1
A Multi-faceted, Hierarchic Analysis of Chemical Micro Process Technology

To give a thorough, rational review of the field of chemical micro-process technology itself, one ideally would like to follow a deductive analysis route, pursuing a bottom-up approach. First, one may provide a definition of micro reactors, then search for the impacts on the engineering of chemical processes, and try to propose routes for exploitation, i.e. applications. Alternatively, for a less comprehensive, but more in-depth description, one could use a top-down approach starting with a selected application and try to design an ideal micro reactor for this.

Such ideal scenarios could not be followed in this book and are not practised in any other publications worldwide so far, since the developments and the theory in the field are not complete. Since mere deduction, therefore, could not be followed, the way of narration chosen gives a multi-faceted, hierarchic analysis of the field of chemical micro processing.

At four hierarchic levels, groups of entities are given in such a way that both the groups and the entities have casual relationships to each other, i.e. adapt a certain linear order (Figure 1.1). This main row may have side arms, comprising entities of minor importance. Each entity as well as the mutual relationships between the entities are not described in a complete, analytical fashion (for the reasons given above), but are outlined in a more heuristic or phenomenological way by discussing multiple facets thereof. Each entity is discussed in a corresponding section within this chapter; the facets are given in a sub-section. Thereby, the analysis given here has a kind of encyclopedia format.

At a first level, *fundaments* related to the use of micro-process devices are discussed. The nature of these fundaments is considered in Section 1.2.

At a second level, a *definition* or *conception* of a micro reactor, the so-called *micro-reactor differentiation*, is provided by analysis of its constituting properties. Conceptual approaches that arose from this definition are highlighted in the following such as *numbering-up*, *the multi-scale concept* and *process intensification*. This is accompanied by supplying auxiliary information and definitions on *interrelated topics* such as green chemistry, micro total analysis systems, and others. At the end of description of the first level, information on the micro-reactor history and *forums/ organizations* acting in the field is given.
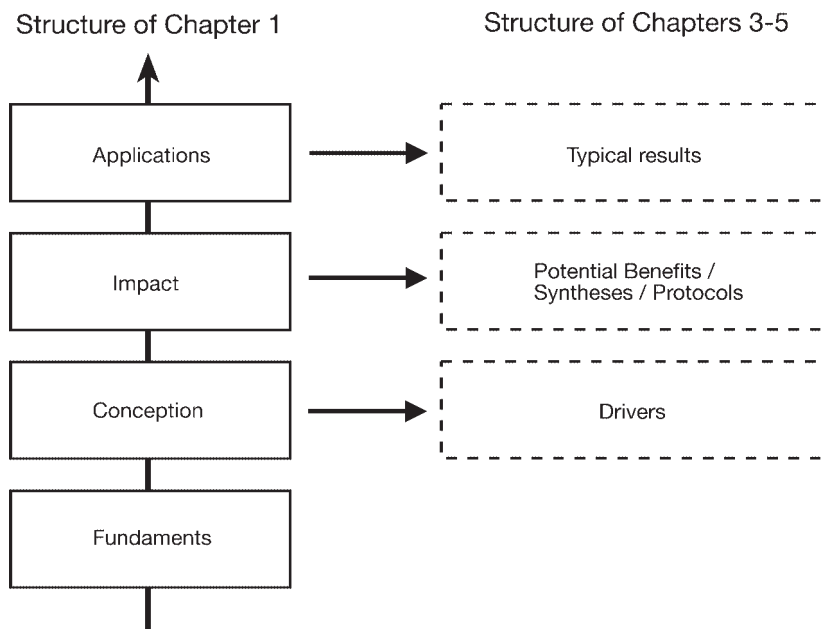
Structure of Chapter 1 Structure of Chapters 3-5

Figure 1.1 Entity hierarchy: four-level architecture of this first chapter resulting in the topics implication – conception – impact – applications. This logic is kept in three of the four following chapters, being sub-divided into drivers – potential benefits/syntheses/protocols – typical results.

A micro reactor according to the logic given here uses the fundaments to permit *impacts* on several entities, all related to chemical micro processing. Further, the new way of processing has impacts on mankind and environment. These various kinds of impacts provide altogether a third level, i.e. a third group of entities. Some of the impacts are in a consecutive relationship, some are in a parallel position. The nature of these fundaments is disclosed in Section 1.2.

Besides naming the third level 'impact', one could also term it *cognition* about what the conception actually can do.

At a fourth and final level, the impacts determine which *applications* are derived from the conception (or from the micro reactor itself).

The four-levelled approach is a guideline for the configuration of three of the four following chapters, describing experimental achievements made with micro reactors. The conception transfers to the *drivers* that trigger investigations with micro reactors. The impacts are evident when cognising on the potential benefits and developing a route to achieve this, i.e. choosing proper *experimental protocols*. The applications are specified and corroborated by *typical results*. This strategy was used for the three experimentally based chapters on gas-phase, liquid-phase and liquid/liquid-phase and gas/liquid-phase reactions. Of course, this could not be applied to modeling and simulation; hence Chapter 2 has a different structure.

1.1
Micro-reactor Differentiation and Process Intensification

1.1.1
Structure or Being Structured? Miniature Casings and Micro Flow

Micro reactors use *chemical micro processing,* which is continuous flow through regular domains with characteristic dimensions much below those applied in conventional apparatus, typically in the sub-millimeter range. There is a mutual relationship between structure and a process medium which is structured. Geometrically defined flow demands precisely structured small units for *casing* it. It is this synergetic interplay between geometric confinement and novel ways of processing that leads to the beneficial properties of micro reactors to be discussed below.

Today's micro-fabrication techniques have contributed substantially to providing miniature casings for chemical micro processing with much wider flexibility and accessibility (see, e.g., [1–4]). Besides simple *confinement,* today's precise manufacturing creates micro-flow elements of virtually any shape. Shaping in this way provides miniature passive elements, such as interdigital structures, which assume a specific *function,* e.g. for multi-lamination mixing, when passed by fluid flow. Accordingly, the high standard and variety of today's microfabrication techniques allow the provision of tailor-made micro-reaction units, possibly with a flexibility higher than for macroscopic reactors. Combined with the aid of modern simulation and the speed of modern screening approaches to determine optimum experimental parameters, there is definitely potential for a steep learning curve. If this potential is brought into application, micro reactors may affect the operation of chemical processes in a way not previously known in chemistry and, with huge value to the development of conventional apparatus, to an extent also not known in chemical engineering.

1.1.2
Symmetry and Unit Cells

A favorable feature of many micro flows is regularity or symmetry, i.e. manifold repetition of internal flow structures as a constituting element. First, this relates to flows in channels or in platelets (with channel arrays) parallel to each other. Second, this flow symmetry may even concern the flow within one micro channel, e.g. regarding the radial extension, the axial evolution, or both. To illustrate this abstract consideration by examples, focused and normal multi-lamination patterns and slug-micro flow are flows of high symmetry (Figure 1.2). The latter flow pattern is composed of a row of alternating segments, consisting of immiscible liquids or gas/liquid segments.

When symmetry is given, there is no need to consider the flow in a micro device or even a micro channel as a whole, but favorably one can refer to only a small part of it and regard this as a true functional region. A first-approach description for slug flow, according to the above consideration, may therefore refer to the repeti-
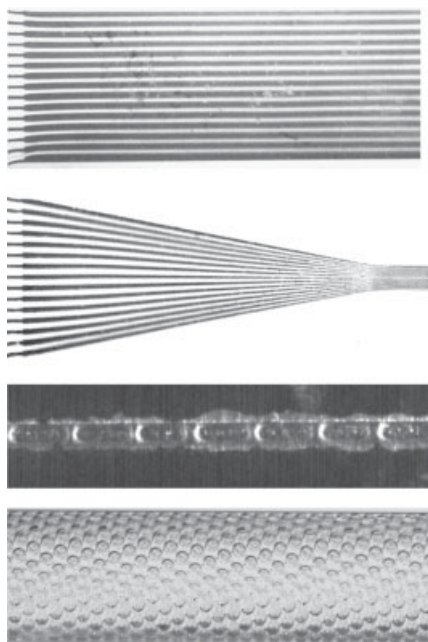
Figure 1.2 Normal and focused multi-lamination flow patterns, slug flow composed of gas/liquid segments ('Taylor flow'), and ordered foam flow ('hexagon flow') (from top to bottom).

tion unit only, i.e. to a single slug. This confined processing region may be termed unit-flow cell or unit cell.

Owing to the repetitive structure of the flow domain, a rational design of micro reactors is alleviated (see also the discussion on first-principle modeling approaches in Section 1.4.4.3). Instead of having to consider the complete system, often the study of a representative unit cell is sufficient to gain valuable information on the behavior of the full set-up. In practical terms, this leads to a more thorough involvement of simulation/modeling in future micro-reactor investigations which, in turn, will demand more microfluidic experiments in advance of the engineering and design phase of microstructured devices.

1.1.3
Process Design Dominates Equipment Manufacture and Choice

Knowing about ideal unit cells has the potential to turn the situation around in process development (Figure 1.3). First, the process is 'designed' for a very confined volume, the unit cell. Here, modern simulation techniques undoubtedly have a key role (see Chapter 2). The choice of the best unit-sized 'process design' is followed by choosing proper micro reactor elements and architectures, then repeating them and, in this way, constituting the total micro-reactor device. As the net result of this novel approach in process development, the reaction (or the process) becomes pre-eminent over the reactor, simply because the best reactor allows the reaction to be in the limelight.
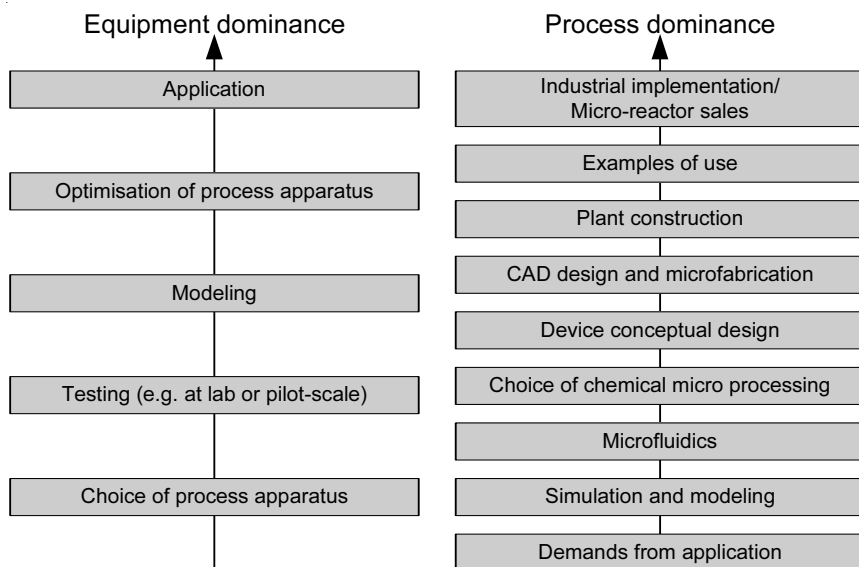
Equipment dominance

↑

Application

Optimisation of process apparatus

Modeling

Testing (e.g. at lab or pilot-scale)

Choice of process apparatus

Process dominance

↑

Industrial implementation/ Micro-reactor sales

Examples of use

Plant construction

CAD design and microfabrication

Device conceptual design

Choice of chemical micro processing

Microfluidics

Simulation and modeling

Demands from application

Figure 1.3 Today's bottom-up (equipment dominance) and sketch of future top-down (process dominance) approaches in process development.

1.1.4
Micro-reactor and Chemical-micro-processing Differentiation

Many authors regard chemical micro engineering as a separate, novel discipline (see, e.g., [5]), the term micro-reactor engineering being used already in an early citation [6]. What is essentially different about micro reactors, i.e. what differentiates micro-reactor and chemical-micro-processing?

Older definitions ascribe to micro reactors their manufacture as a distinguishing feature; a micro reactor accordingly is termed a device that is, at least partly, made by microfabrication or modern precision-engineering techniques (see, e.g., [3]). As a result, micro reactors have sub-millimeter internal dimensions. This definition was very exact and useful at that time, however, in the light of modern investigations, it seems to be somewhat too narrow. What if a device is composed of 'micro channels', albeit not being made by microfabrication techniques? Then undoubtedly one could rely on virtually the same micro-flow processing as with microfabricated devices. Should such a device not be termed a micro reactor? In this sense, the older definitions were technology-driven; therefore, in the following it is aimed at finding a more application-driven definition.

> *Micro-reactor differentiation*
> A micro reactor is a casing for performing reactions that was designed or selected to induce and exploit deliberately micro-flow phenomena, i.e. flow guidance and flow processing with characteristic dimensions much below that of conventional apparatus, typically below the sub-millimeter range.

In the same way, any other micro-flow device performing other processing functions can be defined. By custom, all such micro-flow devices are subsumed under the term 'micro reactor', although strictly this is not correct.

How, then, do we define chemical-micro processing (or micro-reaction technology, micro-chemical process engineering, or whatever substitute naming is used)? Is that synonymous with simply using a micro reactor for an application, i.e. replacing conventional equipment by novel micro reactors? It is not; in lieu of the conceptions made in Section 1.1.3, this is an essential, but not a commensurate condition.

> *Chemical-micro-processing differentiation*
> Chemical micro processing is based on 'process design' in a unit cell before manufacturing new or selecting existing micro-processing equipment, composed of a multitude of such cells. This results in having tailored processing equipment at the micro-flow scale.

A few micro reactors, especially those having large throughput, may fulfil the criteria of *process intensification* (PI) (see Section 1.1.6). Chemical micro processing can then be a branch of process intensification. More often, process intensification will rely on novel, specifically designed reaction equipment of larger scale such as spinning-disk reactors [7], i.e. tools which neither are micro devices nor have micro-flow equipment. Accordingly, micro-flow devices, PI reactors, and conventional apparatus constitute processing equipment of varying scale, the so-called *multi-scale concept* (see Section 1.1.7).

