DOI: http://dx.medra.org/10.17374/CI.2018.100.4.34

ANDREA HENSELER, JOACHIM HECK
EHRFELD MIKROTECHNIK GMBH
WENDELSHEIM (GERMANY)
ANDREA.HENSELER@EHRFELD.COM

SCALABLE FLOW REACTORS FOR INDUSTRY

One of the current challenges for the chemical industry is a continuously changing demand on product portfolios from commodities to customized products. To meet this challenge, flexible production facilities and a short time to market are important prerequisites especially for fine chemical and pharmaceutical industries.

A technology platform which can contribute to meet these needs is flow chemistry also known as microreation technology (MRT). Discontinuous batch methods are replaced by continuous processes within small channel structures in micro- or millireactors. Due to excellent heat transfer and rapid mixing, reaction conditions are uniform and can be precisely controlled, which can lead to considerably higher yields and improved product quality. Moreover, it has also been demonstrated that flow reactors are able to handle processes where batch reactors fail or only give poor results **[1]**.

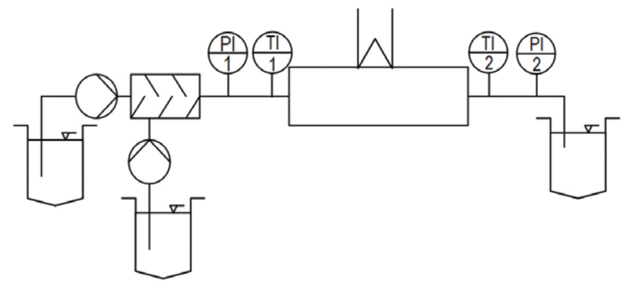

Fig. 1 - Typical setup for a continuous flow process

Operating Principle and Benefits

The main applications of flow equipment are mixing and heat transfer along a defined channel length. To control and monitor these operations, pumps, sensors, valves and process automation systems are typically needed in addition to the reactors (Fig. 1).

The channels in continuous flow reactors are characterized by high surface-to-volume ratios and offer therefore an improved heat transfer compared to conventional batch reactors. Due to small dimensions, short diffusion distances allow for efficient mixing and high mass transfer rates.

In flow chemistry, residence time is a function of channel length and flow rate. By knowing the reactor dimensions and controlling the flow rates of the reactants, the residence time can be accurately defined, which is especially important when instable intermediates with a short life time are involved in the process. In this way, chemical reactions can be run under definite process conditions. Especially fast, highly exothermic reactions with explosive or toxic substances benefit from significantly smaller reactor volumes compared to conventional batch chemistry: only small quantities of hazardous reagents and intermediates are present at any given time. Moreover, the compact plants occupy less space and a high degree of automation reduces the need for manual intervention.

All these features taken together, enable us to run challenging processes with improved yields and selectivities under precisely defined operating conditions. The most important advantages of continuous manufacturing in micro- and millireactors are summarized as follows:

- ultrafast mixing
- highly efficient heat transfer
- short and defined residence times
- simple and precise process control due to low system inertia
- high operational reliability due to minimal hold-up

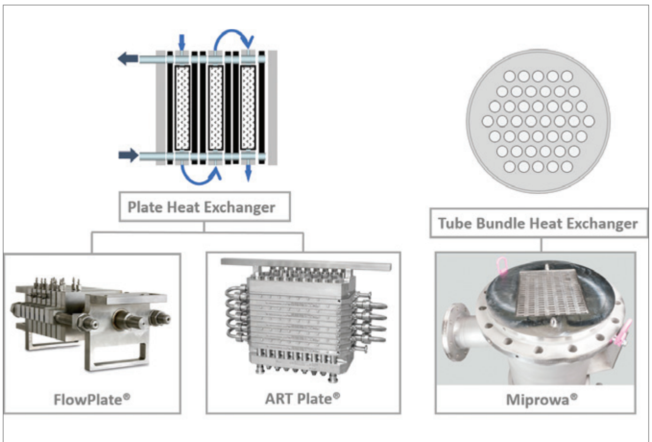

Fig. 2 - Ehrfeld reactors in analogy to established reactor concepts such as plate type and tube bundle heat exchangers

- short development times

Economic benefits:

- higher yields, selectivities and improved product qualities
- simplified downstream due to less by-product formation
- plant safety
- low energy consumption (less cooling/heating) and lower carbon foot print
- reduced production costs

Application Fields

Although flow chemistry is not yet an established process technology within specialty chemicals and pharmaceutical industries, visible references not only in research but also in production scale are getting more and more.

Core segments include explosively fast and highly exothermic reactions, which are particularly difficult to handle in batch reactors such as the synthesis of organic peroxides, ethoxylations and lithiation reactions where an efficient heat transfer is crucial and process safety plays an important role.

Multiphase-reactions (liquid/liquid and liquid/gas) require continuous active mixing and benefit from small channel dimensions combined with integrated mixing structures. This creates large specific contact areas and diffusion paths short enough to allow sufficiently fast mass transfer rates. Examples are ozonolysis, hydrogenation or oxidation reactions.

