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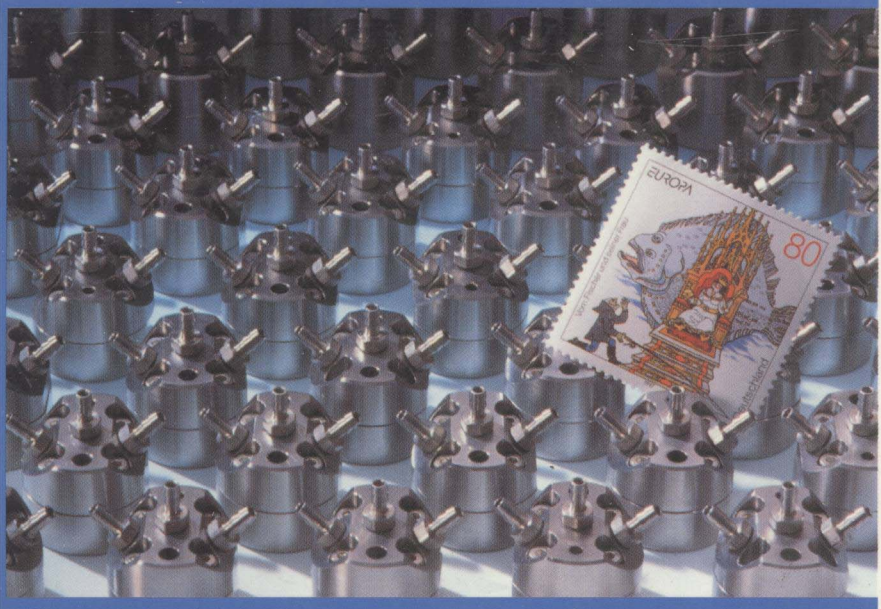
New Technology for Modern Chemistry



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W. Ehrfeld, V. Hessel, H. Löwe
Institut für Mikrotechnik Mainz GmbH
Carl-Zeiss-Straße 18–20
55129 Mainz
Germany

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Preface

Today's microreaction technology is no longer in its infancy. Whereas the first four years of development were characterized by basic feasibility work and the development of methods, sometimes even accompanied by skepticism and lack of understanding, the success of this emerging technology these days is beyond doubt. Small microfabricated reactors have proven to provide excellent mass and heat transfer properties as well as uniform flow patterns and residence time distributions. Some of these devices even are available commercially and being tested by a growing community of researchers. This, for instance, holds for interdigital micromixers, thus stimulating a rapid accumulation of know-how in the field of micromixing.

The numerous teams of researchers investigating microreaction technology belong to many disciplines, e.g. chemists, physicists, chemical engineers, material scientists, and mechanical engineers. Meanwhile, a vivid communication has started, the series of "International Conferences on Microreaction Technology" being the focus of this exchange of scientific results. It seems to be that something which was hidden for a long time is now bursting out, and has the potential to a complete change of today's chemical methodologies and, maybe even more notable, the corresponding habits of the researchers.

Industrial contributions played an important role throughout the recent years' developments. Innovative companies like DuPont and BASF promoted and supported these developments by own activities from the very beginning. The Merck company presented their first example of implementing a new industrial process, at least assisted by means of microreaction technology. Axiva seems to be interested to become a professional provider of modern process development utilizing microreactors. A number of companies followed these examples, e.g. Schering, Degussa-Hüls, and Bayer, just to name a few. But not only German companies are involved, Rhône-Poulenc/Rhodia in France, Shell in the Netherlands and the United Kingdom, as well as DuPont and UOP in the U.S.A. have become more and more active.

The technical and scientific development concerning micoreactors is tremendous. Knowledge concerning microfabrication, modeling, design concepts, and testing is provided and increasingly spread between different journals. Due to this growing number of publications and a so far missing common platform, e.g. a journal on microreaction technology, the authors strongly felt that it is high time to summarize and categorize the research work in recent years. In this context, this book presents the state of the art of this new discipline, but is also designated to reveal its full beauty and breathless excitement.