Owing to their normal size of equipment and of processing volumes, PI devices usually cannot refer to a unit-flow description as given for micro reactors, since they are dealing with non-micro flows. Instead, an analysis of their performance is usually based on a more gross or global description of the flows. In turn, they have the advantage of bridging the gap from conventional chemical apparatus to micro-flow devices. Thus, while still exhibiting improved performance, PI devices may also meet requirements of productivity, costs and reliability in a way which micro reactors cannot satisfy.

1.1.5
Numbering-up

1.1.5.1 Progressive Increase in Capacity by Addition of Modules

There are opinions that micro-flow processing, the repetition of unit cells (see Sections 1.1.2 and 1.1.3), not only holds at the laboratory scale, but may also be applied to – smaller or larger – production as well [5]. This is achieved by numbering-up of the elements, i.e. by multiple repetitions of small, precisely structured regions. In this way, unit-cell processing should be maintained at enlarged to process-unit size, although capacity is increased significantly – very different from conventional processing. By numbering-up, potentially the pilot-scale processing may be bypassed [5] and a phased (gradual) increase in production volumes may be achieved by progressively bringing on-stream micro reactor modules.

1.1.5.2 **Internal vs. External Numbering-up: Scaling-out of Elements or Devices**

Numbering-up can be performed in two ways (Figure 1.4). *External numbering-up* is referred to as the connection of many devices in a parallel fashion [8] (a similar, but less elaborate, definition was already provided in [9, 10]; see also [11] for a realized industrial example). A device in the sense as it is used here is defined as a functional element, e.g. a micro-mixing flow configuration such as an interdigital
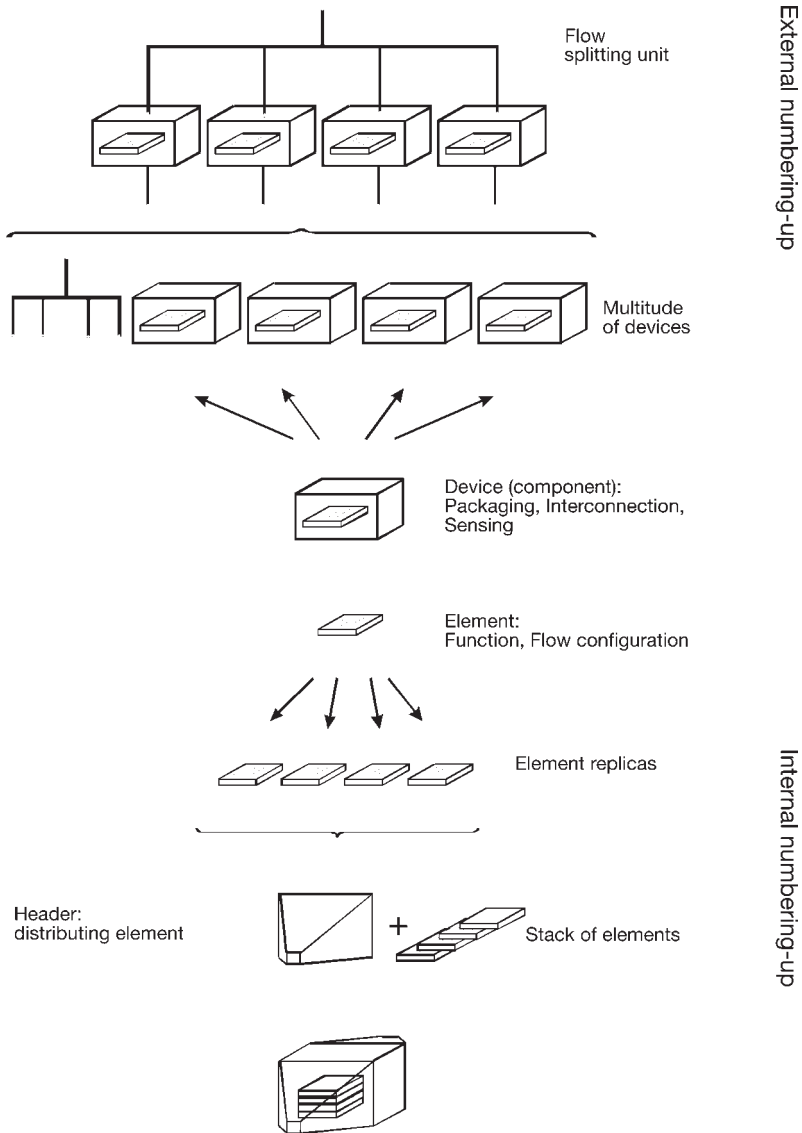

Figure 1.4 Schematic representation of the generic conceptions of external and internal numbering-up [8].
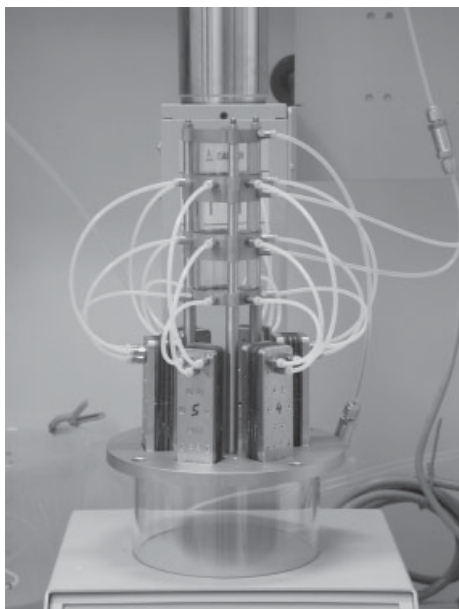
Figure 1.5 Photograph of the liquid-flow splitting unit for liquid/liquid processing with three tanks and six separation-layer micro mixers [8].

feed array with mixing chamber attached, which is encased and has outer connections for fluid supply and withdrawal. Combining of devices is thus achieved via their outer connections which most often follow commercial standards. Accordingly, conventional tubing with standard process-control equipment may be used here, but can suffer from fluid equipartition problems as mentioned in [11]. For this reason, a first specialty fluid-splitting tool was recently proposed and developed. The construction of this six-fold liquid splitting unit is given in Figure 1.5.

External numbering-up is numbering-up in the truest sense. Virtually, the complete fluid path is repeated. This resembles also the real meaning of scaling-out.

Internal numbering-up means the parallel connection of the functional elements only, rather than of the complete devices. These elements are grouped in a new way, usually as a stack, and are encompassed in a new housing. This housing typically contains one flow manifold and one collection zone, most often having a simple design like a header of diffusor. Although often overlooked, internal numbering-up actually is state of the art. To name only a few realized examples, a mixer array with 10 parallel interdigital units [12], a gas/liquid contactor array with 10 packed beds [13], and micro heat exchangers with hundreds of parallel platelets [14] (see [15] for a recent development) have been realized (Figure 1.6). The internal numbering-up of the latter type of device, for instance, permits a throughput of up to 7 t h^{-1} water flow [14]. Hence one device, of a size of a shoebox up to a computer, may be sufficient for a complete production.

External numbering-up benefits from true repetition of the fluidic path, and hence preserves all the transport properties and hydrodynamics, determined in advance for a single-device operation. This is commonly believed to result in a
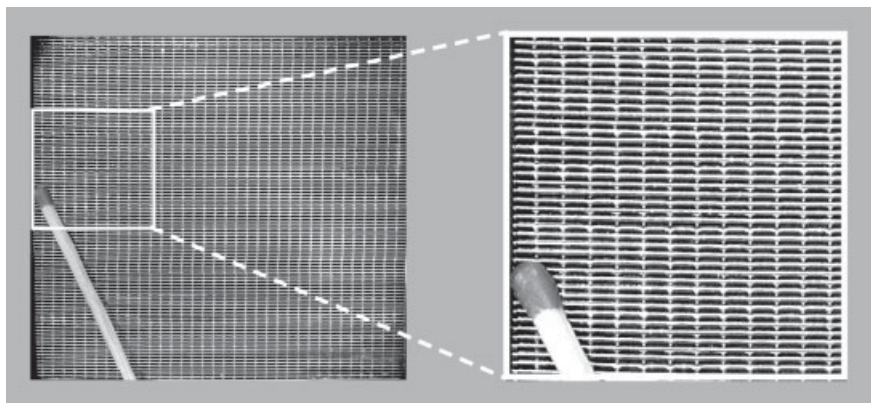
Figure 1.6 Photograph and detailed view of 6685 parallel micro channels which are numbered-up internally to give a micro-flow heat exchanger of large capacity [15].

faster time-to-market of the process development. The disadvantage is the need for a sophisticated monitoring and control system, in particular to achieve fluid distribution. Another drawback stems from the unfavorable ratio of housing (i.e. reactor) material to active internal volume. At the laboratory scale (single-device operation), this does not matter, whereas at a production scale it is almost not practicable. It is easy to imagine that even only a few tens of parallel connected devices with all their tubing attached do not present really elegant, compact engineering solution. Furthermore, the costs for micro-reactor fabrication are raised considerably owing to the increasing material demand and, more especially, to the need to structure the housings multiple times.

In contrast, internal numbering-up provides, as the existing examples demonstrate, compact reactor architecture at reasonably high throughput. Meanwhile, advanced fabrication exists, reducing the costs of such production devices more and more to an acceptable level. Fluid distribution is manageable, in particular using modern simulation methods. The disadvantage is that possibly a slight redesign of the fluidic path, sometimes even of the functional element, has to be made. This, however, can be avoided by the taking into account during design of the initial single device how the internally numbered-up production device may be arranged later.

Obviously, internal numbering-up has more arguments in favor than external numbering-up. Hence why propose a liquid-splitting tool for external numbering-up? There are still good reasons to do so. First, not all micro-reactor processes are amenable to internal numbering-up, e.g. for fluid dynamic reasons. Concerning the latter, the application reported for the first external numbering-up device refers to the field of precipitating organic synthesis and in some way stands also for crystallization. The special feature of the corresponding micro-flow processing is tri-layered droplet formation causing delayed mixing [16, 17]. The droplet can be made using a single separation-layer micro mixer; the same processing cannot, however,

Table 1.1 Some thoughts on features of chemical processing which favor the choice of either external or internal numbering-up. Provided that more in-depth knowledge is gained, such a (modified) list may provide selection criteria for choosing the right splitting concept when looking for scaling-out.

External numbering-up	Internal numbering-up
Low degree of parallelism	High degree of parallelism
Favoring multi-phase processing, including powder making	Favoring single-phase processing
Bubble/droplet/film formation or movement; surface flows	Stream guidance; volume (channel) flows
Specialty, complex processes	Unit operations; standard reactions
Precious products; functional chemicals	Bulk chemicals; fine chemicals
Slow reactions/processes, i.e. demand for laminar-flow post-processing, e.g. by delay-loop	Fast reactions/processes, i.e. no demand for laminar-flow post-processing, process completed within device
Hazardous processes	Safe processes

be simply made by an internal parallel arrangement. As a rule of thumb, such solid/liquid processes and, in a wider sense, multi-phase processes in general may restrict (or at least favor) parallelization to external numbering-up. These and more thoughts in favor of or against a numbering-up concept are given in Table 1.1.

In addition, when carrying out a process in the explosive regime, the whole fluidic path possibly has to be set below a certain characteristic dimension to guarantee inherent safety (see, e.g., [18]). Hence the processing of hazardous reactions may demand an optimized, well-understood specialty device, rather than restarting developments at the level of internal numbering-up. The use of any conventional tubing or any larger-scale own-constructed splitting unit (such as the one here) may be prohibitive, as it does not fulfil the stringent safety requirements.

Finally, external numbering-up may be chosen for simple, practical reasons, if the degree of parallelism does involve only low numbers, e.g. not exceeding 10 devices. Developing an internally numbered-up device will demand development costs and time and, therefore, may be inefficient at a low degree of parallelism. Meanwhile, since micro reactors are available commercially and tentatively will become cheaper, the rapid availability of a small series of devices is no longer impossible.

1.1.5.3 Issues to be Solved; Problems to be Encountered

The numbering-up concept demands achieving absolutely uniform flow equipartition by placing special headers in front of the parallel micro channels [5]. Although this has been solved for tubes in conventional multi-tubular reactors, the expenditure for equipartition in micro channel stacks is assumed to be higher, since the small channels may have more relative differences in structural preci-

sion. In addition, their sensitivity to particulate clogging may be higher, requiring a filtration system. Fouling inside the channels may be even more detrimental, since there may be major difficulties with removal. Heat management, already an issue at the device scale, will demand more elaborate solutions for a scale-out device, taking into account the heat management of each subunit. Another issue also refers to the multi-unit architecture, namely sensing and controlling all of the subunits in a reliable and robust manner. Here, a first approach based on valves, flow meters, power supply, and control circuitry was proposed by industry and academia [19, 20].

The existence and the success of scaled-up industrial plants using micro or mini reactors reported in the open literature [11, 21], however, gives hope for the possibility overcoming all the problems mentioned above, at least for selected applications.

1.1.5.4 Limits of Mini- and Micro Plants for Scale-up

There are not only limitations concerning the achievement of numbering-up, but also concerning the right use of a numbered-up micro-reactor plant.

In this context, the simulation of complete plant behavior, including recycling and energy management, at the mini-plant or micro-plant stage, is critically reviewed by Zlokarnik [22]. Mini plants describe homogeneous-phase processes adequately; scale-dependent processes can be processed satisfactorily. However, Zlokarnik admonishes that mini-plants in the general case are not suited to develop scale-up rules for scale-dependent processes. This holds even more for micro plants, since they will lose their performance upon an increase in device size, i.e. scale-up (even when keeping the relative internal dimensions). (Parallel) numbering-up is hence the only right means to scale-out micro devices.

1.1.5.5 First Large-capacity Numbered-up Micro-flow Devices Reported

Having reviewed the limitations predicted, one should have a look at the achievements that already have been made with numbering-up.

Numbering-up within one device, i.e. internal numbering-up, is no longer a dream, but is reality. For a long time, the Forschungszentrum Karlsruhe has reported on parallel micro heat exchangers that have a productivity of up to $7 \, \text{t h}^{-1}$ liquid flow per passage, leading to a heat-transmission power of 200 kW, at an outer volume of only $27 \, \text{cm}^3$ [23].

