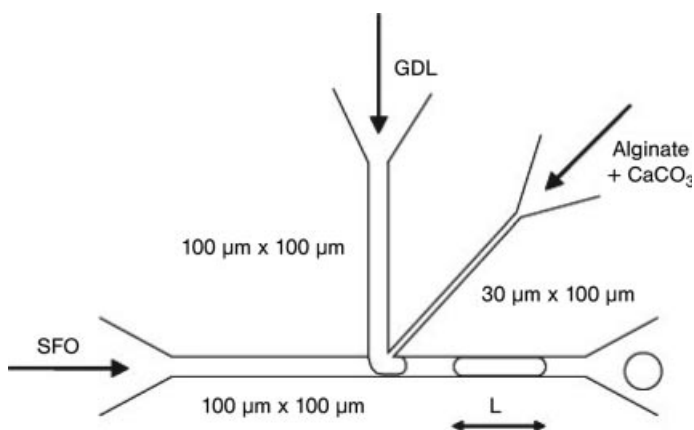


Figure 22.17 Scheme of the modified T-junction microdevice used by Amici *et al.* [28]. The arrows specify the orientation of the flows. SFO, sunflower oil; GDL, D-gluconic- δ -lactone.

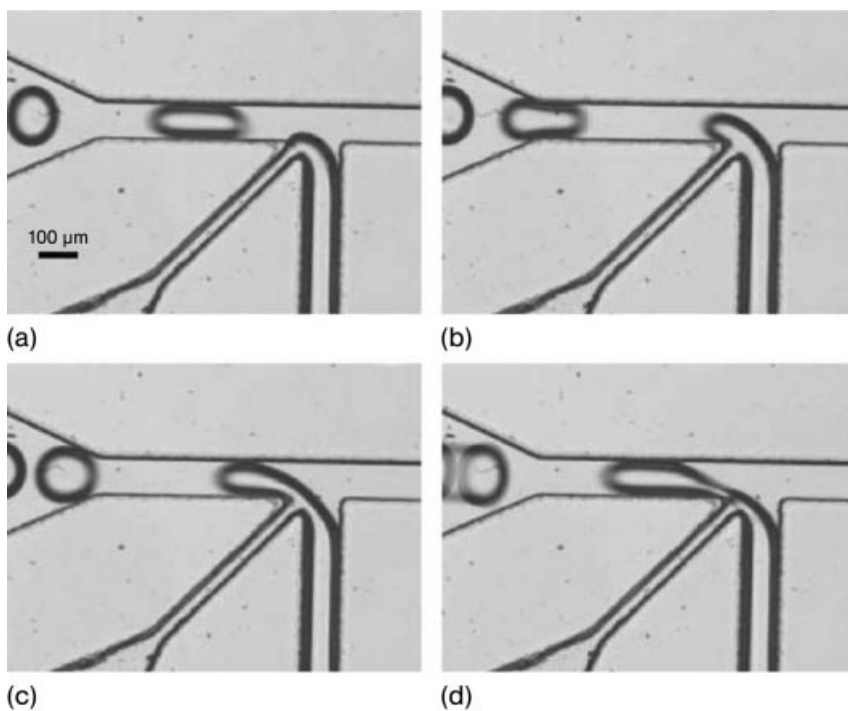


Figure 22.18 Optical microscope images of a drop formation event in the modified T-junction microdevice used for alginate gelation. Flow rates: aqueous phase 0.16 and sunflower oil 0.24 mL h^{-1} . The sunflower oil flows from right to left in the pictures [28].

to permit long-term operation. The flow rate ranges investigated were about $0.1\text{--}1.0 \text{ mL h}^{-1}$ for the oil phase and $0.10\text{--}0.32 \text{ mL h}^{-1}$ for the aqueous phase.

22.12

Production of Base Chemicals Exemplified by SO_3 and Detergent Production

Currently, the major application areas of chemical microprocess engineering are fine and special chemistry. The focus is on the improved production of chemicals. Improvements could be, e.g., a better controllable process, process intensification, safer operation and better product quality. Naturally, the consumer goods industry also depends on chemicals and corresponding production processes. Hence topics discussed in the context of the application of chemical microprocess engineering in the areas of fine and special chemistry should also be of interest for the consumer goods industry. Instead of reviewing all the topics covered in the corresponding chapters, in the framework of this chapter just one production process that shows links to the consumer goods industry will be taken and described in more detail. The

selected process is the production of detergents, or more precisely the production of alkylsulfonates, a high tonnage product. The selection is based on the fact that in the literature sulfonation of toluene by SO_3 and the production of SO_3 itself in microstructured reactors are described. The motivation for these investigations may be not the production of surfactants – at least it is not explicitly stated – but that they represent a starting point for corresponding thinking is obvious.

22.12.1

Introduction

In detergent formulations, surfactants constitute the most important component [29]. Depending on what charge is present in the chain-carrying portion of the surfactant molecule after dissociation in water the surfactant can be grouped either in the class of anionic surfactants, non-ionic surfactants, cationic surfactants or amphoteric surfactants [29]. Alkylsulfonates represent an important group of (anionic) surfactants [29]. Major classes are alkylbenzenesulfonates (LAS and TPS), secondary alkanesulfonates (SAS), α -olefinsulfonates (AOS), alkyl sulfates (AS) and alkyl ether sulfates (AESs) [29]. LAS represent the largest portion: in 1998 the worldwide consumption of LAS amounted to 3.0×10^6 t (all surfactants: 9.9×10^6 t) [29].