In recent years, also the pharmaceutical industry shows an increasing interest in continuous manufacturing [2]. Stable operating conditions with a high degree of control via online analytics are crucial for maintaining constant product quality. Furthermore, multiple process steps, which typically must be divided into several isolated batch operations, can be integrated into one automated continuous process [3]. The FDA is currently encouraging pharmaceutical manufacturers to shift to continuous manufacturing for its numerous advantages such as decreased fluctuations in production and short time-to-market.

From Lab to Production

To implement flow technology in a fast and economic way in production facilities, scalable reactor concepts are essential.

The portfolio of Ehrfeld Mikrotechnik comprises micro- and millireactors from lab to production scale. Millireactor concepts for production scale applications lean on established reactor concepts such as plate type heat exchangers [4, 5] and tube bundle heat exchangers [6] (Fig. 2).

The use of metallic materials such as stainless steel or Hastelloy® guarantees required solidity and robustness of reactors for industrial applications.

The word “millireactor” illustrates that small channel dimensions are applied in the reactor design for the purpose of process intensification but miniaturisation only takes place to an extend that does not compromise robust operation under industrial production conditions.

Miprowa®

Miprowa® reactors are constructed analogously to tube bundle heat exchangers. The concept is based on rectangular channels with planar static mixing inserts (comb layers, Fig. 3). The higher surface-to-volume ratio of the rectangular channels compared to a circular

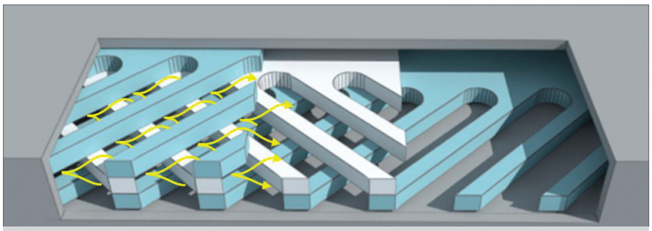
Fig. 3 - Rectangular channel with comb layers

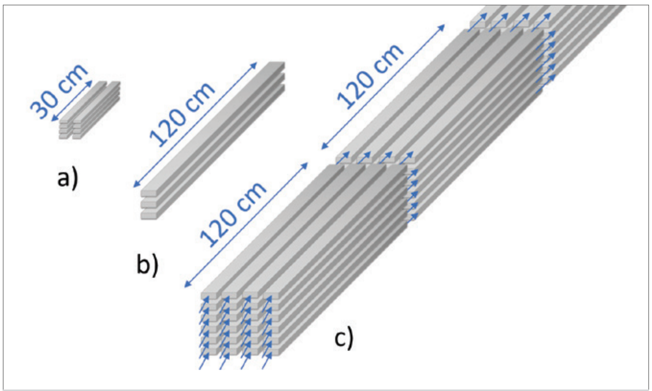

Fig. 4 - Scale-up concept: Channels in a) Miprowa® Lab reactor (channel cross section: 12x1.5 mm^2), b) Miprowa® Matrix Pilot reactor (channel cross section: 18x3.2), c) Production Scale (channel cross section 18x3.2)

tube, enables a significantly improved heat exchange between process- and heat transfer medium.
Static mixers are placed inside the channels to increase this effect and are responsible for efficient and fast mixing, which is crucial for multiphase reactions. For instance, in aqueous systems, heat transfer coefficients of about 2.200 W/m^2K can be achieved.
In addition, the mixing inserts cause a narrowing of the residence time distribution compared to an empty channel which is free of any lateral flow velocity components. Due to the high level of temperature control, higher selectivities and yields can be achieved especially for highly exothermic reactions.
For industrial applications, scalability is crucial. Ehrfeld Mikrotechnik has introduced an integrated scale-up concept for this reactor technology, which allows a seamless upscaling from smallest scale to production level. Once, a process has been developed and optimized in the Miprowa® Lab reactor (schematic Fig. 4a), long-term stability runs using technical raw materials are conducted in the Miprowa® Matrix reactor. This device includes channel geometries which are equal to the later production unit, providing identical process characteristics. Also start-stop strategies are tested (schematic Fig. 4b).
The throughput is increased to the desired production capacity by a parallel arrangement of multiple channels within one reactor segment. With this strategy, several hundred parallel Miprowa® channels can be fitted into one compact apparatus (Fig. 5). Since reaction time (residence time) in continuous production plants is a function of flow rate and channel length, the desired total reactor length can be adapted to the required reaction time by serially connecting the corresponding number of cores (schematic Fig. 4c).
In this manner, volume flows such as 1 m^3 per hour can result in production capacities of up to 10.000 t/a with only one continuous reactor (Fig. 6).
This means that a scale-up from lab to production can be done in just two scaling steps with no need for major process adaptation, which facilitates a short time to market.