The Institut für Mikrotechnik Mainz GmbH (IMM) recently introduced a production- and pilot-scale gas/gas counter-flow heat exchanger comprising microstructured channel arrays [15] (see Figure 1.6). This stainless-steel device is equipped with industrial flanges, and is about 36 kg in weight and 54 cm long. It is operated at gas throughput in the range of $\text{m}^3 \, \text{min}^{-1}$ at 100 mbar pressure drop, having a power capacity of about 10 kW at a thermal efficiency above 95%. The internals consist of a stack of microstructured plates having multi-channel arrays of a channel width of 2 mm, depth of 250 µm, and length of 240 mm. In total, 6685 micro channels are operated in parallel in this device. The flanges allow installation in large-scale industrial plants.

1.1.5.6 First Complete Test Station for Multiple-micro-reactor testing

DuPont and MIT built a so-called *turnkey multiple-micro-reactor test station* providing reactors with fluidic distribution and control components in a scaleable fashion (Figure 1.7) [2, 19]. A detailed design description for a whole plant concept starting from one generic idea is provided. A key feature of this concept is the use of standard components originating from the semiconductor industry for micro chemical processing, either in the original version or partially modified. This holds for, e.g., the so-called *known good die sockets* of Texas Instruments and for the special type of arrangement chosen that was oriented at the concept of *printed circuit boards*. Available microtechnical standard components such as MEMS-based mass flow controllers of Redwood Microsystems and further commercial equipment such as *programmable logic controllers* of Siemens are also integrated. With respect to these monitoring and controlling functions, the time-scale of temperature change is given exemplarily. Temperature is reported to be changeable within about 3 ms, allowing real-time algorithms. Besides the use of standard components, the micro-reactor test station is characterized by showing up technical solutions for a fluid manifold, the essential component for numbering-up.
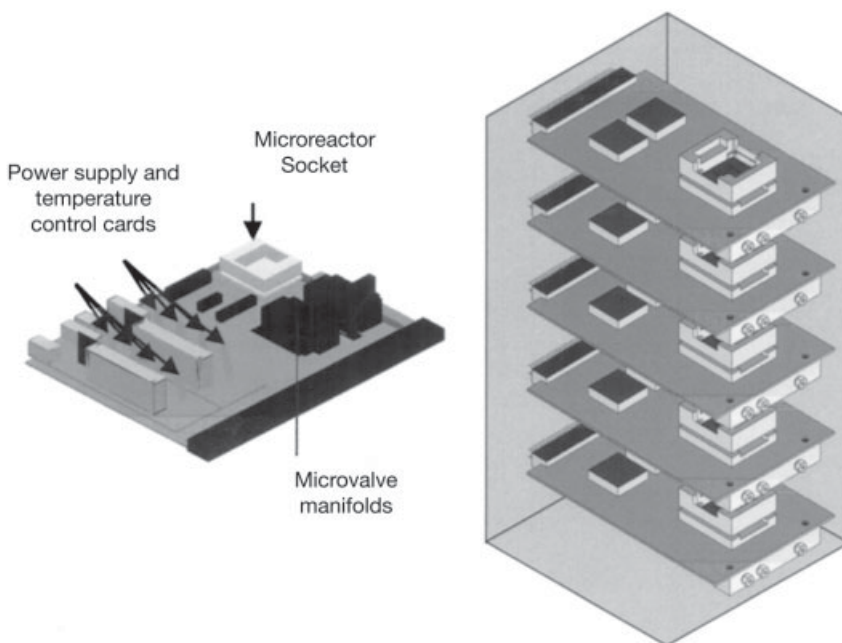

Figure 1.7 Schematic outline of the constructional principle of the multiple-micro-reactor test station [2].

1.1.6
Process Intensification

1.1.6.1 Definitions

Process intensification is a concept aimed at notable improvements in chemical processing. Ramshaw, one of the pioneers in the field, defines process intensification as a design approach for making dramatic reductions in the physical size of a plant while achieving a given production objective [24] (see also [25] and [5]). A volume reduction of 100-fold or more was regarded as dramatic by Ramshaw [24], whereas newer publications, with the achievements of the last decade, give two as a realistic number [25]. The size reduction in equipment, which is typically a plant or a system, can come from shrinking the parts of the equipment, i.e. device miniaturization, or from omitting complete parts, i.e. unit operations, from the equipment.

Stankiewicz and Moulijn extend the definition of process intensification from size reduction of apparatus to dramatic improvements in key features of chemical processing [25]. Substantial decreases in the following process-engineering properties are listed:

- ratio of equipment size to production capacity
- energy consumption
- waste production

Therefore, in this definition process intensification encompasses both novel apparatus and techniques which are designed to bring dramatic improvements in production and processing (Figure 1.8) [25]. As a result, safe, cheaper, compact, sustainable (environmentally friendly), and energy-efficient technologies are obtained.

Process intensification means following engineering methods and using appropriate apparatus; improvements in materials, e.g. catalysts, or chemical paths, are not regarded as falling into this category [25]. The list of engineering methods includes the integration of operations such as reaction and separation [26] (multifunctional reactors), the use of alternative energy sources such as ultrasound, and new process-control methods such as unsteady operation. There is a tendency that process intensification will no longer be based on pure unit operations, but rather will involve hybrid forms. The impact on equipment is seen to be even more prominent; it is said that some types of apparatus will disappear from plants because of process intensification [25].

Phillips of the BHR Group, UK, provides a compact definition of process intensification, saying it is '… a design philosophy whereby the fluid dynamics in a process are matched to its chemical, biological and/or physical requirements, …' [27]. In this way, significant benefits are gained, those listed above.

1.1.6.2 Matching Fluidics to Physico-chemical Requirements of a Reaction

Following the latter definition, the BHR Group <www.bhrgroup.co.uk> gives straightforward goals reflecting how they envisage a chemical process becoming
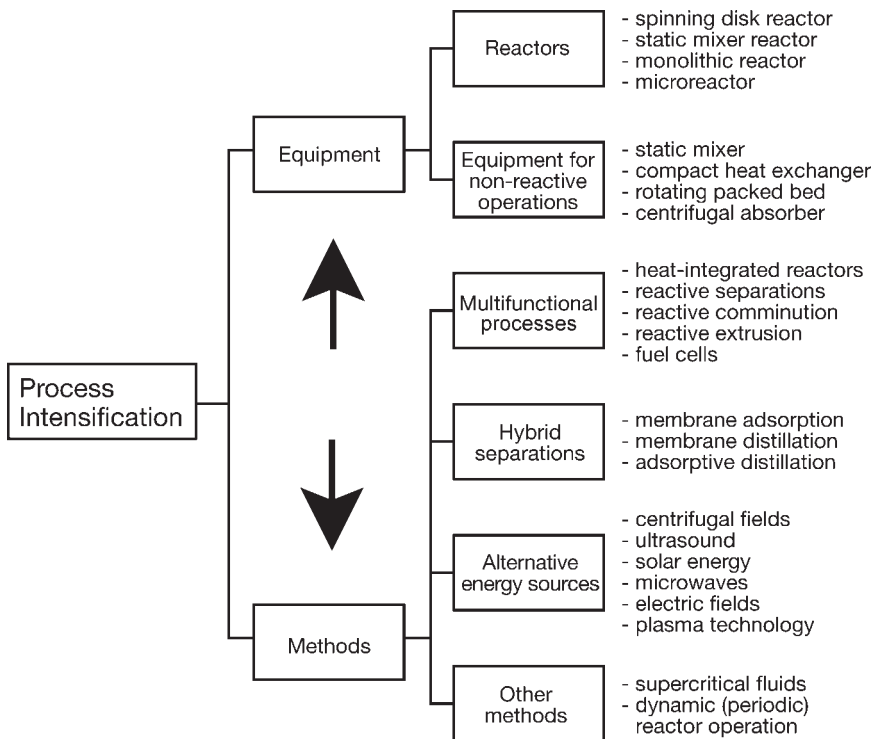
Figure 1.8 Branching of process intensification into engineering methods and corresponding equipment [26].

ideal. They propose to match variaous dynamic features with the physico-chemical requirements of the reaction:

- match reaction rate with mixing rate
- match mechanism with flow pattern
- match reaction time with residence time
- match exothermicity with heat transfer

1.1.6.3 Relationship of and Difference between of PI and Micro-reaction Technology

Micro-reaction technology can be one of the tools that process intensification may use [5]. Hence chemical micro processing and process intensification have a share, where the former supplies devices for the latter concept or purpose. However, both chemical micro processing and process intensification also cover unique aspects that the other field does not comprise.

Strictly, chemical micro processing, in addition to being a device field based on micro channels, is a means to use micro flows, which is oriented not at one, but rather at a multitude of purposes. Process intensification, also strictly, is a concept (but specifying no concrete means) and apparatus for a specific purpose (see above).

Hence chemical micro processing may also be applied for purposes other than PI, e.g. screening, which is not related to production and, accordingly, does not fall into the category of process intensification (see the definition given above).

1.1.6.4 **Process Intensification Achieved by Use of Micro Reactors**

As examples of micro-channel process intensification and the respective equipment, in particular gas/liquid micro reactors and their application to toluene and various other fluorinations and also to carbon dioxide absorption can be mentioned [5]. Generally, reactions may be amenable to process intensification, when performed via high-temperature, high-pressure, and high-concentration routes and also when using aggressive reactants [5].

1.1.7
The Multi-scale Concept

Hessel and Löwe report on hybrid, i.e. multi-scale, approaches which are currently most often favored for micro-reactor plant construction, simply for practical time and cost reasons [9, 10]. In addition, such an approach allows one to fit micro reactors in existing industrial, producing and academia, measuring environments. The micro reactor is only used where it is really needed and costs for changing the processing are kept to a minimum in such a way (Figure 1.9).

The hybrid concept is generically different from the monolithic concept, such as practiced for Lab-on-a-Chip designs, aiming at integrating all processing and controlling functions into one miniature device. It stands to reason that the monolithic concept has advantages for analytics and screening, whereas the hybrid (multi-scale) concept is demanded for production and synthesis of preparative quantities. A review on concrete multi-scale architecture, including the first commercial ones (Figure 1.10), is given in [9, 10].

The hybrid approach seems to be the more pragmatic procedure [9, 10]. The impressive results gathered so far, especially on the industrial side, substantiate that this – and so far only this – concept is not lacking innovative character besides pragmatism [11, 28]. Set-ups with many micro-reactor components, pointing to a monolithic concept, will find use when each of these components on its own or the interplay between all of them gives advantages. This holds, for instance, for applications in the field of automobiles and consumer care. Here, space and weight savings are important technical drivers, thereby demanding miniaturization of all components. In turn, chemical applications typically target other issues. In any case, one should be aware that the fluidic peripherals of many of today's micro-reactor plants still take a considerably large portion of the total plant space.

The time of the hybrid approach has come already [9, 10]. It allows one without delay to analyze the advantages of micro reactors, especially facing today's industrial time demands. The monolith approach needs more time for development, but can be built on the progress achieved so far. The respective developments will certainly gain an additional impetus when more and better tailor-made applications especially for this concept are identified.
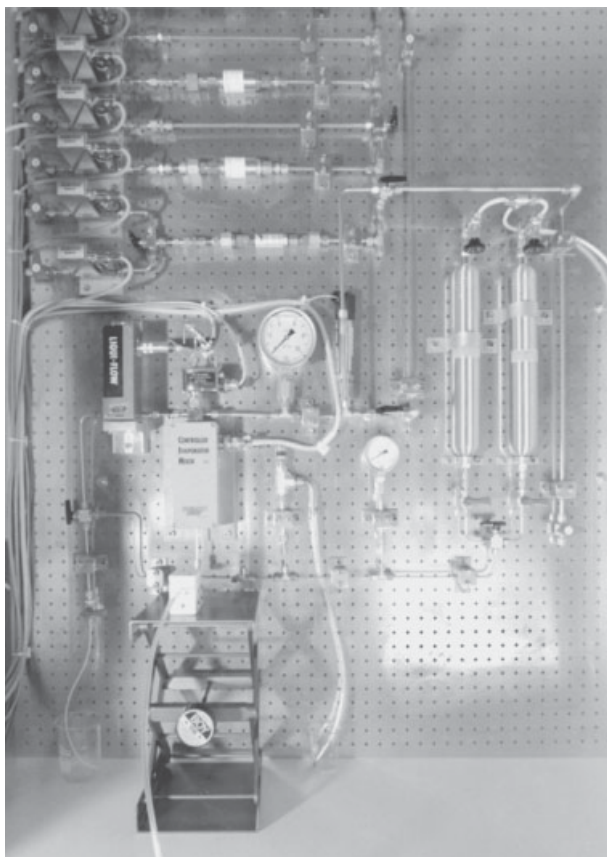
Figure 1.9 Hybrid, multi-scale micro-reactor plant for catalyst testing for propane steam reforming [15].

Figure 1.10 Hybrid, multi-scale micro-reactor plant, a commercial product of mgt mikroglas technik AG, Mainz, Germany [9].

1.1.8
A Word of Caution on the Probability of a Deductive Analysis

Needless to say, all conclusions drawn in Sections 1.1.1–1.1.7 are ideal-case considerations of an abstract nature aimed at showing the maximum potential of chemical micro processing, and the ideas behind. In reality, a performance less than ideal (but often better than conventional) may be found, at least initially, e.g. for reasons of imperfect exhibition of flow patterns or due to limits of micro flow compared with existing technology. This reality description is given in Chapters 3–5.

1.1.9
Other Concepts Related to or Relevant for Chemical-Micro Processing

1.1.9.1 **µTAS: Micro Total Analysis Systems**
Micro Total Analysis Systems (µTAS) are chip-based micro-channel systems that serve for complete analytics. The word 'Total' refers to the monolithic system character of the devices, integrating a multitude of miniature functional elements with minimal dead volumes. The main fields of application are related to biology, pharmacology, and analytical chemistry. Detailed applications of µTAS systems are given in Section 1.9.8. Recently, µTAS developments have strongly influenced the performance of organic syntheses by micro flow (see, e.g., [29]). By this, an overlap with the micro-reactor world was made, which probably will increase more and more.