This book is written both for the newcomer and the expert as well as for researchers from industry and research institutions. It is neither intended to attract chemists or chemical engineers only nor being dedicated to "microtechnicians". Hence, the book, as microreaction technology itself, should be of interdisciplinary character in the true sense. It tries to join the different disciplines, to evidence the success of mutual interaction, and to high-light the benefits of such a strategy.

The book contents are subdivided into two major parts. The beginning of each chapter is aimed to present general aspects of a specific class of microdevices, while in separate sections details are discussed therein. Consequently, large parts of this book contain a multitude of single information compiled in a comprehensive volume. Nevertheless, concepts are introduced as well and the respective fields of applications are indicated. Presently, such a systematic analysis in most cases is limited since a number of activities regarding microreactors still remain in their starting phase. However, there is an ultimate need to expand this systematic analysis in a future version of this book.

A book, as all hard and genuine work, seldom is elaborated by a single person or a small group on their own, but rather in a framework of human co-operation. In this context, the authors would like to acknowlegde the aid of all members of the Microreaction Technology and Chemistry Departments at the Institut für Mikrotechnik Mainz. In particular, this refers to L. Agueda for organization, J. Schiewe and Th. Richter for discussion and proof-reading, and Ch. Hofmann for illustration. Additionally, all funders and believers in this technology are acknowlegded, in particular from chemical industries as well as the DECHEMA and DARPA organizations. The same holds for the VCH-Wiley publishers, early recognizing the importance of microreaction technology and providing the possibility for this comprehensive volume. Finally, the authors are deeply indebted to the scientific community active in microreaction technology. For instance, a number of researchers helped a lot by providing illustrations and proof-reading of sections.

IMRET 4 in Atlanta is just around the corner. The technology development certainly will speed up. Standardization and system assembly as well as commercialization of microreactors may become relevant key topics. Production issues based on microreactors – a topic only mentioned in a whisper two years ago – attracts increasing interest. These interesting topics certainly will contribute to the growing progress in microreaction technology.

We are really glad that we actively could take part in such a fascinating development.

W. Ehrfeld, V. Hessel, H. Löwe Mainz, March 2000

Contents

1 State of the Art of Microreaction Technology

The aim of this chapter is to define the field referred to as microreaction technology, to analyze principal advantages, to comment on these benefits, reviewing current achievements, to document the state of the art of industrial implementation, and finally to outline future developments.

1.1 Definition

1.1.1 Microsystems Termed Microreactor

In accordance with the term "microsystem", which is widely accepted, microreactors usually are defined as miniaturized reaction systems fabricated by using, at least partially, methods of microtechnology and precision engineering. The characteristic dimensions of the internal structures of microreactors like fluid channels typically range from the submicrometer to the sub-millimeter range. Some people also prefer the terms nanoreactors or milli-/minireactors for devices with characteristic dimensions at the lower or the upper boundary of this dimensional range. In this book, however, only the term "microreactor" will be used.

1.1.2 Structural Hierarchy of Microreactors

The construction of microdevices generally is performed in a hierarchic manner, i.e. comprising an assembly of units composed of subunits and so forth. This holds particularly for microreactors which are based on an architecture characterized by multiplying unit cells, the so-called concept of numbering-up [1, 2]. In the following it is aimed to commonly define different units which most often are assembled in microreactors.

Definitions with Regard to Structural Hierarchy
The smallest units of a miniaturized continuous flow system are *microstructures*, in the vast majority of cases referring to *channel* structures (see Figure 1-1). Usually parallel channels are combined to an array surrounded by inlet and outlet flow regions, sometimes referred to as headers. A typical single or multiple flow channel configuration of distinct geometric nature is named *element*. A typical example for a mixing element is an interdigital channel configuration. In some cases, elements can consist of chambers too, e.g. carrying additional microstructures such as pores.