22.12.2

Sulfonation of Toluene with Gaseous Sulfur Trioxide in a Microreactor Setup

Müller *et al.* [30] used the sulfonation of toluene with gaseous SO_3 as a reaction to characterize and test a microreactor plant based on a standardized microfluidic platform for laboratory and small-throughput production purposes. The reaction paths during sulfonation of toluene with gaseous SO_3 are given in Figure 22.19. Sulfonic acid is the desired product, which is formed via the direct reaction of toluene and SO_3 [reaction (23.1)]. In a consecutive reaction, sulfone [reaction (23.2)] is formed, which cannot be converted further. Also, a mixed anhydride and sulfonic

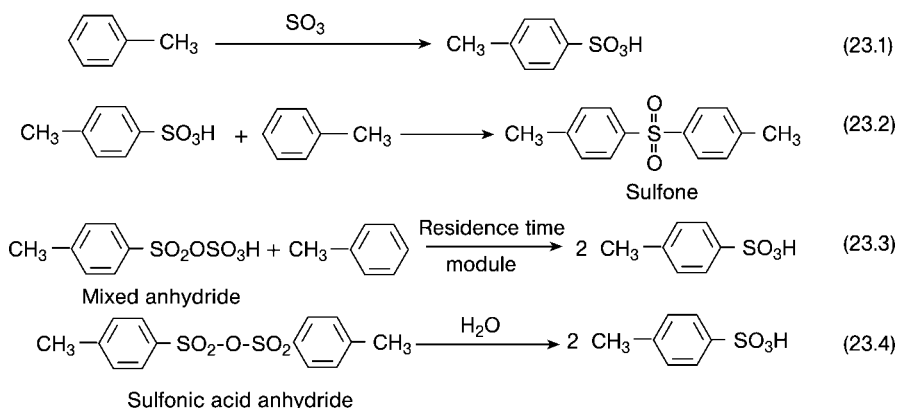


Figure 22.19 Reaction paths during sulfonation of toluene with gaseous SO_3 [30].

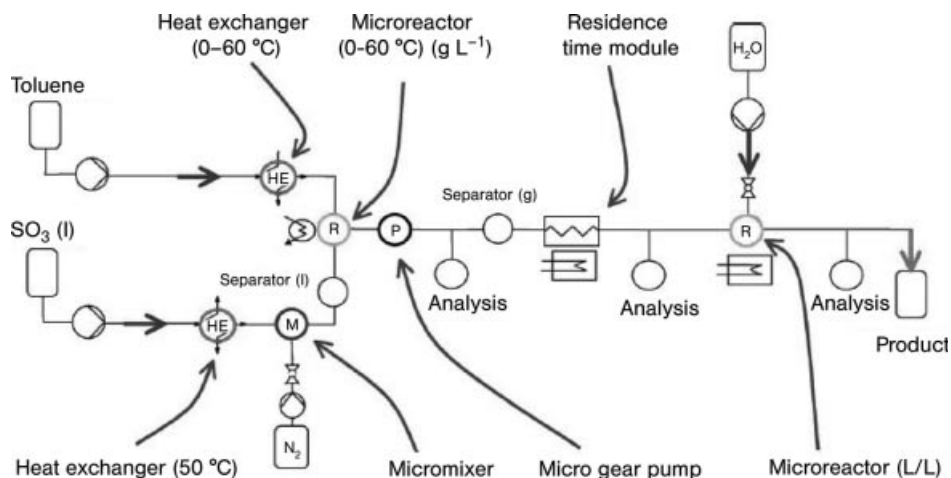


Figure 22.20 Flow sheet of the setup used for the sulfonation of toluene with gaseous SO₃ [30].

acid anhydride is formed. The mixed anhydride can be converted to the desired sulfonic acid by reaction with toluene [reaction (23.3)]. The sulfonic acid anhydride can also be converted to sulfonic acid by hydration [reaction (23.4)].

The flow sheet of the setup used for the highly exothermic reaction is shown in Figure 22.20. Figure 22.21 gives an overview of the microplant used. Toluene is heated to 40 °C by a microstructured heat exchanger. At the same time, liquid sulfur trioxide is heated to 60 °C in order to evaporate it. After diluting the sulfur trioxide with nitrogen, traces of liquid are removed in a separator. Then the toluene is contacted with the sulfur trioxide gas in a microstructured falling film microreactor. This reflects that the most important industrial use of conventional falling film reactors without rotating internals is the sulfonation of organic compounds with sulfur trioxide [31]. A residence time module follows in which the mixed anhydride formed can be converted to sulfonic acid. Finally, water is added to convert the sulfonic acid anhydride to sulfonic acid. Experiments including the hydration steps have been performed. Müller *et al.* [30] judged the results as promising. Exemplary results are given in Figure 22.22.

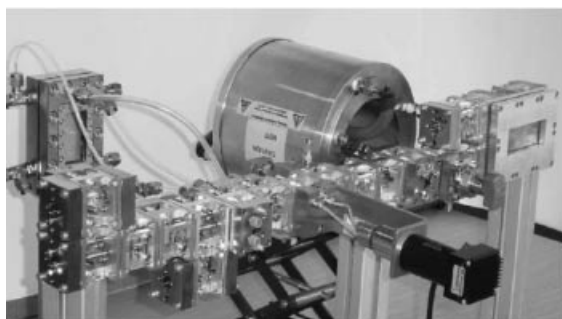


Figure 22.21 Microplant used by Müller *et al.* [30] for the sulfonation of toluene with gaseous SO₃.