There is no doubt that the description of µTAS investigations could fill several volumes on their own. In the following chapters, only those applications with relevance to synthetic chemistry are presented. For reviewing all other µTAS applications, actually the majority, the reader is referred to reviews in the field (pioneering literature [30–40]; up-to-date literature [41–44]; essays [45]; see also [46] for a description of a consortium) and to the proceedings of the µTAS conferences.

1.1.9.2 **Green Chemistry**
Haswell and Watts use the term *Green Chemistry* in way similar to the definitions for methods for process intensification (see Section 1.1.6) [47]. This refers to optimum use of material, energy, and consequent waste management, with an appreciation of the environmental resources and the need for reducing pollution. While traditionally waste was reduced at the end of the pipeline, a change is needed to reduce waste at the source. In this context, micro-reaction devices fulfil the criteria of sustainability in the way described below, e.g. because they have high selectivity, have efficient heat management, and use high reactant concentrations, reducing solvent volumes.

1.1.9.3 **Sustainable Development and Technology Assessment**
Jischa gives an overview of sustainable development and technology assessment, particularly from the German point of view and reviewing the German initiatives

over the last four decades [48]. Technology assessment is the older term, essentially of similar meaning to sustainable development, mainly used nowadays. Concerning sustainable development, no unambiguously accepted, detailed definition can be given, but it is related to planned resource use and focused resource development. As relevant problem areas, world-population growth, provision of energy and raw materials, and environmental destruction are seen. Micro reactors certainly are of relevance to the latter two areas. Consequently, sustainable development is concerned with environmental, social, and economic aspects.

One coalition of 165 international companies united by a shared commitment to sustainable development is the *World Business Council for Sustainable Development* (WBCSD; <www.wbscd.org>). The three pillars economic growth, ecological balance, and social progress constitute the idea of sustainable development. This movement is joined by companies from more than 30 countries and from more than 20 major industrial sectors. The aims of WBCSD are business leadership, policy development, best practice, and global outreach. The mission of WBCSD is to be a catalyst for a change towards sustainable development. Key projects refer to accountability and reporting, advocacy and communication, capacity building, energy and climate, and sustainable livelihoods. As cross-cutting themes are considered corporate social responsibility, eco-efficiency, ecosystems, innovation/technology, risk, and sustainability and markets.

1.1.9.4 Microfluidic Tectonics (µFT)

Moorthy and Beebe subsume under this term '... the fabrication and assembly of microfluidic components into a universal platform, in which one starts with a "blank state" (shallow cavity) and proceeds to shape microchannels and components within the cavity by liquid-phase photopolymerization ...' [49]. Tectonics is the science and art of assembling or shaping of materials during construction. µFT is seen as new strategy to generate organic and biomimetic designs for microfluidic systems. Especially the large freedom in design and fabrication on an *ad hoc* basis are seen as benefits. Hydrogels are cross-linked polymers that can adsorb and move water by swelling and have responsive functions and were considered as construction material of particular interest.

1.1.9.5 Compact Flow-through Turbulent Reactors, also Termed Microreactor (MR) Technology

For a longer time than the onset of chemical micro processing, the term micro reactor was also used for small-scale testing continuous-flow equipment without micro channels and micro flow (see, e.g., [50]). Instead, turbulent flow was usually utilized. By this, numerous benefits over existing batch technology could be figured out, which are similar to the 'real' micro reactors. This stems from process-engineering implications which are basically the same for the two classes of micro reactors: high mass and heat transfer, shortening of residence time, and so on. Particularly interesting is that economic data are available for the use of the first type of equipment, perhaps providing valuable hints for the future industrial use of micro reactors.

Table 1.2 Key data for production of polymers in the compact reactor/mixer/heat exchanger, termed micro reactor, by cationic polymerization yielding propylene, piperylene, butylenes, etc. [50].

Process parameter	Micro reactor	Batch reactor in CIS	Batch reactor of Amoco USA
Reactor volume [m^3]	0.02–0.06	1.5–4.0	22.7
Output on raw stock [$m^3\ h^{-1}$]	5–10	2	9
Residence time [h]	10^{-3}	1	2.5
Metal consumption [t]	0.05	7.5	40
Specific expenses [relative units]:			
– raw stock	0.84	1	1
– catalyst	0.6–0.8	1	1
– electric energy	0.75	1	–
– water	0.6–0.85	1	–

As an example, a compact high-throughput turbulent flow reactor/mixer/heat exchanger was used for various applications, including polymer and rubber manufacture [50]. Further applications refer to emulsification and intensified heat exchange.

Typical properties (Table 1.2) of these micro reactors preserved the basic characteristics of the existing processes, reduced the reactor volume with even slightly increased output and distinctively reduced residence time, thereby having a very large specific output [50]. In addition, the quality of the final product was improved, a high process flexibility was achieved, less raw material and catalyst were needed, specific expenses were reduced, and gains in economy of the process were achieved. Fewer staff members were needed for process operation.

Other types of non-micro-channel, non-micro-flow 'micro reactors' were used for catalyst development and testing [51, 52]. A computer-based micro-reactor system was described for investigating heterogeneously catalyzed gas-phase reactions [52]. The 'micro reactor' is a Pyrex glass tube of 8 mm inner diameter and can be operated up to 500 °C and 1 bar. The reactor inner volume is 5–10 ml, the loop cycle is 0.9 ml, and the pump volume adds a further 9 ml. The reactor was used for isomerization of neopentane and n-pentane and the hydrogenolysis of isobutane, n-butane, propane, ethane, and methane at Pt with a catalyst.

1.1.9.6 Supramolecular Aggregates, Also Termed Micro Reactors

Supramolecular organic structures such as micelles, vesicles, liposomes, or monolayers were often also termed micro reactors when being used for reaction processing (Figure 1.10) [53]. Hollow structures created by inorganic crystallites such as zeolites were named and used in a similar way [54]. All these represent reaction vessels of nanometer dimensions, spatially and parametrically segregated from the homogeneous solution. For the latter reason, these 'nano reactors', which is probably the more appropriate term, can change reactions in a way not accessible to real micro reactors. They create unique, localized chemical environments
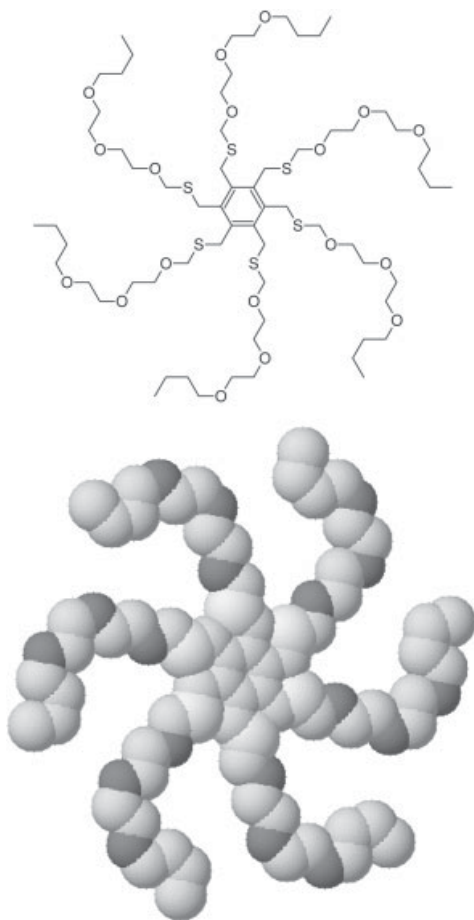
Figure 1.11 Hexapus, a multi-polar amphiphile providing a supramolecular structure [55]. Similar types of multi-polar amphiphiles were used as nano-reactors for changing the course of reactions [56].

with, e.g., modified solubility, solvent polarity, and reactant concentration. In addition, they may exhibit steric interactions not given in bulk solution such as hindered rotation in the case of molecules encapsulated in the zeolites' cavities.

In [53], segregated catalyst and polymer particles act as 'micro reactors' where the polymerization process takes place. Each particle is an individual reactor with its own energy and material balance. During polymerization, the catalyst particles undergo a change in volume by a factor of 10^3–10^4, thereby generating the corresponding polymer particles. The particle size distributions of catalyst and polymer are the same.

1.1.10
Some Historical Information on Micro-reactor Evolution

Hessel and Löwe give some information on the 'pre-history' of micro reactors by mentioning that this approach is not fundamentally novel as the foundation of the American Microchemical Society in 1934 is a relevant factor (Figure 1.12) [57, 58]. Wörz (BASF, Ludwigshafen, Germany) overstates this argument when making the – undoubtedly correct – remark that 'Microreactors are not really new, because every capillary tube is a microreactor' [28]. It is, however, also a matter of fact that a proper transformation of this system of thought into practice was pushed to the sidelines and at times is still being pushed.

The developments at the Kernforschungszentrum Karlsruhe (KfK), now the Forschungzentrum Karlsruhe, in the late 1980s and early 1990s, belong to the earliest, if not the first, reported activities on micro reactors [59–62]. In particular, Schubert et al. report on probably the first activities within industry documented in the open literature in 1993 [63]. KfK's activities were isolated until about 1994 (albeit being intense in themselves), i.e. not many other reports of other groups followed this example.

Accordingly, it is valid to claim the joint onset of micro-reaction technology in 1995 and to try to name those who were the pathfinders in this development (see, e.g., [3] for a description of such an opinion). Regarding the birth of micro-reaction

Some important steps in microreactor development	a list possibly incomplete
'Prehistory', e.g. foundation of American Microchemical Society	1930-1980
GDR patent from former German Democratic Republic	1985
First mention of microreactors + µChem processing at KfK (now FZK) in Karlsruhe; first micro heat exchangers manufactured	1989
Fundamental microfluidic studies reported at µTAS series	1994
First DuPont + BASF activities; PNNL, MIT, IMM, FZK, Dechema, AIChE First workshop in Mainz: paved the way for later IMRET series	1995
Focused activities on µChem processing all over the world	1996-2001
First µChem companies founded, all four in Germany µChem components and plants commercially available LOC: Lab-on-a-Chip, RSC journal with many µChem contributions Platforms: NeSSI (U.S.) and IPµVT (Germany) —Standartisation PAMIR: a µChem market survey states profit, but also 'R&D control' Japan, Korea, Australia; South Africa become active	Today 2003

Figure 1.12 Timetable for the micro-reactor evolution, marking important steps in the two last decades.

technology as a discipline, many researchers refer to the year 1995, when the first Workshop on Microsystems Technology for Chemical and Biological Microreactors was held in Germany [5]. A section on the pre-history of micro reactors, covering MEMS (*Micro ElectroMechanical Systems*) fabrication and the start of µTAS developments, is provided in, e.g., [5]. In [57, 58], it is stressed in the same sense that 'Microfabrication techniques have made headway with the total development of chemical microprocessing …'.

The status of micro reactor and µTAS developments from the beginnings to 1998 is given in [64]. Selected micro devices and applications are presented, and also key players, the foundations and the main drivers for undergoing such development.

A similar overview of German activities in 1998 is provided in [65]. The German working party on micro-reaction technology is presented, a federal funding program is introduced, and three top-priority research projects are presented. They show the activities at the edge of acceptance by industry.

Wegeng et al. give an overview of US and Japan funding programs in 1996 and plans for future funding [1]. They also name interest groups, funding programs and conferences in the field of MEMS at that time. They then identify major players in Europe in 1996 and, finally, comment on German activities which were then just starting the series of *International* Conferences on *Micro-REaction Technology* (IMRET).

1.1.11
Micro-reactor Consortia/Forums

1.1.11.1 The Laboratory on a Chip Consortium (UK)

<www.labonachip.org.uk>
This is said to be UK's largest collaborative research project on miniaturized chemistry, mainly concerning the use of chip technology. Members are universities, vendors and user companies (see also [45]). The consortium initiates a large, multidisciplinary collaboration, which combines academic excellence, user steering, and manufacturer input.

The project is managed through the Laboratory of the Government Chemist in Teddington, UK, and is part of the British government's Foresight Link program [45]. The cost of the Lab-on-a-Chip project was £ 3.2 million. Two key tasks are the exploration of reactions and processes on a micro-scale and the commercialization of the results.

1.1.11.2 MicroChemTec and IPµVT (D)

<www.microchemtec.de>
The strategic project *Modulare Mikroverfahrenstechnik* (modular micro-chemical engineering) is funded in the framework of the German program Mikrosystemtechnik 2000+ by the German ministry for education and science, BMBF. The project was started in October 2001 and lasts 3 years.

It was initiated by work results of an industrial platform on micro chemical engineering, the so-called *Industrie Plattform Mikro Verfahrens Technik* (IPµVT). This forum combines industrial users and commercial providers of the technology, meeting in Frankfurt/Main at the Dechema organization. This forum has several reporting sub-groups which each dealing with special topics such as future device development (e.g. standardization) and chemical and biological applications.

The main aims of MicroChemTec are the development of a unit construction kit for micro reactors, definition of standardized interfaces, investigations of modules on the market for their suitability for affiliation in the unit construction kit, documentation for this purpose, and demonstration of functioning of the concept with the example of selected unit operations or processes.

1.1.11.3 NeSSI (USA)

<www.cpac.washington.edu/NeSSI/NeSSI.htm>
NeSSI is a non-affiliated international *ad hoc* group composed of over 250 people (and growing) including end-users such as Dow and ExxonMobil, and manufacturers such as A+, ABB Analytical, Siemens, Fisher-Rosemount, Swagelok, Tescom, Parker-Hannifin, Circo and many others who are looking to modularize and miniaturize process analyzer sample system components. NeSSI operates under the sponsorship and umbrella of CPAC (Center for Process Analytical Chemistry) at the University of Washington in Seattle. The membership focus of NeSSI has been on manufacturers who are willing to supply parts and components for this initiative and also end-users who are willing to do 'in-house' testing. There are now several NeSSI sampling manifold designs which conform (approximately) to the SEMI 1.5″ manifold. An ISA standard is concurrently being drafted, called SP76; this, however, is not an integral part of NeSSI.

NeSSI's driver is to simplify and standardize sample system design. There is also a huge opportunity to adapt the emerging class of 'lab-on-a-chip' sensors to a miniature/modular 'smart' manifold which could fundamentally change the way in which industry does process analysis.