A combination of an element, connecting fluid lines and supporting base material, is termed *unit*. For instance, a mixing platelet with an interdigital structure and feed lines is a micromixing unit. In order to increase throughput, units may form a *stack*, e.g. a stack of catalytic platelets in a chamber of a gas phase microreactor. Alternatively, identical devices

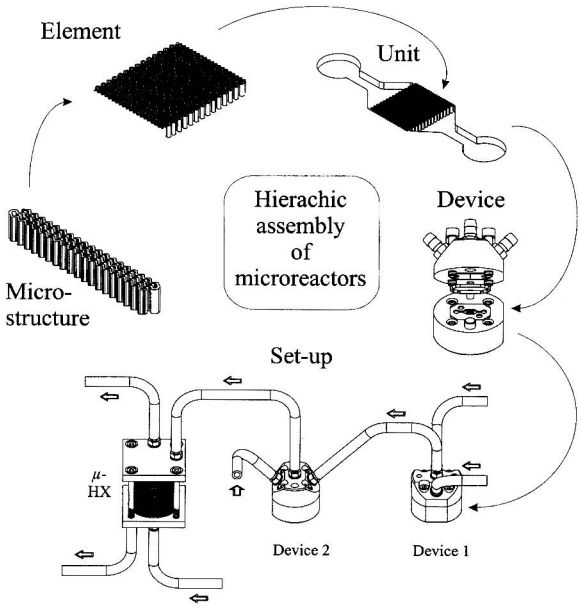

Fig. 1-1. Hierarchical assembly of microreactors, as evidenced for micromixer components.

can be arranged in parallel in a plane, e.g. a micromixer array consisting of thousands of unit cells.

Neither units nor stacks can be operated alone, hence, they are not real microreactors, since they need *housings* or, at least, *top and bottom plates* for fluid connection to external periphery. A *device* refers to a unit embedded either in a housing or between two end caps. The build-up of complex *systems* can be performed by integration of several units within one common housing. A system can also be based on a connection of devices, in this case referred to as *components*.

Any parallel or serial interconnection of components, systems or mixed combinations may be termed *set-up* or *plant*, dependent on the type of application, being lab- or industrial scale oriented, respectively. These set-ups or plants consist of either only microdevices or -systems, or, more likely, may contain microreactors next to conventional larger equipment.

Conceptual Division of Contents of This Book

The structural hierarchy – microstructure/channel, element, unit, device/component, system, set-up – is related to the conceptual division of the contents of this book. Chapters discuss components and systems with respect to different types of reactions and unit operations:

- Micromixers
- Micro heat exchangers
- Microseparators
- Gas phase reactors
- Liquid phase reactors
- Gas/liquid reactors

In the case of a combination of several operations, i.e. referring to a microsystem, the most characteristic function is chosen for classification. For instance, a system consisting of a mixer, heat exchanger and catalyst platelets, designated for carrying out gas phase reactions, will be discussed in the chapter "Gas Phase Reactors". The remaining components of this microsystem will not be described in separate chapters, e.g. in "Micromixers" or "Micro Heat Exchangers", except if they represent a unique flow configuration regarding their microelement. In this case, the presentation of the system is split into a chapter for the (unit) operation and a chapter for the system (reactor).

Very complex assembled microsystems including several types of reactors are discussed in separate chapters. These microreaction systems are referred to their respective type of application. Currently, two special fields of applications are of extremely high commercial interest, namely catalyst/material screening and energy generation. For these applications, two separate chapters were planned in this book. In addition, the assembly of several microsystems into a complete plant, e.g. for distributed production, is discussed in the Chapter 11 "The Miniplant Concept".

In the case of the description of components, sections refer to selected flow configurations, i.e. microelements, typical for a certain function. Since these elements are directly correlated to principles of function, e.g. a certain mixing concept, it was aimed to present a comprehensive overview of present approaches. Thereby, potential advantages of miniaturization are given practical application. Hence, a performance comparison of the various concepts, i.e. components or systems with specific elements, is crucial for a deep understanding of microreaction technology.