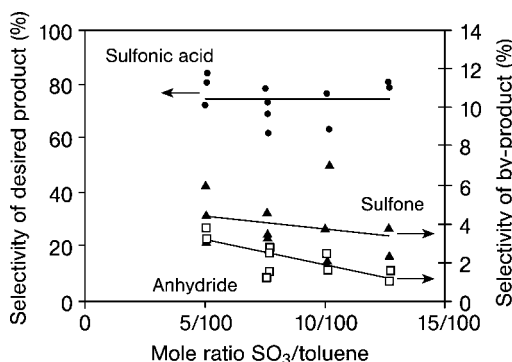


Figure 22.22 Exemplary results of the sulfonation of toluene with gaseous SO₃ in a microplant by Müller *et al.* [30]. The results refer to analysis after the residence section and before the hydration step.

22.12.3

One-pass Synthesis of Pure Sulfur Trioxide in Microreactors

Industrially, SO₃ is produced in dilute gaseous form by the heterogeneously catalyzed oxidation of SO₂ on vanadium species with air. Maximum conversion is linked to the temperature-dependent equilibrium between SO₂ and SO₃, which is shifted towards SO₂ with increase in temperature. The reaction is strongly exothermic. Due to the adiabatic temperature rise obtainable, conversion for a single reactor pass is considerably lower than expected from equilibrium calculation based on the reactor inlet temperature. To circumvent this problem, industrially four or five stages of catalyst bed with inter-stage cooling by heat exchangers or by direct air quenching are used. The SO₂ inlet concentration is thereby limited to about 10 vol.% with a maximum temperature of 600 °C in the first stage.

Driven by the high heat transfer potential of microreactors, investigations of Pfeifer *et al.* [32] on the laboratory scale were aimed at providing the basic principle of a microchannel reactor to produce SO₃ in a one-pass process without stepwise cooling or quenching and at performing conversion with pure oxygen. Higher SO₃ concentrations will favor a reduction in reactor size and simplify exhaust gas treatment. The authors judged the application of microreactors for this process as promising, especially when pure SO₃ as product is aimed at, e.g. for following sulfonation or sulfation reactions. The authors mentioned in this context the production on demand of SO₃ in the range 1–10 kg h⁻¹. A corresponding process design including the SO₂ formation process was outlined by the authors (Figure 22.23). Compared with conventional processes, exhaust gas treatment with SO₃ absorption in sulfuric acid is simplified by oxygen recycling instead, where higher sulfur residues are tolerable. The increase in oxygen concentration lead to higher reaction rates of SO₂ oxidation, but is also practical for a preceding SO₂ generation by sulfur burning. Based on the results achieved so far, the channel volume required for a 1 kg h⁻¹ SO₃ reactor is estimated to be 0.22 L.

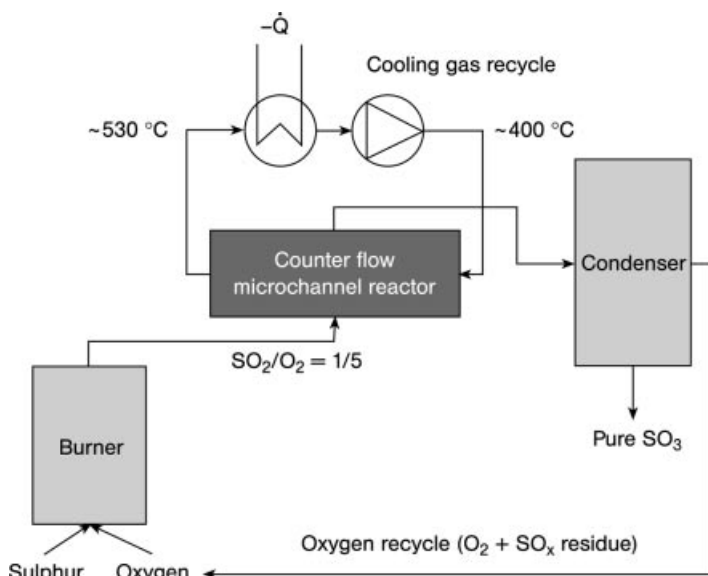


Figure 22.23 Schematic presentation of a potential microreactor-based process for SO₃ production including a sulfur burning step for SO₂ formation and gas exhaust treatment as outlined by Pfeifer *et al.* [32].

The experiments dealing with the one-pass synthesis of SO₃ were performed using a catalyst-containing microchannel reactor made of titanium heated by five heat cartridges with a total maximum power input of 1250 W. Heating is necessary because of the heat loss to the environment when operating the laboratory-scale reactor with its low flow rates. Under the operating conditions, the reaction heat is in the range of a few watts compared with 150–250 W from the heating cartridges required during steady-state operation. To avoid heat conduction along the channel axis via the housing, the housing bears slotted holes where possible. The reactor contained seven reactor plates with the catalyst whereby two concepts of plates were investigated. In one case the plates bear microchannels (200 μm × 200 μm × 8 mm) with a wall coating of titanium dioxide-supported platinum catalyst (in total about 250 mg of TiO₂ and 50 mg of Pt). In the other case, the plate bears a larger reaction space with a hexagonal arrangement of cylindrical pillars with a diameter and height of 800 μm allowing the space to be filled with catalyst in analogy to a fixed bed. A commercial vanadium catalyst was crushed and milled and a particle size fraction of 200–300 μm was sieved for use in the reactor. The total reaction volume here is 11.5 cm³ compared with 2.4 cm³ in the first case. Figure 22.24 shows the microchannel reactor with its two possibilities for catalyst incorporation.