1.1.11.4 Micro Chemical Process Technology, MCPT (J)

<www.mcpt.jp>
The Research Association of Micro Chemical Process Technology (abbreviation: MCPT) was established in July 2002 with the aim to conduct experimental research on micro-chemical process technology through the collaborative work of its members. The association has been implementing R&D together with its members from 29 different firms of various industries including the chemical industry, the precision machinery industry, and the electrical equipments and electronics industry. In addition, the participation of national, public, and private universities as well as independent administrative institutions has been greatly appreciated.

With the support of the Ministry of Economy, Trade and Industry (METI) and the New Energy and Industrial Technology Development Organization (NEDO),

The Research Association of Micro Chemical Process Technology will establish micro-chemical plant technology and microchip technology, which is the core of micro-chemical process technology. By integrating these two technologies in an effort to establish micro-chemical process technology as the fundamental technology that is common to all technologies of the industrial world, the association will continue to dedicate itself to the R&D of the systematization of micro-chemical process technology.

Concrete aims of MCPT are to implement experimental research on high-efficiency micro-chemical process technology, to apply micro-spaces to chemical reactions and analysis technologies by utilizing semiconductor production technologies that have developed rapidly in recent years. Furthermore, the work conducted is said to contribute to the establishment of high-efficiency chemical plants, which is expected to reduce resource and energy consumption in the chemical industry. In a similar way, contributions to the development of high-speed analysis technologies using minute quantities are foreseen, which is expected to create a large-scale market of life-science products such as diagnostic chips, etc. for household and other uses. As a sum of all these targets, it is hoped to establish a fundamental technology beneficial to the industrial world, through the systematization of the aforementioned knowledge and technologies.

1.1.11.5 CPAC Micro-reactor Initiative (USA)

<www.cpac.washington.edu/micro-reactor/cpac_micro.htm>
The Center for Process Analytical Chemistry (CPAC) in Seattle (WA, USA) released a white paper specifying its capabilities on micro reactors and trying to initiate collaborations to fill vacancies in this portfolio. For these reasons, the CPAC Micro-reactor initiative will focus on the acquisition and operation of commercially available micro-reactor systems as test beds for the testing and development of analytical sensing technologies, process integration, and process control issues. CPAC also envisions the platform as a valuable educational tool in the chemistry and chemical engineering disciplines, particularly as part of the engineering unit operations laboratory section of chemical engineering. The three main aspects for implementing the CPAC Micro-reactor initiative are:

- acquire commercially available micro-reactor platforms
- select appropriate chemistries for test applications running on the micro-reactor platforms
- operate the micro-reactor platforms as test beds for research and testing.

1.2
Consequences of Chemical Micro Processing

1.2.1
Limits of Outlining Top-down Impacts for Micro Reactors

The field of chemical micro process engineering is moving fast, having impacts on chemical process industry, academia, markets, and society (see Section 1.3), and is starting to bring the technical progress made into application (see Section 1.9). Hence it is not surprising that not all impacts of this field have so far been fundamentally described, ideally in the format of a bottom-up scenario (see Section 1.4.3), and that some applications still remain underdeveloped. In the first 10 years, developments focused on establishing fabrication technology, to a considerable extent by microtechnology development, and on chemical feasibility studies. Detailed, e.g. mechanistic, scientific and technical analyses, as well as practical scenarios, e.g. cost analysis of a process, are left to future studies.

Nevertheless, based on our own considerations and on expert opinions given in the literature, it is aimed in the following to provide as far as possible a comprehensive overview.

1.2.2
Categories of 'Micro-reactor Fundaments and Impacts'

Many authors have described the consequences of chemical micro processing (see Section 1.4.3) in reviews. When following the multi-faceted hierarchic structure proposed at the beginning of this chapter, one is able to specify the entities grouped at four levels by studying the expert information supplied in the reviews (Figure 1.13). As a result, at the first level physical and chemical basics (see Sections 1.3 and 1.4), named briefly fundaments in the following, have to be described. At the second level is micro-reactor development, which has impacts on chemical engineering, process engineering, process results, society/ecology and the economy (see Sections 1.5–1.8). Knowing the process results, one is able to evaluate the potential for the use of micro reactors for applications in various fields (see Section 1.9).

Some reviews provide information on impacts of various types, whereas others focus on one aspect in detail. Most descriptions cover physical fundaments and the impact on chemical engineering; the impact on process results, although indispensable for the field of micro reaction engineering, has so far not been described in a systematic and comprehensive manner (probably for this more progress in experimental results is needed). Process engineering visions originally developed for transportable bench-scale plants composed of small conventional devices, but also relevant and adjustable to micro reactors, were given at very early stage of development. A vision of the socio-economic aspects of the field is given in a few specialist articles.
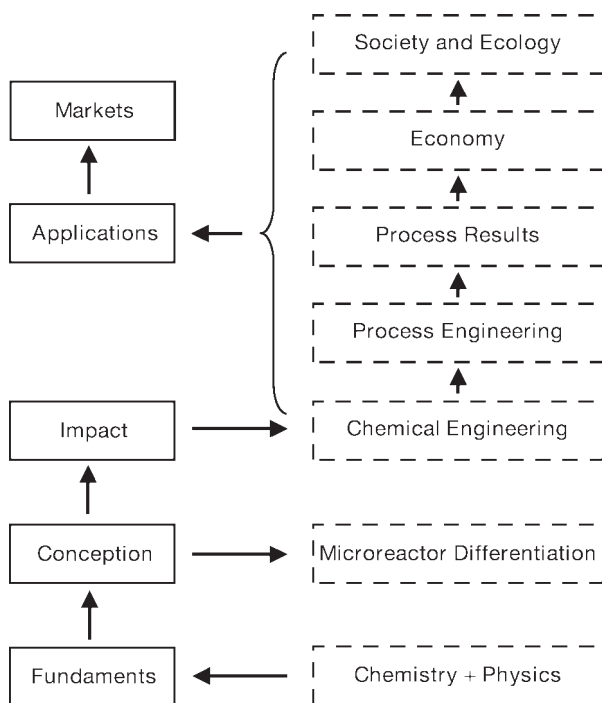
Figure 1.13 Hierarchic structure of entities that are related to using micro reactors – fundaments, impacts, and applications. An analysis and specification of the entities and their relation gives a multi-faceted knowledge on chemical micro processing, the content of this chapter.

1.2.3
Comprehensive Reviews and Essays

At an early stage of development, Wegeng et al. gave a near-comprehensive view covering all of the above-mentioned fundaments and impacts (with the exception of the chemical one) [1]. Naturally, information on applications was limited, hence the review had to be visionary in many parts, but it made correct predictions, as we now know. Much later and based on the much wider knowledge available then, Hessel et al. provided a series of reviews of comprehensive and extended character, full of details on applications and up-to-date references [9, 10, 57, 58, 66]. The two CIT and CET series by these authors contain particularly a section on plant concepts with regard to micro reactors. Gavriilidis et al. gave similar information in a compact manner in one review, included a section on modeling, and reported in detail on chemical applications [5].

The first book on the field aims at combining all this information and to group it according to the way of processing [4].

1.2.4
Reviews and Essays on Physical Fundaments and the Impact on Chemical Engineering and Process Engineering

Ehrfeld et al. gave a particularly systematic description of the physical fundaments, the resulting fundamental advantages, generic device concepts, and some early-stage, relevant applications [3]. Ehrfeld et al. also reviewed microfabrication techniques and in a phenomenological way described many kinds of devices [67–70]. Wegeng et. al also reported at an early stage physical fundaments, microfabrication methods needed for micro-reactor manufacture, and the first micro-flow devices [1]. Later, the first ideas on industrial implementation and commercialization were also sketched by Ehrfeld et al. [71]. Further, at an early stage of development, Jäckel [72, 73] and Lerou et al. [74] each gave a description of the physical fundaments and the impact on process engineering from an industrial perspective, touching also upon economic aspects. Jensen reported on chemical engineering aspects, but also summarized the microfabrication issues, considering especially chip micro reactors [2, 75, 76]. One reference addresses the impact on process engineering in a compact form [75].

1.2.5
Reviews and Essays on the Impact on Process Results, Society/Ecology and the Economy

Haswell et al. prepared very detailed reviews on the use of chemical micro processing in chip-based micro reactors for organic synthesis [29, 77] and for chemistry in general [78], covering also green chemistry aspects [47]. Other reviews also concern the chemical field [79–81]. An especially detailed review on the chemical fundaments was recently provided by Jähnisch et al. [82]. Schwalbe et al. gave a first insight into the relationship between potential-energy profiles of the reaction course and setting proper micro-reactor operation [81]. Löwe et al. gave information on the chemical misuse of micro reactors [83]. Rinard et al. focused on socio-ecologic-economic analysis with strong consideration of the social aspects of future chemical processing [84–86]. Hessel et al. discussed hybrid/multi-scale plant concepts and the state of market implementation [9, 10, 57, 58, 66, 86, 87].

1.2.6
Reviews and Essays on Application Topics and Microfabrication

Concerning one application only and the design concepts involved, reviews were given on micro mixing [88], micro heat exchange [14], energy [64, 89, 90], and extraterrestrial applications [91, 92]. Some reviews give in-depth information on selected micro-fabrication techniques: electroforming in the framework of the LIGA process for metal micro reactors [93], μEDM [94–96], specialty-tool milling [61], and ceramic moulding [97–100]. In [3], a summary and many references on microfabrication technologies applied are given.

1.2.7
Reviews and Essays on Institutional Work

Other reviews explicitly concern summaries of the work of the author's group, supplemented by a short introduction in the field: see [75, 76, 101] for MIT work, [87, 93, 102, 103] for IMM work, [104] for TU Eindhoven work, [105] for Sandia National Laboratories work, [106] for PNNL work, and [23] for the work of the Forschungszentrum Karlsruhe.

Reviewing all these experts' analyses, in the following it is aimed to give a summary of these considerations, supplemented by our own or otherwise newly presented thoughts. Special attention is given to achieving a thorough separation and classification of the fundaments and impacts according to their origin.

1.3
Physical and Chemical Fundaments

1.3.1
Size Reduction of Process Equipment

The most obvious, trivial consequence of micro-device miniaturization is a

- decrease in volumes, e.g. for reaction flow-through chambers or for interconnects.

Many other, less obvious physical consequences of miniaturization are a result of the scaling behavior of the governing physical laws, which are usually assumed to be the common macroscopic descriptions of flow, heat and mass transfer [3, 107]. There are, however, a few cases where the usual continuum descriptions cease to be valid, which are discussed in Chapter 2. When the size of reaction channels or other generic micro-reactor components decreases, the surface-to-volume ratio increases and the mean distance of the specific fluid volume to the reactor walls or to the domain of a second fluid is reduced. As a consequence, the exchange of heat and matter either with the channel walls or with a second fluid is enhanced.

Generally, whenever fluids are processed in a confined space, two different types of phenomena are observed: surface and volume effects. An example of a surface effect is a heterogeneously catalyzed reaction occurring at the walls of the vessel, whereas the motion of a fluid due to gravitational forces would be described as a volume effect. In brief, it can be stated that the surface effects gain in importance compared with the volume effects when the size of a reactor decreases. In particular, the reduction of length scale leads to a

- decrease in diffusion distances, e.g. for mixing and heat transfer
- increase in respective gradients, e.g. concentration or temperature
- increase in specific surfaces, e.g. when using films or catalysts
- increase in specific interfaces, e.g. in multi-phase flow.

A more specific discussion of the importance of various hydrodynamic phenomena when the length scale is reduced is given in the following section.

1.3.2
Scaling Effects Due to Size Reduction: Hydrodynamics

In order to assess the importance of various physical phenomena relevant to standard and micro-process technology, it is helpful to compare two scenarios of typical processes. In standard process technology, a generic reactor is the stirred vessel which is used for liquid/liquid and gas/liquid reactions. When the goal is to process a gas/liquid mixture, the impeller blades may contain spargers for introduction of gas bubbles. A schematic representation of such a device is shown on the left in Figure 1.14 and a generic micro reactor design on the right. In such a device, either liquid/liquid or gas/liquid reactions can be conducted, depending on the types of fluids fed to the two inlets (gas-phase reactions are not considered in this section). The figure indicates the transport of gas bubbles through the reaction channel. In contrast to the standard process, which is of batch type, the micro reactor allows the fluids to be proceeded in a continuous-flow manner.

In general, a multitude of different phenomena of flow, heat and mass transfer occur during a liquid/liquid or gas/liquid reaction. Rather than discussing all relevant effects, which would be a tremendous task, the focus of this section is solely on flow phenomena in either single-phase aqueous systems or air/water systems. The purpose is to highlight some of the relevant scaling laws to be taken into account when reducing the size of process equipment.

To be specific, a liquid with the properties of water at 20 °C and 1 atm, i.e. a density of $\rho_l = 998.21$ kg m^{-3}, a dynamic viscosity of $\mu_l = 1.002 \cdot 10^{-3}$ Pa s and a surface tension of $\sigma = 72.7 \cdot 10^{-3}$ N m^{-1}, is considered. For the gas, the properties of air under the same conditions are assumed ($\rho_g = 1.188$ kg m^{-3}, $\mu_g = 18.24 \cdot 10^{-6}$ Pa s). The velocity scale u was taken to be 1 m s^{-1} for the stirred vessel and 0.01 m s^{-1} for the micro reactor, and the fluids are assumed to be subject to a gravi-
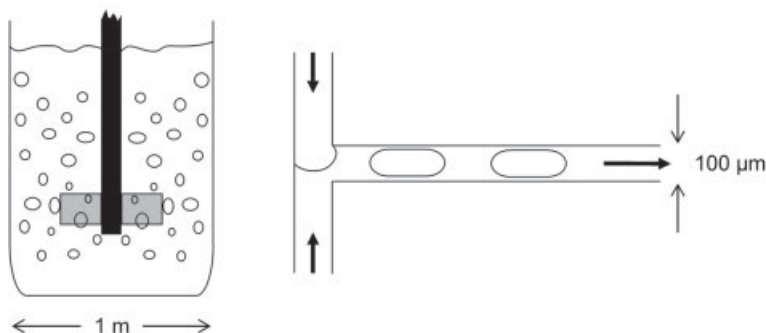

Figure 1.14 Schematic representation of a stirred vessel (left) and a T-shaped micro reactor (right). Both devices can be used for liquid/liquid and for gas/liquid reactions. The length scales indicate typical physical dimensions.

tational acceleration $g = 9.81$ m s^{-2}. The central quantity the present analysis is based on is the relevant length scale L in both types of reactors. For the stirred vessel, a diameter of 1 m is assumed, while the channel diameter of the T-shaped micro reactor is fixed at 100 µm. When gas/liquid flows are considered, a second length scales comes into play, which is the bubble diameter. Characteristic bubble diameters in heavily agitated tanks are about 500 µm [108], whereas in a micro reactor the dimension of the bubbles is typically the same as the channel diameter. Alternatively, the T-shaped micro reactor might also be used to process droplets or slugs instead of bubbles.