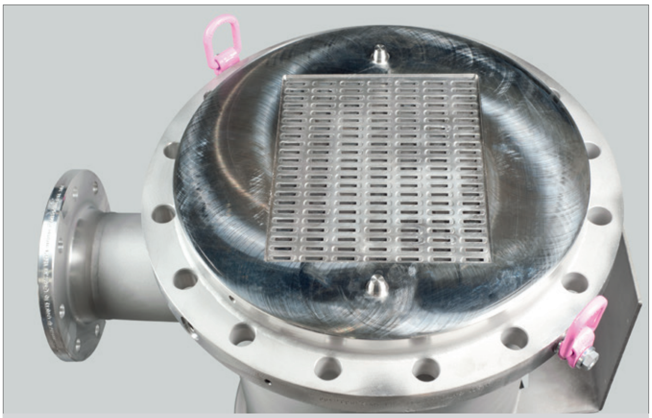

Fig. 5 - Equalling up of multiple rectangular channels within one reactor core

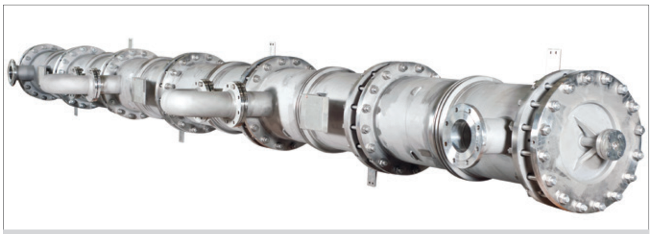

Fig. 6 - Miprowa® with 6 reactor cores for multi-ton production scale

Millireactor for Multi-Ton Production

Despite numerous advantages, there is still a modest number of usually not visible industrial references for continuous flow production reactors in specialty chemicals and pharmaceutical industries. Many potential users know the potential but lack the experience of this technology, especially compared to conventional batch processing. Therefore, potential risks are often overestimated and especially the European industry hesitates. At the same time, a number of companies are using flow reactors but are keeping it unpublished. Only recently, visible references started to appear.
In 2016, Ehrfeld Mikrotechnik designed, manufac-

tured and supplied a Miprowa® production reactor for the Chinese producer Shaoxing Eastlake High-Tech. The producer of agrochemical active ingredients was founded in 1990 near Shanghai and supplies both, the Chinese market and more than 20 countries worldwide. They have been seeking for new, promising technologies over the past decade to replace more than 20 batch reactors for a highly exothermic alkoxylation process. Driven by guidelines, environmental regulations and safety considerations, they purchased a Miprowa® millireactor, which contains about 150 rectangular channels and handles a throughput of 1 m^3/h. Based on results from corrosion tests, the reactor was made of Hastelloy® to ensure the required corrosion resistance.

The reactor was commissioned in China within two weeks, already meeting the production specifications (Fig. 7).

For control purposes, the reactor was opened after six months and the inspection showed no corrosion, clogging or contamination. This shows the high degree of selectivity of the process, accompanied by a full conversion. Since then the Miprowa® reactor is running smoothly until today with a production capacity of up to 10.000 t/a.

Fig. 7 - Top end of the 7.50 m long Miprowa® Reactor installed at Shaoxing Eastlake High-Tech in China with connectors for heat transfer medium

The continuously running reactor replaces more than 20 batch reactors and moreover yield and product quality could be significantly improved compared to the batch process.

In 2017, Shaoxing Eastlake High-Tech ordered two further identical reactors in order to further increase production capacity.

REFERENCES

[1] J.-i. Yoshida, H. Kim, A. Nagaki, *J. Flow Chem.*, 2017, **7**, 60.

[2] S. Fogal, R. Motterle, E. Rossi, *La Chimica e l'Industria*, 2015, **5**, 33.

[3] S.A. May, *J. Flow Chem.*, 2017, **7**, 137.

[4] P. Plouffe, M. Bittel, J. Sieber *et al.*, *Chem. Eng. Sci.*, 2016, **143**, 2016.

[5] F.G.J. Odille, A. Stenemyr, F. Pontén, *Org. Process Res. Dev.*, 2014, **18**, 1545.

[6] P. Biessey, M. Grünewald, *Chem. Eng. Technol.*, 2015, **38**, 602.

Reattori scalabili per produzioni industriali in continuo

I processi in reattori batch operanti in modalità discontinua possono essere effettuati in maniera alternativa, utilizzando reattori significativamente più piccoli operanti in modalità flusso. Pur non essendo un argomento nuovo, la chimica in flusso continuo è di estrema attualità perché questa tecnologia è ora implementata su capacità produttive elevate (multi-ton). Grazie alla robustezza e all'elevato rendimento, la nuova parola chiave per questa tecnologia è millireattore anziché microreattore. La sfida per la creazione della piattaforma tecnologica dei micro- e millireattori è la concorrenza con le tecnologie consolidate nell'industria di processo. Lo scopo di questo articolo è quello di approfondire la conoscenza della piattaforma tecnologica, e delle sue interessanti applicazioni, così come delle basi progettuali e della robustezza necessarie per le esigenze degli impianti produttivi. Un concetto di scale-up integrato sarà esposto come metodo facile, sicuro e veloce per passare dal laboratorio alla produzione. Lo scale-up si basa su apparecchiature consolidate in analogia con scambiatori di calore a fascio tubiero e scambiatori di calore a piastre. Per dimostrare questo concetto, presenteremo un'applicazione industriale di rilevante importanza e il percorso dal laboratorio alla produzione su ampia scala.