The best results so far (about 98% conversion) were obtained using the platinum catalyst with 30 mL min⁻¹ SO₂ and 390 mL min⁻¹ O₂ plus 300 mL min⁻¹ nitrogen (nitrogen was used here for experimental reasons) with heat cartridge settings

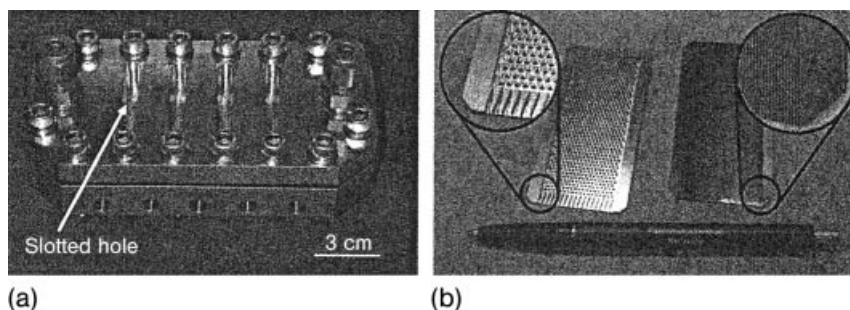


Figure 22.24 (a) Assembled microreactor. (b) Micropillar and microchannel foil (outer dimensions 4×8 cm) [32].

between 500 and 530 °C. It is assumed that operation of the reactor with a pronounced falling temperature profile conversion near to 100% with an $O_2:SO_2$ ratio of 3–5 should be feasible. This would form the basis for the process outlined above (see Figure 22.23).

22.13

Homogenization of Dairy Products

In the following, an example dealing with the application of microstructured reactors in the food area is given.

Köhler *et al.* [33] investigated a microstructured system for homogenization of dairy products with high fat content. High-pressure homogenizers are widely used for technical emulsification processes also in the food industry, where milk, dairy products, fruit juices and concentrates are application examples [33]. Homogenization reduces the drop size and thereby improves product characteristics such as creaminess, texture and shelf-life stability by retarded creaming or sedimentation [33]. In the case of pasteurized milk, the mean diameter of the fat droplets has to be well below $1 \mu\text{m}$ to ensure sufficient shelf-life stability [33]. Processing consists conventionally of one or two stages with pressure drops between 100 and 200 bar while the temperature is in the range 50–70 °C. Milk fat droplets are disrupted by shear and inertia forces when flowing through homogenization valves of the flat valve type [33]. Generally, raw milk is separated prior to homogenization into a low-fat (0.03–0.3 vol.% fat, “skim milk”) and a fat-enriched phase (30–42 vol.%, “cream”). So far it is not possible with conventional processes to homogenize dairy products with a high fat content (>17 vol.%) in one step due to an increase in coalescence and agglomeration linked with the higher concentration [33]. Therefore, prior to homogenization the cream has to be diluted again with skim milk. The aimed for fat content in the final product is then adjusted by mixing this homogenized high-fat milk again with further skim milk [33].

The basic idea of Köhler *et al.* [33] to resolve the problem of homogenizing high-fat dairy products is to inject skim milk directly into the disruption zone. On the one

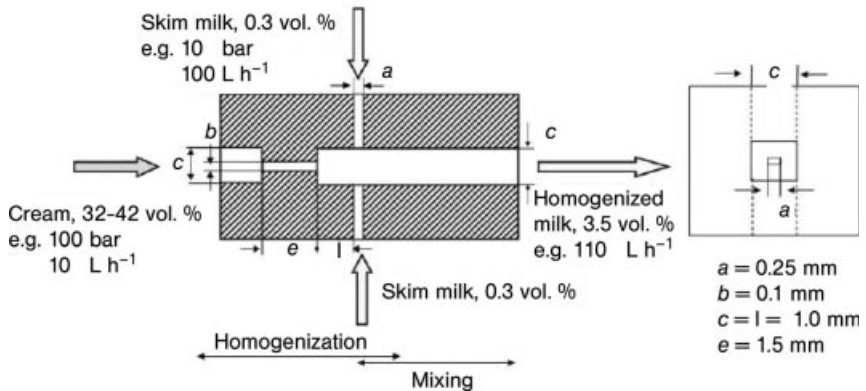


Figure 22.25 Design of the microstructured reactor used by Köhler *et al.* [33] for the homogenization of milk with high fat content [33].

hand, the skim milk contains fat droplet-stabilizing molecules, thereby suppressing coalescence, and on the other hand, the dilution with skim milk reduces droplet collisions and thereby agglomeration. The corresponding microstructured device (Figure 22.25) therefore consists of a combination of a homogenization valve directly followed by a T-shaped micromixer for the injection of the skim milk.

The device has been investigated experimentally, whereby pressure drops up to 300 bar over the valve occurred. The flow rate of cream was up to 14 L h^{-1} and that of the skim milk up to 112 L h^{-1} . The investigations demonstrated that it is feasible also to homogenize cream with up to at least 32 vol.% fat without a decrease in product quality compared with conventional processing.

This approach to homogenization allows product volume to be homogenized at high pressure and the number of processing units in dairy homogenization processes to be reduced [33]. The simplification of the processing is illustrated in Figure 22.26. Only 60% of the energy input used in conventional homogenization is required [33]. This results in considerable energy and cost savings. In addition, two mixing units can be eliminated from the process line, resulting in lower investment, cleaning and maintenance costs [33].