In Table 1.3, some of the most important dimensionless groups characterizing the flow in both the standard macroscopic vessel and the micro reactor are listed. If not stated otherwise, the geometric dimensions (1 m and 100 µm) were used as the length scale L. Likewise, the properties of water were normally used to compute the expressions in the second column. The evaluation of the Bond number in the second line shows that in both the macro and micro devices, gravitational forces can usually be neglected when compared with surface-tension forces. However, the Froude number indicates that in these two cases gravitational forces dominate over inertial forces. The product of both numbers gives the Weber number, listed

Table 1.3 Comparison of miscellaneous dimensionless groups characterizing different hydrodynamic regimes in macroscopic vessels and micro reactors.

Name	Formula	Phyical interpretation	Typical macro value	Typical micro value	Comments
Bond number	$Bo = \dfrac{(\rho_l - \rho_g)\, L^2\, g}{\sigma}$	$\dfrac{\text{gravitational force}}{\text{surface-tension force}}$	$3 \cdot 10^{-2}$	$1 \cdot 10^{-3}$	Relevant for bubble (droplet) flows. Length scale: bubble diameter
Capillary number	$Ca = \dfrac{\mu\, u}{\sigma}$	$\dfrac{\text{viscous force}}{\text{surface-tension force}}$	$1 \cdot 10^{-2}$	$1 \cdot 10^{-4}$	Relevant for bubble (droplet) flows
Froude number	$Fr = \dfrac{\rho_g\, u^2}{(\rho_l - \rho_g)\, g\, L}$	$\dfrac{\text{inertial force}}{\text{gravitational force}}$	$2 \cdot 10^{-1}$	$1 \cdot 10^{-4}$	Relevant for bubble (droplet) flows. Length scale: bubble diameter
Reynolds number	$Re = \dfrac{\rho\, L\, u}{\mu}$	$\dfrac{\text{inertial force}}{\text{viscous force}}$	$1 \cdot 10^{6}$	1	
Weber number	$We = \dfrac{\rho_g\, L\, u^2}{\sigma}$	$\dfrac{\text{inertial force}}{\text{surface-tension force}}$	$8 \cdot 10^{-3}$	$2 \cdot 10^{-7}$	Relevant for bubble (droplet) flows. Length scale: bubble diameter

in the last line. Hence, for gas/liquid flows the ranking of surface-tension, gravitational and inertial forces is the same in both types of devices, with surface-tension forces being the most important. Viscous forces, represented by the capillary number, are of about the same importance as gravitational forces in such reactors. Naturally, the perhaps surprising similarities between the macro- and micro reactors disappear when not the gas/liquid interface of the bubbles, but the interface between the bulk liquid and the surrounding gas in the stirred vessel is considered. In that case the relevant length scale is 1 m rather than 500 μm, with the result that gravitational and inertial forces dominate over surface-tension forces.

The most pronounced difference between the stirred vessel and the micro reactor is to be seen in the Reynolds number, which is the ratio of inertial and viscous forces. The Reynolds number is a dimensionless group relevant for both single-phase and two-phase flows. In a macroscopic vessel, viscous forces are usually completely negligible compared with inertial forces. This is no longer true in micro reactors, where both are of the same order of magnitude. As a result, flow in macroscopic devices is turbulent in most cases, whereas usually laminar flows are found in micro devices. This fact bears far-reaching consequences for process modeling. Except for a few special cases, turbulent flows require special heuristic models which incorporate the effects of stochastic velocity fluctuations [109]. The range of validity of these models is often limited and it is often not clear which model is best suited for a specific problem.As a result, the predictive power of, e.g., methods of computational fluid dynamics, is often not sufficient for a rational design of complex macroscopic reactors. In contrast, first-principle modeling techniques can be applied for flow prediction in micro reactors. In this context, the term 'first principle' refers to the fact that the fundamental equations for flow, heat and mass transfer are solved directly, without any reference to heuristic models. Hence, the predictive power of micro reactor models is often higher than their counterparts for macroscopic devices are able to achieve. In such a way, a rational design of micro reactors and even a virtual prototyping process seem within reach.

1.3.3
Chemical Fundaments

The majority of syntheses described in the literature belong to the class of homogeneous organic reactions. These are typical bulk reactions and the underlying chemistry is typically performed at the molecular level. Hence it is not likely that micro channels of a typical size of a few micrometers or more will have an impact on the reaction course, unlike nanometer-sized reaction vessels such as micelles or zeolites, which e.g. may hinder rotation, impact on electron density distribution or change the state of solvent environment. The majority of industrially practised processes belong to heterogeneous reactions, the chemistry of which is also not likely to be changed.

However, it is known that, even when using construction materials only (no functional polymer resin or catalyst), bulk reactions can change to surface reactions with the surface acting as a real 'reactant'. Here, the functional groups of the surface act as reactants. Such findings have only recently been identified (see Section 1.6.10).

1.4
Impact on Chemical Engineering

1.4.1
Basic Requirements on Chemical Engineering from an Industrial Perspective

Arguing from an industrial point of view, Wörz et al. list three basic tasks which an industrial reactor has to fulfil [110–112].

- provision of the residence time needed for reaction
- efficient heat removal or supply
- provision of a sufficiently large interface (for multi-phase reactions)

Wörz et al. describe in detail why micro reactors can give advantages concerning all three tasks [110–112]. They illustrate their analysis by two application examples, concerning a liquid/liquid reaction and a catalyzed gas-phase reaction, both representing industrial chemical production processes.

Note that the tasks defined by Wörz et al., when matched perfectly to the reaction requirements, exactly correspond to the criteria introduced by the BHR Group for defining process intensification (see Section 1.1.6.2). CPC give a similar selection of basic (micro-) reactor tasks [113].

1.4.2
Top-down and Bottom-up Descriptions

The conclusion of Wörz et al. given above is the concentrated result of a number of heuristic bottom-up descriptions, having access to micro-reaction technology, knowing about the corresponding impact on chemical engineering, and selecting by this an application of interest. In total, all these descriptions provide valuable expert opinions and thus are cited in Section 1.4.4. To approach the topic from an industrial and sales view, the study of these conclusions is indispensable. However, the current status of chemical-engineering know-how allows an even more in-depth analysis. Based on a systematic, non-heuristic analysis, a top-down description of the impact of chemical engineering will also be provided. It would be very desirable to have such top-down descriptions also for the process-engineering, chemical, socio-ecologic and economic impacts. However, it stands to reason that the complexity of these topics currently or even hardly ever will not allow such an approach. There is definitely a chance for the first two types of impacts, but more results are needed and an in-depth methodology has to be developed going beyond the scope of this book.

1.4.3
A Top-down Description of Chemical Engineering Impacts

Most of this section is based on the work of Jean-Marc Commenge of CNRS, Nancy, France [114], to whom we are indebted.

1.4.3.1 A Case Study on Gas-phase Reactions

In an economics context, the question has to be raised for which applications micro process technology offers a superior performance to conventional processes. An attempt to answer this question should include various aspects such as reactor efficiency, reliability, maintenance costs, and expenditures for investment and plant operation. However, a complete analysis assessing the benefits and drawbacks of micro process technology in a holistic context has rarely been given. Most reviews are based on a bottom-up approach, describing the achievements of specific operation units and deriving implications for specific applications in chemical engineering. Rather than that, a deductive or top-down approach starts with the requirements related to a specific process and seeks to derive a design allowing one to fulfil these requirements, potentially subject to various constraints and aiming at the minimization of certain cost functions. As an example, the requirement could be to produce a specific quantity of a chemical species per unit time in a continuous-flow process, where a limit on the pressure drop is given and the mole fraction of an undesired by-product should be as small as possible.

One of the most far reaching analyzes along these lines of thought was given by Commenge [114] in the context of gas-phase reactions in continuous-flow processes. Specifically, he analyzed four different aspects of micro reaction devices, namely the *expenditure in mechanical energy*, the *residence-time distribution*, *safety in operation*, and the *potential for size reduction* when the efficiency is kept fixed.

1.4.3.2 Energy Gain from Microstructuring

A standard way of conducting gas-phase reactions in a continuous-flow process is through the use of fixed-bed reactors. A fixed-bed reactor contains a dense packing of catalyst pellets through which the process gas is guided. The chemical species contained in the gas phase diffuse to the pellets and inside their pores where a reaction occurs. Alternatively, a heterogeneously catalyzed gas-phase reaction may be conducted in a micro-channel reactor. In such a set-up, the process gas is guided through a multitude of parallel micro channels which are coated with a catalytically active porous layer. The heat management in corresponding reactors may be done via heating or cooling gas channels, which may be arranged in alternating layers with the micro channels. Alternatively, heating cartridges in thermal contact with the reactor monolith may be employed.

The two different concepts are depicted schematically in Figure 1.15. The fixed bed is assumed to have a cross-section S_F and a height H_F and is filled with non-deformable spherical particles with diameter d_F, where the density of the packing (particles per m^3) is denoted by n_F. The micro-channel reactor has a cross-section S_M and a height H_M and comprises channels of diameter d_M with a specific density (number of channels per m^2) n_M.

In order to compare the micro-channel and the fixed-bed reactor, the design and operation parameters should be adjusted in such a way that certain key quantities are the same for both reactors. One of those key quantities is the porosity ε, defined as the void fraction in the reactor volume, i.e. the fraction of space which is not occupied by catalyst pellets or channel walls. The second quantity is the specific
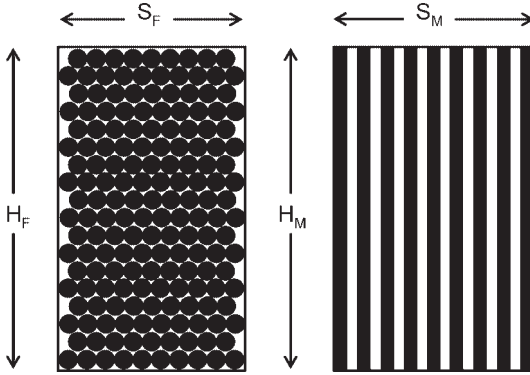
Figure 1.15 Schematic representation of a fixed-bed reactor (left) and a micro-channel reactor (right) [114].

surface area a (surface area/reactor volume), which, in the case of the fixed bed, is defined via the surface area of the catalyst pellets. Finally, the gas flows should be adjusted in such a way that the mean residence time τ is the same for both reactors. Specifically, for equal gas flows, this means that the cross-sections and the heights of the reactors need to be the same. From the equivalence of porosities and specific surface areas, a relation between the pellet size and the micro-channel diameter is obtained:

$$d_F = \frac{3}{2}\frac{1-\varepsilon}{\varepsilon}d_M . \tag{1}$$

For this purpose, cylindrical channels have been assumed. In randomly packed fixed beds the porosity is about 0.4, from which the relationship $d_F = 2.25\,d_M$ is obtained. Since the focus is on heterogeneously catalyzed gas-phase reactions, it is important to not only ensure comparable conditions from a hydrodynamic point of view, but also as far as chemical reaction kinetics is concerned. Therefore, it is assumed that both reactors contain the same amount of catalyst.

In order to verify that the fixed bed and the micro-channel reactor are equivalent concerning chemical conversion, an irreversible first-order reaction $A \rightarrow B$ with kinetic constant k_s was considered. For simplicity, the reaction was assumed to occur at the channel surface or at the surface of the catalyst pellets, respectively. Diffusive mass transfer to the surface of the catalyst pellets was described by a correlation given by Villermaux [115].

$$\frac{k_d\,d_F}{D} = 2 + 1.8\,\mathrm{Re}^{1/2}\,\mathrm{Sc}^{1/3} \tag{2}$$

where k_d denotes the mass transfer coefficient and D the molecular diffusivity of the chemical species. The Reynolds number Re and the Schmidt number Sc are given by

$$\text{Re} = \frac{u\,\rho\,d_{\text{F}}}{\mu}\,; \quad \text{Sc} = \frac{\mu}{D\,\rho}\,, \tag{3}$$

where u, ρ and μ are the velocity, density, and dynamic viscosity of the gas, respectively. In the context of heterogeneously catalyzed reactions, an important quantity characterizing the interplay between reaction and diffusion dynamics is the Damköhler number, defined as

$$\text{Da} = \frac{k_{\text{s}}\,d_{\text{F}}}{D}\,. \tag{4}$$

For fast reactions Da becomes large. Based on that assumption and standard correlations for mass transfer inside the micro channels, both the model for the micro-channel reactor and the model for the fixed bed can be reformulated in terms of pseudo-homogeneous reaction kinetics. Finally, the concentration profile along the axial direction can be obtained as the solution of an ordinary differential equation.

For a specific comparison of the two different reactor types, channels of 300 μm diameter were considered. The equivalent pellet size for that case is 675 μm. As a characteristic quantity, the conversion at the reactor exits was computed for different flow velocities and a range of Damköhler numbers spanning three orders of magnitude. The results for the two different reactor types obtained in such a way were practically indistinguishable. This suggests that the different reactors considered in this study are equivalent as far as chemical conversion is concerned.