For instance, the chapter on micromixers is composed of sections, referring to the microelements termed with respect to the specific flow configuration. To illustrate this type of classification, the following examples of micromixing elements are given:

- Contacting of two substreams, e.g. in a mixing tee configuration
- Collision of two substreams of high energy and generation of a large contact surface due to spraying/atomizing
- Manifold splitting and recombination of a stream consisting of two fluid lamellae of two components

Subsections correspond to specific variants or adaptations of one concept, merely being examples which show the range of possibilities to realize a common idea. For instance, the section "Manifold Splitting and Recombination of a Stream Consisting of Two Fluid Lamellae of Both Components" is subdivided into the following subsections:

- Multiple Flow Splitting and Recombination Combined with Channel Reshaping
- Multiple Flow Splitting and Recombination Using Fork-like Elements
- Multiple Flow Splitting and Recombination Using a Separation Plate etc.

In the case of microreaction systems, this type of classification has not been followed, for reasons listed therein. For instance, in the chapter "Gas Phase Reactors" the microsystems were grouped according to the type of reactions carried out.

1.1.3 Functional Classification of Microreactors

Two classes of microreactors exist, referring to applications in analysis, especially in the field of biochemistry and biology, or chemical engineering and chemistry. Although these fields are distinctly different in most cases, as analytical and preparative equipment are, some microreactors cover both aspects. This holds particularly for combinatorial chemistry and screening microdevices which serve as analytical tools for information gathering as well as synthetic tools providing milligram quantities of products.

A further classification of microreactors is based on the operation mode, either being continuous flow or batch-type. The vast majority of microdevices presented in this book refer to continuous flow systems. Instead, batch systems such as micro and nano titer plates, e.g. for solid-supported chemical synthesis of drugs, will not be reported. In this field, the reader is referred to comprehensive overviews supplied by a number of excellent reviews and books [3–5].

The same holds for a large number of continuous flow microfluidic devices which were developed for analytical purposes starting in the late 1980s. If a series of processes such as filtration, mixing, separation and analysis is combined within one unit, the corresponding microsystems usually were termed micro total analysis systems (μTAS) [6–12]. Most often, these systems were applied for biochemical and chemical analysis. Modern developments consider e.g. polymerase chain reaction, electrophoretic separation, or proteome analysis, just to mention a few [13–15].

Concerning this field already comprehensively described [16], only component development will be presented in the framework of this book which turned out to be relevant for purposes of chemical microreactors. This is especially the case for analytical micromixers yielding a conceptual base for similar constructions for synthetic applications. Hence, in terms of consistency and novelty, the following chapters within this book will only refer to developments concerned with flow-through chemical microreactors, used for process development, production or screening.

1.1.4 Dividing Line Between Analysis and Reaction Systems

Reaction systems generally differ from analysis systems by producing or converting materials or substances. The latter devices are designed to gather information, e.g. to measure

the content of a certain analyte in a water sample taken from a lake. However, comparing extremely small individual systems, this difference apparently vanishes, because miniaturization of reaction devices ultimately will decrease the amount of converted materials to a level close to that of analytical devices. Therefore, the productivity of such small reaction devices, which is not sufficient anymore for synthesis purposes, can be used for process development or for screening only.

Both applications clearly refer to measuring tasks, the former regarding the finding of optimum process conditions, the latter of application-tailored materials. Actually, such measuring tools gather information similar to analytical devices. However, the purpose of using the information is distinctly different. In analytics, information gathering is an end in itself. For instance, the detection of ozone concentration in a certain layer of the atmosphere provides important information for ecological research. In contrast, information obtained in small reaction systems is used to optimize a lab synthesis or a large-scale process as well as to produce a new material with advanced properties, thus, finally is related to production issues. Hence, there is a clear dividing line between miniaturized analysis systems and microreactors for chemical applications.