22.14

Outline of Additional and Potential Aspects of Microreactor Applications in the Consumer Goods Industry

In the following, additional and potential aspects of microreactor applications in the consumer goods industry are outlined. The topics are more explorative and should be thought more as a means to stimulate a broader thinking with regard to future microreactor applications in the consumer goods industry. No linkage to consumer goods and the consumer goods industry is given explicitly in the cited examples. Topics discussed in the following are the use of microreactors for analytical tasks, the

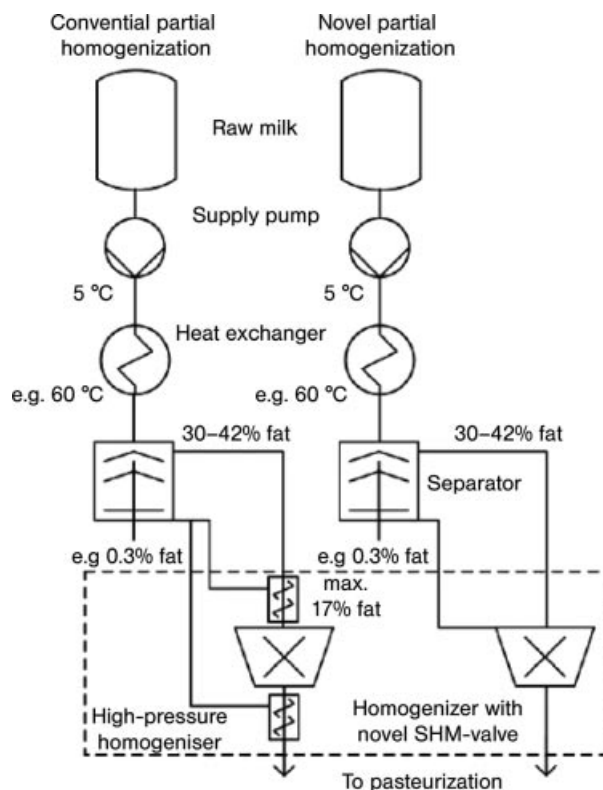


Figure 22.26 Flow chart of conventional (left-hand side) and novel (right-hand side) homogenization processes [33].

accessibility of new materials and the accessibility of high directed control of process conditions. Not mentioned in the following but maybe also worth considering from the perspective of the consumer goods industry are activities in the field of energy (for an overview of microstructured fuel processors for energy generation, see e.g. [23]).

22.14.1

Microfluidic Devices in Chemical Sensing of Flavors and Fragrances

Microfluidic systems are well established in the area of biochemical analysis. A similar exploitation of this aspect of microreactor technology against the background of consumer good applications is a possibility. It is outwith the scope of this chapter to review all the activities in the area of biochemical analysis (lab-on-a-chip; see [34] for the latest developments) with regard to potential applications in the consumer goods industry. In the following, only an example is given dealing with efforts in the area of chemical sensing of flavors and fragrances based on microfluidic devices.

Odor-sensing systems are required in many fields such as foods, beverages, cosmetics and environmental testing [35]. One approach is to use a simple colorimetric method for odor discrimination [35]. Nakamoto *et al.* [35] described a method in which a dye-coated plate is illuminated with various LEDs of different colors followed by detection of the reflected light. The color of the plate changes when the dye coating is exposed to odors. Pattern recognition of multi-LED sensor outputs makes it possible to discriminate among odors.

Dornbusch *et al.* [36] reported on efforts to miniaturize such systems. They are targeting small measuring volumes in the region of 25 μL and a volume of only 5 cm^3 for the analysis system, allowing the implementation at almost all desired positions in a production process or in quality control. The current investigations are focused on the detection and discrimination of molecules such as triethylamine, alcohols, acetic acid and acetaldehyde in a gas stream. A complete analysis setup is outlined in a related paper by the same group [37]. Although the report focused on the development of a required micromixer, it is also mentioned that micropumps and microvalves belong to the required key components of a complete microfluidic system. Figure 22.27 shows schematically the complete targeted measuring system.

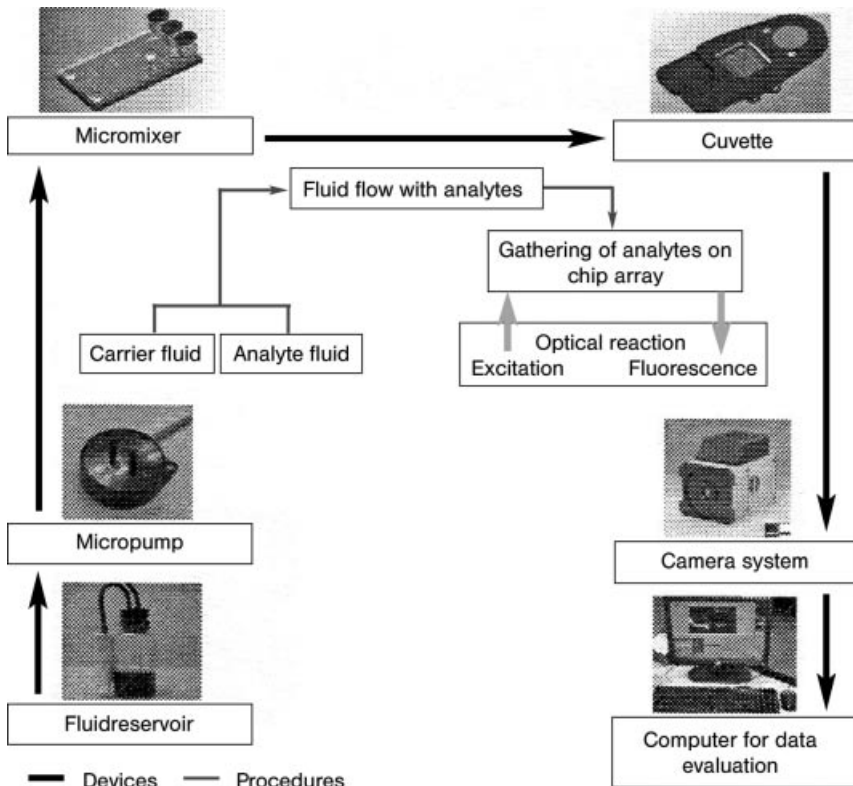


Figure 22.27 Scheme of a microfluidic system for chemical sensing of flavors and fragrances [37].