In continuous flow systems, the expenditure in mechanical energy necessary to run a process is directly proportional to the pressure drop over the system. Hence the pressure drop is an important figure determining the operating costs of a device. After having verified the chemical equivalence of the two reactor types introduced above, the question arises of whether using a micro-channel reactor instead of a fixed-bed reactor allows a decrease in the pressure drop. In order to estimate the pressure drop in the fixed-bed reactor, the Carman–Kozeny hydraulic diameter model (see, e.g., [116]) was used:

$$\frac{\Delta P}{L} = \frac{36\,h_{\text{k}}\,\mu}{d_{\text{F}}^2}\,\frac{(1-\varepsilon)^2}{\varepsilon^2}\,u \tag{5}$$

where ΔP denotes pressure drop, L the length of the fixed bed, h_{k} the Kozeny coefficient, and u the average gas velocity in the pore system. For the micro-channel reactor, the pressure drop is obtained from the usual Poiseuille flow profile. Accordingly, a comparison of the two reactor types yields

$$\frac{(\Delta P/L)_{\text{F}}}{(\Delta P/L)_{\text{M}}} = \frac{h_{\text{k}}}{2}\,. \tag{6}$$

For a fixed bed of spherical particles, the Kozeny coefficient lies between 4.5 and 5. Hence the pressure drop in the fixed bed is up to 2.5 times larger than that in the micro-channel reactor, for otherwise comparable conditions. This suggests

that micro-structured reactors bear a great potential for energy gain when compared with fixed-bed technology.

1.4.3.3 Residence-time Distributions

When a number of competing reactions are involved in a process, and/or when the desired product is obtained at an intermediate stage of a reaction, it is important to keep the residence-time distribution in a reactor as narrow as possible. Usually, a broadening of the residence-time distribution results in a decrease in selectivity for the desired product. Hence, in addition to the pressure drop, the width of the residence-time distribution is an important figure characterizing the performance of a reactor. In order to estimate the axial dispersion in the fixed-bed reactor, the model of Doraiswamy and Sharma was used [117]. This model proposes a relationship between the dispersive Peclet number:

$$\text{Pe}'_A = \frac{u \, d_F}{D_{A,F}} \tag{7}$$

the modified Reynolds number:

$$\text{Re}' = \frac{\varepsilon \, u \, \rho \, d_F}{\mu} \tag{8}$$

and the Schmidt number. In the definition of the dispersive Peclet number, $D_{A,F}$ denotes an effective diffusion coefficient which contains the effects of axial dispersion in the fixed bed. The relationship is given as

$$\frac{1}{\text{Pe}'_A} = \frac{0.5}{1 + \dfrac{3.8}{\text{Re}' \, \text{Sc}}} + \frac{0.3}{\text{Re}' \, \text{Sc}} \, . \tag{9}$$

For axial dispersion in the micro-channel reactor, the usual relationships from Taylor–Aris theory were employed. In order to assess the performance of both reactor types, the widths of two initially delta-like concentration tracers are compared after they have passed through the flow domain. The results of this comparison are displayed in Figure 1.16.

The figure shows the ratio of the widths of initially delta-like concentration tracers at the reactor exits as a function of the micro-channel Peclet number for different values of the porosity. Taking a value of $\varepsilon = 0.4$ as standard, it becomes apparent that the dispersion in the micro-channel reactor is smaller than that in the fixed-bed reactor in a Peclet number range from 3 to 100. Minimum dispersion is achieved at a Peclet number of about 14, where the tracer width in the micro-channel reactor is reduced by about 40% compared with its fixed-bed counterpart. Hence the conclusion may be drawn that micro-channel reactors bear the potential of a narrower residence time than fixed-bed reactors, where again it should be stressed that reactors with equivalent chemical conversion were chosen for the comparison.
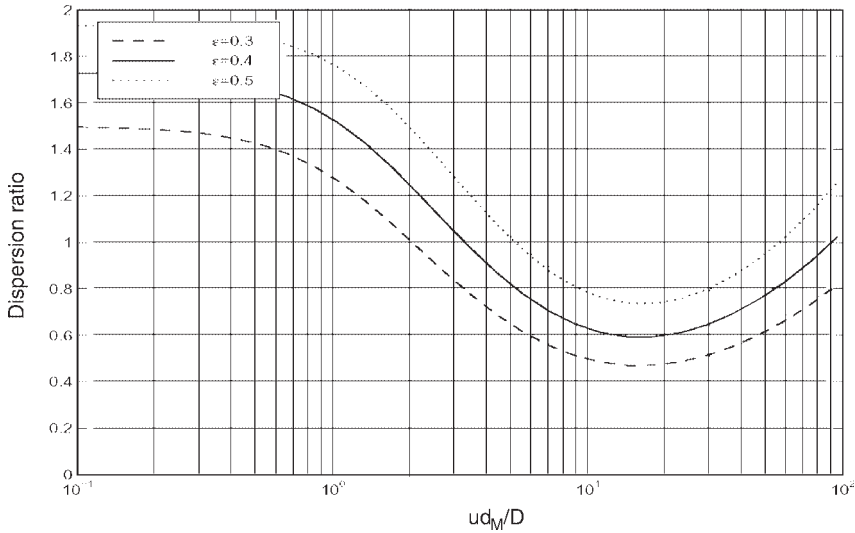
Figure 1.16 Ratio of the width of concentration tracers at the exit of the micro-channel reactor to the corresponding quantity in the fixed-bed reactor as a function of the micro-channel Peclet number $u\,d_{M}/D$, as obtained in [114].

1.4.3.4 Heat Transfer: Safety in Operation

Micro-structured reactors offer a gain in operational safety for at least two different reasons. In the first place, chain reactions may be quenched when molecules of the gas phase collide with the channel walls. In many cases the channel walls may act as a catalyst, with the result that reactions at the surface are different from the reactions occurring in the bulk, or at least the speed of various elementary reactions is modified. In micro devices, the specific surface area is larger than in macroscopic vessels, associated with an increasing importance of surface reactions and, potentially, enhanced safety due to quenching of chain reactions. Secondly, thermal explosions may also be prevented. The driving mechanism behind thermal explosions is a reaction rate rapidly increasing with temperature. However, due to the very efficient heat transfer between the fluid phase and the reactor housing in micro devices, thermal energy may be subtracted so rapidly that a significant temperature rise is avoided and a thermal explosion can be suppressed. The following discussion focuses exclusively on the second effect, since, owing to the variety of possible chain reaction mechanisms, a sufficiently general treatment of such safety hazards does not seem to be feasible.

In the following, the impact of the micro-channel diameter on the temperature rise due an exothermic gas-phase reaction is investigated. For simplicity, a homogeneous reaction A → B of order n with kinetic constant k is considered. Inside the micro channel, the time evolution of the radially averaged species concentration c and temperature T is governed by the equations

$$\frac{dc}{dt} + k\,c^{n} = 0 \tag{10}$$

$$\frac{\mathrm{d}T}{\mathrm{d}t} + \frac{4\,h}{\rho\,d_{\mathrm{M}}\,c_{\mathrm{p}}}\,(T - T_{\mathrm{W}}) = -\frac{k\,c^n\,\Delta H}{\rho\,c_{\mathrm{p}}} \tag{11}$$

where h is the heat transfer coefficient between the fluid and the channel walls, c_{p} the specific heat of the gas, T_{W} the temperature of the wall (assumed to be constant), and ΔH the reaction enthalpy. For the gas passing through the micro channel, the conversion between time and space coordinates is done using the average flow velocity. The temperature dependence of the kinetic constant is given by Arrhenius' law:

$$k = k_0\,\exp\left(-\frac{E_{\mathrm{a}}}{R\,T}\right) \tag{12}$$

where k_0 is a pre-exponential factor, E_{a} the activation energy, and R the gas constant. The temperature rise in the channel due to the chemical reaction is governed by two different time-scales, a reaction time-scale t_{r} and a heat-exchange time-scale t_{he}:

$$t_{\mathrm{r}} = \frac{1}{k_0\,\exp\left(-\dfrac{E_{\mathrm{a}}}{R\,T_{\mathrm{W}}}\right)}\;;\quad t_{\mathrm{he}} = \frac{\rho\,d_{\mathrm{M}}\,c_{\mathrm{p}}}{4\,h}\,, \tag{13}$$

where a first-order reaction was assumed.

When t_{he} is large compared with t_{r}, the reaction gas can be heated considerably before the heat is subtracted through the reactor housing. In the opposite case, hardly any temperature rise is observed, since heat is removed rapidly through the channel walls.

In order to derive specific numbers for the temperature rise, a first-order reaction was considered and Eqs. (10) and (11) were solved numerically for a constant-density fluid. In Figure 1.17 the results are presented in dimensionless form as a function of $t_{\mathrm{r}}/t_{\mathrm{he}}$. The y-axis represents the temperature rise normalized by the adiabatic temperature rise, which is the increase in temperature that would have been observed without any heat transfer to the channel walls. The curves are differentiated by the activation temperature, defined as $T_{\mathrm{a}} = E_{\mathrm{a}}/R$. As expected, the temperature rise approaches the adiabatic one for very small reaction time-scales. In the opposite case, the temperature rise approaches zero. For a non-zero activation temperature, the actual reaction time-scale is shorter than the one defined in Eq. (13), due to the temperature dependence of the exponential factor in Eq. (12). For this reason, a larger temperature rise is found when the activation temperature increases.

In order to show how specific guidelines for the reactor layout can be derived, the maximum allowable micro-channel radius giving a temperature rise of less than 10 K was computed for different values of the adiabatic temperature rise and different reaction times. For this purpose, properties of nitrogen at 300 °C and 1 atm and a Nusselt number of 3.66 were assumed. The Nusselt number is a dimensionless heat transfer coefficient, defined as

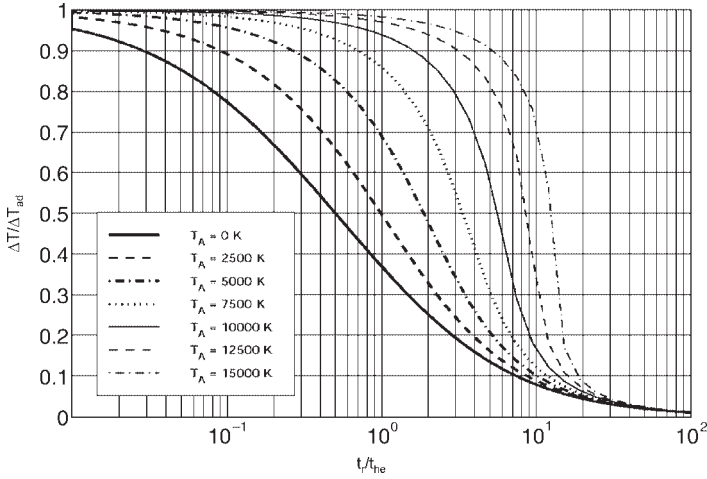$$\mathrm{Nu} = \frac{h\,d_{\mathrm{M}}}{\lambda} \tag{14}$$

Figure 1.17 Normalized temperature rise for a first-order exothermic reaction as a function of the ratio of reaction and heat-exchange time-scale, obtained from [114]. Different activation temperatures are considered.

where λ is the thermal conductivity. Furthermore, the activation energy was set to zero. The results of that calculation are depicted in Figure 1.18. Each curve corresponds to a fixed channel radius, ranging from 100 μm to 1 mm, and a calculated temperature rise of 10 K. The plane is spanned by the adiabatic temperature rise
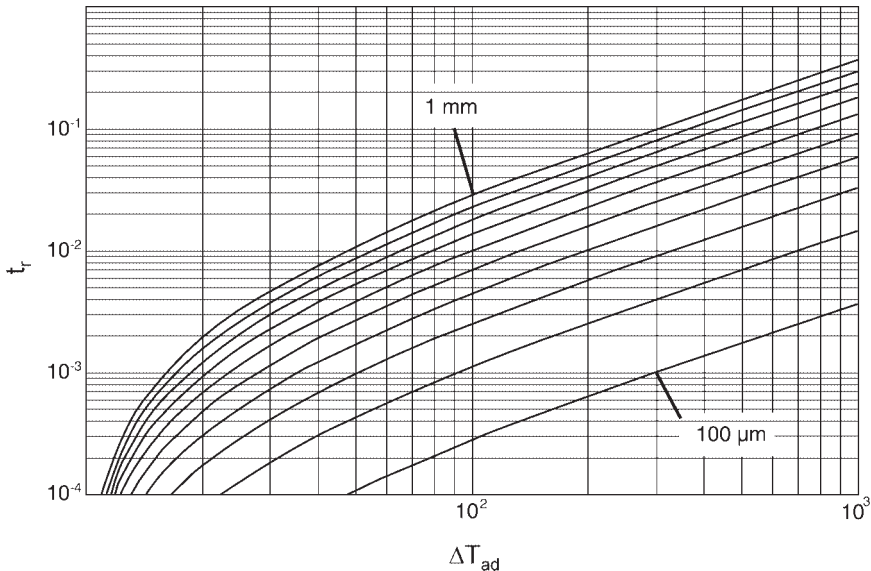
Figure 1.18 Lines of constant temperature rise ($\Delta T = 10$ K) for micro channels of different radius in a plane spanned by the adiabatic temperature rise of the reaction and the reaction time-scale, obtained from [114]. The properties of nitrogen at 300 °C and 1 atm and a Nusselt number of 3.66 were used for this calculation.

(*x*-axis) and the reaction time-scale (*y*-axis). When one of the two criteria is relaxed, i.e. either the reaction time-scale is increased or the adiabatic temperature rise is reduced, successively larger channel diameters are sufficient to limit the temperature rise to 10 K.

In order to exemplify the potential of micro-channel reactors for thermal control, consider the oxidation of citraconic anhydride, which, for a specific catalyst material, has a pseudo-homogeneous reaction rate of $1.62 \ \mathrm{s}^{-1}$ at a temperature of 300 °C, corresponding to a reaction time-scale of 0.61 s. In a micro channel of 300 µm diameter filled with a mixture composed of N_2/O_2/anhydride (79.9 : 20 : 0.1), the characteristic time-scale for heat exchange is $1.4 \cdot 10^{-4}$ s. In spite of an adiabatic temperature rise of 60 K related to such a reaction, the temperature increases by less than 0.5 K in the micro channel. Examples such as this show that micro reactors allow one to define temperature conditions very precisely due to fast removal and, in the case of endothermic reactions, addition of heat. On the one hand, this results in an increase in process safety, as discussed above. On the other hand, it allows a better definition of reaction conditions than with macroscopic equipment, thus allowing for a higher selectivity in chemical processes.