1.2 Fundamental Advantages of Microreactors

Before analyzing the fundamental advantages of microreactors it is worthwhile to shortly review the benefits of miniaturized analysis systems, designed with similar characteristic dimensions as microreactors, and nano-scale reactors of much smaller size.

1.2.1 Fundamental Advantages of Miniaturized Analysis Systems

A large number of applications within the last decade clearly demonstrated fundamental advantages for miniaturized analysis systems compared to lab-scale equipment (see also Section 1.1.3). The smaller devices needed less space, materials, and energy and often had shorter response times [7]. In particular, more information per space and time is gained. By parallel microfabrication and automated assembly, the costs per device could be kept low. Decreasing the component size, in addition, allowed the integration of a multitude of small functional elements, thereby enhancing the system performance [7].

1.2.2 Fundamental Advantages of Nano-Scale Reactors

In the following, a nano-scale reactor is defined as any supramolecular assembly which acts as a reaction unit, i.e. being a host providing a small reaction volume, sometimes encasing only one molecule. To mention only a few, supramolecular assemblies such as molecular tweezers, zeolites, micelles, liposomes and Langmuir–Blodgett layers were, among other applications, utilized as small "reaction vessels". Most often, the molecular

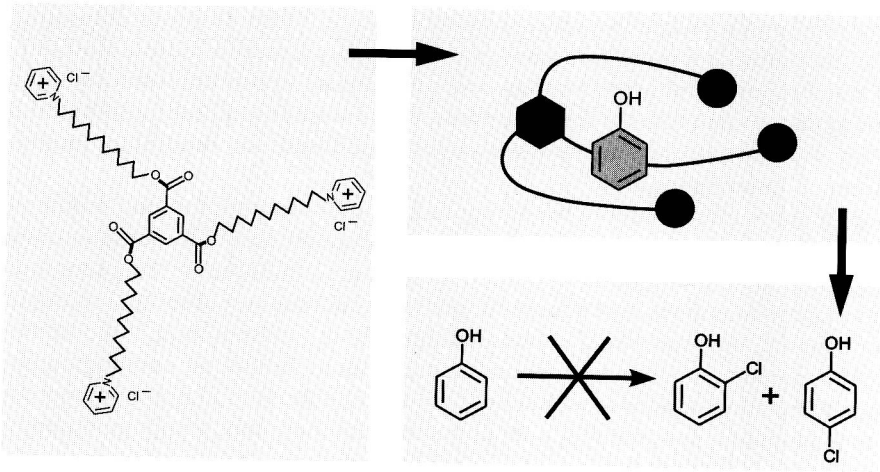

Fig. 1-2. Bola-type amphiphile forming a small nano-sized reaction vessel by means of self-organization. The chlorination of encapsulated phenol is thereby prohibited.

encapsulation strongly modified the reactivity of the reactants, e.g. by electronic interaction of π systems within a bola-type amphiphile [17], by adsorption and isolation in a zeolite cavity [18, 19], or by separation within micelles in order to prevent radical recombination [20].

Hence, small vessels, cavities and clefts provided in nanoreactors allow an interaction by means of molecular forces and modify the electronic structure of reactants. In addition, steric interactions are possible, e.g. influencing the conformation of a molecule or the free rotation of a group attached to a molecule. All these factors, known to modify the reactivity of "free" molecules as well, have a similar effect on "encapsulated" reactants. In this sense, nanoreactors behave like a solvent or a weak complexing agent.

To summarize, the most remarkable feature of nanoreactors is that they are actively changing chemistry, although the encasement certainly influences transport properties as well.

1.2.3 Advantages of Microreactors Due to Decrease of Physical Size

The volumes of microreactors are too large in order to interact with reactants significantly on a molecular level. Their main impact focuses on intensifying mass and heat transport as well as improving flow patterns. Therefore, benefits concerning chemical engineering is the main driver for microreactor investigations, while chemistry, in terms of reaction mechanism and kinetics, remains widely unchanged.