22.14.2

Accessibility of New Materials Exemplified by the Controlled Synthesis of Polymer Particles

Microreactor technology allows access to new materials. An example of this is illustrated in the following on the controlled synthesis of polymer beads. Polymer beads cover a wide range of applications from paint formulations to drug delivery, so there is relevance also in the context of consumer goods. Bouquey *et al.* [38] reported on the microfluidic-based synthesis and assembly of reactive polymer beads, finally forming new structured polymer materials, in this case polymer bead necklaces. Figure 22.28 illustrates the formation process. By contacting a polymerizable solution (containing monomer and a curing agent) at a microstructured junction with the continuous aqueous phase, polymerizable microdroplets are formed. In a following microstructured junction another sort of polymerizable microdroplets can be formed and added to the drop flow. By suitable operation of the feed pumps, an alternating flow of these two kinds of microdroplets can be achieved. A photoinitiator is present. By application of UV light downstream, free radical copolymerization is induced. By mixing different functional co-monomers to the two monomer phases, it is possible to obtain two different kinds of microparticles bearing on their surface antagonistic chemical groups capable of forming a covalent bond by condensation reactions. Through suitable design of the microfluidic network, it is possible to bring neighboring droplets in contact. Finally, the chemical reaction between the antagonistic chemical groups is thermally initiated, resulting in a covalent bond between the microparticles and the formation of a polymer necklace.

In principle it is possible to control the size of the droplet by the applied flow rates: Also, alternative arrangements of initial microdroplets can be realized (Figure 22.29).

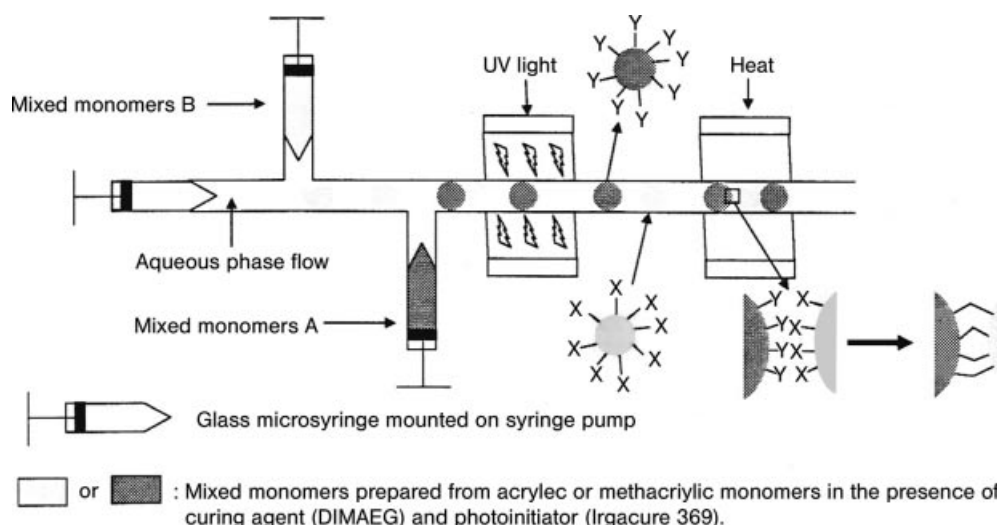


Figure 22.28 Scheme of the synthesis of polymer bead necklaces in a microfluidic device [38].

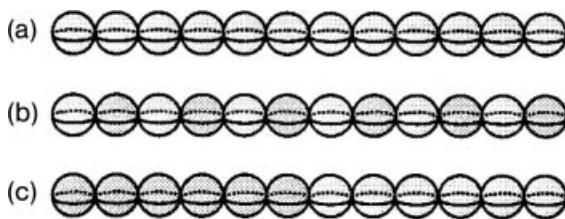


Figure 22.29 Different types of accessible polymer beads necklaces: (a) plain, (b) alternated and (c) block polymer bead necklaces [38].

Furthermore, by varying the amount of cross-linking agent and the nature of the co-monomers, it is possible to adjust some of the physical properties of each bead such as rheological characteristics.

This work demonstrates that the use of microfluidic devices allows the synthesis of totally new polymer materials such as polymer bead necklaces, with a large range of morphologies and properties.

22.14.3

Controlled Formation of Monodisperse Double Emulsions in a Microfluidic System

In double emulsions, droplets of the dispersed phase themselves contain dispersed droplets. Double emulsions can thereby be used again as a kind of encapsulation method for chemical substances for diverse later applications. Conventional processes struggle with broad size distributions, poor controllability and reproducibility of the droplet size and low entrapment yields [39].

Nisisako *et al.* [39] reported a microfluidic approach which permits the formation of monodisperse double emulsions. The principle design and working principle is shown in Figure 22.30. Both water–oil–water and oil–water–oil emulsions are accessible. Both the internal and external drop size and also the number of entrapped drops in the internal phase can be controlled by the flow conditions. So far, external droplet sizes in the range 40–200 μm have been obtained. Maximum throughput per unit is currently about 1 g h^{-1} . The major challenge to an increase in throughput by parallelization of a multitude of units is seen in the flow distribution. Nisisako *et al.* [39] pointed out that the microfluidic-based production of double emulsions with well-defined and controlled sizes and entrapment yields could greatly increase the application range of double emulsions. Also, they could act as ideal model systems to give a better understanding of release properties and stability conditions. Furthermore, the microfluidic system allows the formation of double emulsions of differing composition by variations in flow rates, which might be a basis also for screening tasks.

Similarly to the example above of the controlled synthesis of polymer particles, this example illustrates again the accessibility of new materials and also an unprecedented control of the formation process.

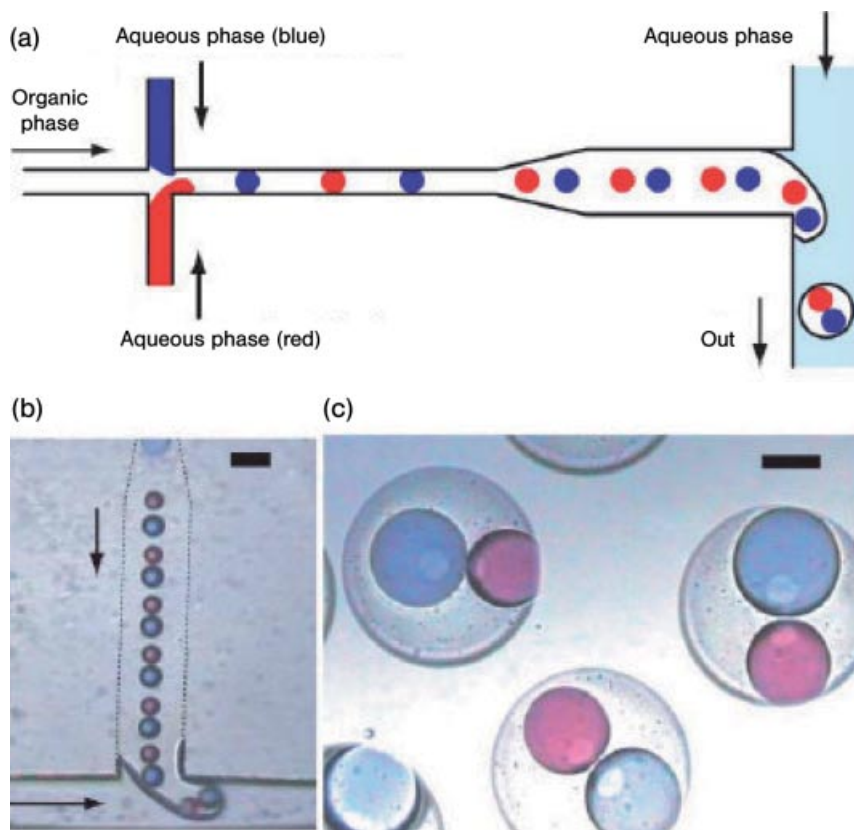


Figure 22.30 (a) Schematic design and functional principle of the microfluidic device used by Nisisako *et al.* [39] to form double emulsions exemplified for oil droplets containing blue and red colored water droplets inside dispersed in water. (b) Photograph showing the dispersion of the oil phase with the water droplets inside the external aqueous phase. (c) Photograph of the formed double emulsion. The scale bars are $100\ \mu\text{m}$ (b) and $50\ \mu\text{m}$ (c) [39].

22.15

Summary and Outlook

As mentioned in the Introduction, the topic of microreactor applications in the consumer goods industry has so far no sharp contour. The above examples cover a fairly broad range of application fields and are most often only loosely connected. Therefore, in the following an attempt is made to structure the topic somewhat. Owing to the state of the topic, this structuring is naturally preliminary and incomplete but may function as a starting point.

The examples given cover the following main application areas: pharmaceuticals, food products, adhesives, personal care products, cosmetics and detergents

Table 22.1 Microreactor application areas in the consumer goods industry.

Area	Application
Pharmaceuticals	Micromixers and microreactors for improved emulsification processes [2, 3, 9, 14, 15] Product improvement – reduction of emulsifiers and preservatives in emulsions [16, 18] Customer-based production of emulsions [19, 20] Customer-based production of formulations (besides emulsions) based on a package system with an incorporated static micromixer [19] Vesicle formation in microfluidic structures [21] Microencapsulation in microreactors [25–28]
Food products	Micromixers and microreactors for improved emulsification processes [2, 3, 9, 14, 15, 33] (homogenization of dairy products) Product improvement – reduction of emulsifiers and preservatives in emulsions [16, 18] Customer-based production of emulsions [19, 20] Customer-based production of formulations (besides emulsions) based on a package system with an incorporated static micromixer [19] Microencapsulation in microreactors (e.g. flavors, enzymes) [25–28] Analytical devices – odor sensing. [35, 36]
Adhesives	Micromixers and microreactors for improved emulsification processes [2, 3, 9, 14, 15] Mixing of high-viscosity liquids [10, 11] Customer-based production of formulations (besides emulsions) based on a package system with an incorporated static micromixer [19]
Personal care products	Micromixers and microreactors for improved emulsification processes [2, 3, 9, 14, 15] Mixing of high-viscosity liquids [10, 11] Product improvement – reduction of emulsifiers and preservatives in emulsions [16, 18] Customer-based production of emulsions [19, 20] Microencapsulation in microreactors (e.g. enzymes, fragrances) [25–28]
Cosmetics	Micromixers and microreactors for improved emulsification processes [2, 3, 9, 14, 15] Mixing of high-viscosity liquids [10, 11] Product improvement – reduction of emulsifiers and preservatives in emulsions [16–18] Customer-based production of emulsions [19, 20] Customer-based production of formulations (besides emulsions) based on a package system with an incorporated static micromixer [19] Microencapsulation in microreactors (e.g. fragrances) [25–28] Screening of cream formulations [17] Analytical devices – odor sensing [35, 36]
Detergents	Micromixers and microreactors for improved emulsification processes [2, 3, 9, 14, 15] Vesicle formation in microfluidic structures [3, 21] (dispersion of surfactants)

Table 22.1 (Continued)

Area	Application
	Process investigations with microreactor setup [3] (dispersion of surfactants)
	Microencapsulation in microreactors (e.g. fragrances, enzymes) [25–28]
	Production of base chemicals – SO ₃ and detergents [30, 32]
Others	Microencapsulation in microreactors (e.g. inks) [25–28]

(Table 22.1). When surveying the major motivations for applying microreactors in these areas, the following main topics are addressed: emulsification, high-viscosity liquids, customer-based production, vesicular dispersions, screening, encapsulation, improved production of base chemicals, new processing methods, analytical tasks, tailored products and numbering-up instead of scale-up for reaching the required production throughput (Table 22.2).

Table 22.2 Microreactor application topics in the consumer goods industry.

Base theme	Topics
Emulsification	<p><i>Micromixer applications:</i></p> <p>Attaining narrow size distribution [4]</p> <p>Predictability of drop size [5]</p> <p>Better process understanding [3]</p> <p>Higher energy efficiency [6, 7]</p> <p>Handling of shear-sensitive ingredients [2]</p> <p>Enabling new processes (homogenization of dairy products with high fat content [33])</p> <p><i>Microreactor applications:</i></p> <p>Better adjusted process conditions and formulation compositions [2], e.g. aiming at reduction of the amount of emulsifiers and preservatives by micromixer application [16, 18]</p> <p>Better controlled process conditions, more reliable process [3]</p> <p>Customer-based production [3]</p> <p>Higher flexibility [3]</p> <p>Numbering-up instead of scale-up [4]</p> <p>Low capital costs [2]</p> <p>Easy maintenance [2]</p> <p>Cost-effective transport to new markets because of compact and possible modular design of microreactors [2]</p> <p>Small equipment size, small liquid inventory, i.e. less off-specification product during equipment charging, starting and taking down, lower solvent requirement during cleaning [2]</p>
High-viscosity liquids	<p>Dispersion of high-viscosity liquids [9]</p> <p>Mixing of high-viscosity liquids [10, 11]</p>

(Continued)

Table 22.2 (Continued)

Base theme	Topics
Customer-based production	<p>Of emulsions [19, 20]</p> <p>Of gas–liquid and solid–liquid -dispersions [19]</p> <p>Of mixtures [19]</p> <p><i>In the field of cosmetics, e.g.:</i></p> <p><i>In situ</i> production of shampoos, deep conditioners, hair or skin milk [19]</p> <p><i>In situ</i> production of hair colors [19]</p> <p>Mixing of reactive solutions with thickeners [19]</p> <p><i>In the field of pharmaceuticals, e.g.:</i></p> <p>Mixing of water-sensitive formulations [19]</p> <p>Ointments, emulsions, milks, etc., at the moment of application with avoidance or reduction of normally needed stabilizers [19, 20]</p> <p><i>In the field of adhesive technology, pharmaceuticals, e.g.:</i></p> <p><i>In situ</i> formation of multicomponent formulations [19]</p> <p><i>In the field of foods, e.g.:</i></p> <p>Formation of mayonnaise, mustards, etc. [19]</p> <p>Homogenization of milk, milk products, etc. [19]</p> <p>Formation of cream without mechanical whipping [19]</p>
Vesicular dispersions	<p>Control over vesicle size distribution [2, 3]</p> <p>Targeted encapsulation of active ingredients [2]</p> <p><i>In the case of liquid detergent production by surfactant dispersion:</i> [3]</p> <p>Attaining narrow size distribution</p> <p>Better controlled process conditions, more reliable process</p> <p>Higher flexibility</p> <p>Microreactor setup as tool for process development</p> <p>Numbering-up instead of scale-up</p>
Screening	<p>Screening of cream formulations [17, 24]</p> <p>Microreactor setup as tool for process development (in the case of liquid detergent production [3])</p>
Encapsulation	<p>Better control over size and properties of microcapsules (encapsulation by interfacial polymerization [26, 27])</p> <p>Encapsulation of bioactive or cellular material for biotechnical or biomedical applications in spheres formed by alginate gelation [28]</p> <p>Continuous processing [3, 21, 26–28]</p> <p>Also vesicular dispersion can transfer active ingredients [3, 21]</p> <p>Also double emulsions can be used for encapsulation [39]</p>
Improved production of base chemicals	<p>Microreactor-based production of alkylsulfonates [30]</p> <p>Microreactor-based production of SO₃ [32]</p>
New processing methods	<p>Enabling new processes (homogenization of dairy products with high fat content [33])</p> <p>Continuous processing (e.g. encapsulation processes [3, 21, 26–28])</p> <p>Controlled formation of polymer particles [38] and double emulsions [39]</p>
Analytical tasks	<p>Microfluidic devices in chemical sensing for flavors and fragrances [36, 37]</p>
Tailored products	<p>Controlled synthesis of polymer particles [38]</p>

Table 22.2 (Continued)

Base theme	Topics
	Defined microcapsules [26, 27] and microspheres [28]
	Defined dispersions [2–5, 16, 18–20]
	Monodisperse double emulsions [39]
Others	Numbering-up instead of scale-up [3, 4]

There are similarities with the topics addressed in the current major application areas of chemical microprocessing, fine and speciality chemistry, continuous processing, new processing approaches (novel process windows), screening, process improvement (process intensification) and numbering-up for reaching the required production throughput. However, some issues are in stronger focus, such as emulsification, customer-based production and tailored products. It is clearly shown that chemical microprocessing is taken up from the consumer goods industry and that this helps in rethinking existing processes and products. The future will show in which direction this will be further developed and which aspects will be the most important for the consumer goods industry, which may differ from today's views.

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