1.4.3.5 Potential for Size Reduction

On shrinking the size of micro-channel reactors by reducing the channel dimensions, a number of characteristic quantities such as pressure drop and the degree of chemical conversion are affected. In order to permit a meaningful comparison of the reactor geometry with a scaled geometry, it is important to keep one or a few key quantities fixed and study the influence of size reduction on the remaining quantities. One strategy is to compare reactors with equal efficiency for heat exchange or chemical conversion. In order to study the problem in a generalized framework, it is helpful to define a characteristic time-scale τ_{op} for specific operations such as heat exchange or reaction. A process can be characterized by its number of transfer units

$$NTU = \frac{\tau}{\tau_{op}} \qquad (15)$$

where $\tau = L/u$ is the mean residence time in the reactor, defined via the channel length L and the average velocity u. When the number of transfer units is kept fixed, the efficiency of a reactor for specific operations, for example heat transfer or chemical conversion, is also fixed. Comparing reactors of different scales with fixed chemical efficiency ensures that the product concentrations at the channel exits are the same.

In Table 1.4, the characteristic time-scales for selected operations are listed. The rate constants for surface and volume reactions are denoted by k_s and k_v, respectively. Furthermore, the Sherwood number Sh, a dimensionless mass-transfer coefficient and the analogue of the Nusselt number, appears in one of the expressions for the reaction time-scale. The last column highlights the dependence of τ_{op} on the channel diameter d_M. Apparently, the scale dependence of different operations varies from $(d_M)^0$ to $(d_M)^2$. Owing to these different dependences, some op-

Table 1.4 Characteristic time-scale and length scale-dependence for selected operations [114].

Type of operation	Characteristic time-scale τ_{op}	Dependence on channel diameter
Heat exchange	$\dfrac{\rho\, c_p\, (d_M)^2}{4\, \lambda\, \mathrm{Nu}}$	$\sim (d_M)^2$
Heterogeneously catalyzed reaction		
• Diffusion limited	$\dfrac{(d_M)^2}{4\, D\, \mathrm{Sh}}$	$\sim (d_M)^2$
• Reaction-rate limited	$\dfrac{d_M}{4\, k_s}$	$\sim d_M$
Homogeneous reaction	$\dfrac{1}{k_v}$	constant

erations are better suited for miniaturization than others, as will be discussed in the following.

In cases where the operation time-scale is independent of the channel diameter, as for a homogeneous reaction, it is necessary to keep the residence time fixed when downscaling a reactor in order keep the efficiency constant. When the flow-rate Q_{tot} of the process gas is given, this means that a reduction in the channel diameter has to be accompanied by an increase in the channel length L or the number of channels N, according to

$$N\, L\, (d_M)^2 \;=\; \text{constant} \tag{16}$$

More favorable for miniaturization are processes with an operation time-scale proportional to d_M or $(d_M)^2$. For a linear dependence on the channel diameter, the product $N\, L\, d_M$ is conserved under the conditions described above. This means that with shrinking d_M and for fixed efficiency, the reactor volume decreases proportionally with the channel diameter. For a quadratic dependence of the operation time-scale with channel diameter, the product $N\, L$ is conserved and the reactor volume decreases as the channel diameter squared.

In some cases, it may not be desirable to reduce the volume of a reactor, and rather a decrease of pressure drop or channel length may be the goal. In Table 1.5, the dependence of several characteristic quantities on channel diameter is given, where the efficiency and at least one specific quantity is kept fixed in each line.

The comparison given above shows that a reduction in channel dimensions offers some substantial benefits in cases where surface reactions are involved or efficient heat and mass transfer are needed. One important conclusion to be drawn is that a decrease in the channel diameter at fixed efficiency does not necessarily mean an increase in pressure drop. Rather, the pressure drop can be kept constant

Table 1.5 Dependence of the number of micro channels N, their length L, the cross-sectional area of the reactor S and the pressure drop ΔP on the micro-channel diameter, when the efficiency (i.e. a fixed number of transfer units) and at least one specific characteristic quantity are kept fixed in each line. Three cases with operation time-scales varying as $(d_M)^0$, d_M, and $(d_M)^2$ are considered [114].

τ_{op}	τ	V	N	L	S	ΔP
constant	constant	constant	constant	$\sim(d_M)^{-2}$	$\sim(d_M)^2$	$\sim(d_M)^{-6}$
			$\sim(d_M)^{-2}$	constant	constant	$\sim(d_M)^{-2}$
			$\sim(d_M)^{-3}$	$\sim d_M$	$\sim(d_M)^{-1}$	constant
$\sim d_M$	$\sim d_M$	$\sim d_M$	constant	$\sim(d_M)^{-1}$	$\sim(d_M)^2$	$\sim(d_M)^{-5}$
			$\sim(d_M)^{-1}$	constant	$\sim d_M$	$\sim(d_M)^{-3}$
			$\sim(d_M)^{-2}$	$\sim d_M$	constant	$\sim(d_M)^{-2}$
			$\sim(d_M)^{-5/2}$	$\sim(d_M)^{3/2}$	$\sim(d_M)^{-1/2}$	constant
$\sim(d_M)^2$	$\sim(d_M)^2$	$\sim(d_M)^2$	constant	constant	$\sim(d_M)^2$	$\sim(d_M)^{-4}$
			$\sim(d_M)^{-2}$	$\sim(d_M)^2$	constant	constant

when the number of channels is increased, while still reducing the total reactor volume [for operation time-scales proportional to d_M and $(d_M)^2$]. At the same time, the channel length decreases. When accepting a constant or only slightly decreasing reactor volume, the pressure drop can even be reduced. However, it should be kept in mind that for a large number of micro channels the flow distribution manifold itself might occupy a considerable volume.

In practice, the process regime will often be less transparent than suggested by Table 1.4. As an example, a process may neither be diffusion nor reaction-rate limited, rather some intermediate regime may prevail. In addition, solid heat transfer, entrance flow or axial dispersion effects, which were neglected in the present study, may be superposed. In the analysis presented here only the leading-order effects were taken into account. As a result, the dependence of the characteristic quantities listed in Table 1.5 on the channel diameter will be more complex. For a detailed study of such more complex scenarios, computational fluid dynamics, to be discussed in Section 2.3, offers powerful tools and methods. However, the present analysis serves the purpose to differentiate the potential inherent in decreasing the characteristic dimensions of process equipment and to identify some cornerstones to be considered when attempting process intensification via size reduction.

1.4.3.6 Proposing a Methodology for Micro-reactor Dimensioning and Layout

In the following, a methodology is derived allowing dimensioning of a micro-channel reactor according to specifications and requirements of a specific process which should be implemented on a micro-reactor platform. The methodology rests on the assumptions made in the previous paragraphs. Specifically, gas-phase reactions are considered. It should be pointed out that in general the micro reactor is

only a sub-unit in a more complex set up. The question of global process design is still more involved, with a complex interdependence between the performance of the sub-units and that of the complete system. In an immediate manner, the present analysis can only give hints on the dimensioning of a single multi-channel reactor and not on the design of a complex plant. However, as the component and the system level are closely intertwined, it is hoped that this analysis also contains some valuable information for the process designer.

Step 1: Dimensioning of the channel diameter
The micro-channel diameter d_M plays a crucial role for heat and mass transfer. When chemical reactions are involved, the channel diameter should be chosen small enough to render the time-scales for heat and mass transfer smaller than the reaction time-scale. A listing of the most relevant time-scales is provided in Table 1.6, where the crosses indicate for which step of the design process the time-scales play a role. In addition to heat- and mass-transfer limitations, there might be constraints on the maximum allowable temperature change in the channel. Hence the adiabatic temperature rise of the reaction also has to be taken into account. A dimensioning of the channel diameter along these lines might result in either very wide or very narrow channels. Wide channels may not give a satisfactory flow equipartition from the distribution manifold to the multi-channel reactor. In that case, the channel diameter may be decreased beyond the limits derived from heat- and mass-transfer considerations. On the other hand, very narrow channels may induce a prohibitive pressure drop. In that case, the number of micro channels could be increased.

Step 2: Dimensioning of the channel length
After the channel diameter has been fixed, the length of the channels has to be determined. Usually in a process, the number of transfer units as defined in Eq. (15) is fixed, which means that the residence time in the micro channel has to be considered as given. Via the equation $\tau = L/u$ this induces a relationship between the channel length and the flow velocity The average flow velocity can be determined be demanding that the broadening of a concentration tracer while being transported through the channel is as small as possible. Based on the expression for the axial dispersion coefficient obtained from Taylor–Aris theory, it is easy to show that this occurs at a Peclet number of $8\sqrt{3}$. With a correspondingly adjusted flow velocity and a given value for the residence time, the channel length can be determined. Again, it should be noted that channel dimensions derived from that rationale may lead to an elevated pressure drop. In such cases, a compromise between narrow residence-time distributions and a low pressure drop should be envisaged.

Step 3: Dimensioning of the channel walls
During the time the process gas spends in a micro channel, heat is transferred from the gas to the channel walls or vice versa. If in an exothermic reaction the time-scale for heat conduction in the channel walls is larger than the residence time of the fluid, considerable temperature gradients will build up along the walls

and an isothermicity assumption will not be valid. Hence, in the case of predominantly longitudinal heat transfer, it is advisable to adjust the heat conduction time-scale in a proper way by providing channel walls of sufficient thickness. In a dynamic regime where temperature ramping becomes important (e.g. for start-up), it is advisable to take into account the time-scale for reactor heat-up which reflects the thermal inertia due to the heat capacity of the construction material.

Step 4: Determining the number of micro channels

After the channel diameter and length and the flow velocity have been fixed, the number of micro channels determines the total throughput and product yield. In applications focused on chemical production, the number of channels is then simply given by throughput requirements. In applications focused on research and development, such as kinetic measurements, a small number of channels might be preferable, since flow equipartition and data analysis can be more difficult when the number of channels is large.

Table 1.6 Characteristic quantities to be considered for micro-reactor dimensioning and layout. Steps 1, 2, and 3 correspond to the dimensioning of the channel diameter, channel length and channel walls, respectively. Symbols appearing in these expressions not previously defined are the effective axial diffusion coefficient D_A, the density ρ_w, thermal conductivity λ_w, specific heat $c_{p,w}$ and total cross-sectional area S_w of the wall material, the total process gas mass flow $\dot{m}$, and the reactant concentration c_0 [114].

Quantity	Expression	Step 1	Step 2	Step 3
Residence time	$\dfrac{L}{u}$		×	
Heat-exchange time-scale	$\dfrac{\rho\, c_p (d_M)^2}{4\,\lambda\, Nu}$	×		
Radial diffusion time-scale	$\dfrac{(d_M)^2}{4\,D}$	×	×	
Axial diffusion time-scale	$\dfrac{L^2}{D_A}$		×	
Time-scale of homogeneous reaction (1st order)	$\dfrac{1}{k_v}$	×	×	
Time-scale of heterogeneous reaction (1st order)	$\dfrac{d_M}{4\,k_s}$	×	×	
Time-scale for reactor heat-up	$\dfrac{\rho_w\, c_{p,w}\, S_w\, L}{\dot{m}\, c_p}$			×
Time-scale for longitudinal heat conduction	$\dfrac{S\, L^2\, \rho_w\, c_{p,w}}{S_w\, \lambda_w}$			×
Adiabatic temperature rise	$\dfrac{\Delta H\, c_0}{\rho\, c_p}$	×		

Step 5: Layout of the flow distribution system

When the number of micro channels is fixed, a flow distribution system for feeding the process gas to the different channels has to be devised. A major requirement for such a system is a narrow residence-time distribution. There are in principle two different ways in which a flow distribution system can effect a broadening of the residence time distribution. First, if flow equipartition over the multi-channel domain cannot be achieved, the mean flow velocities and thus the residence times vary over the different channels. Secondly, the flow distribution system itself may induce a considerable broadening of the residence-time distribution, for example when recirculation zones are present. Among the design concepts for a distribution manifold are a comparatively wide flow coupler interfacing with the inlet and the multi-channel domain, and a tree-like network with successive bifurcations. In the first case, flow equipartition is achieved via the large pressure barrier of the micro channels. In the second case, the geometry of the flow distribution network itself ensures an equipartition over the micro channels. When the number of channels is very large, it may be preferable to split a reactor into various sub-units. In that case, flow equipartition is a two-level problem: first, the flow is distributed between the different sub-units, followed by a distribution manifolds feeding the multi-channel flow domain.

1.4.4

A Bottom-up Description of Chemical Engineering Impacts

1.4.4.1 **Mixing**

The increase in mass transfer by micro-channel processing is frequently cited in the literature [5].

Confined flows typically exhibit laminar-flow regimes, i.e. rely on a diffusion mixing mechanism, and consequently are only slowly mixed when the diffusion distance is set too large. For this reason, in view of the potential of microfabrication, many authors pointed to the enhancement of mass transfer that can be achieved on further decreasing the diffusional length scales. By simple correlations based on Fick's law, it is evident that short liquid mixing times in the order of milliseconds should result on decreasing the diffusion distance to a few micrometers.

In many cases, speed-up of mixing by miniaturization is achieved by lamellar flow configurations. When the width of the fluid lamellae is reduced, the diffusional length scale decreases and mixing is speeded up. In order to increase the mixing speed even further, hydrodynamic focusing can be employed to create fluid lamellae of a width even smaller than defined by the inlet geometry of a mixer [118]. When a high throughput is required, several lamellar streams are usually combined, giving periodic multi-lamellar arrangements (see Figure 1.19) [119, 120]. As an alternative to multi-lamellar mixers, a number of other concepts have been developed. In split–recombine mixers, two fluid streams are successively split and recombined in such a way that, at least in an ideal situation, multi-lamellar arrangements are created [121]. In another class of mixing devices, channels with corrugated walls, recirculating flows are induced which increase the mixing effi-
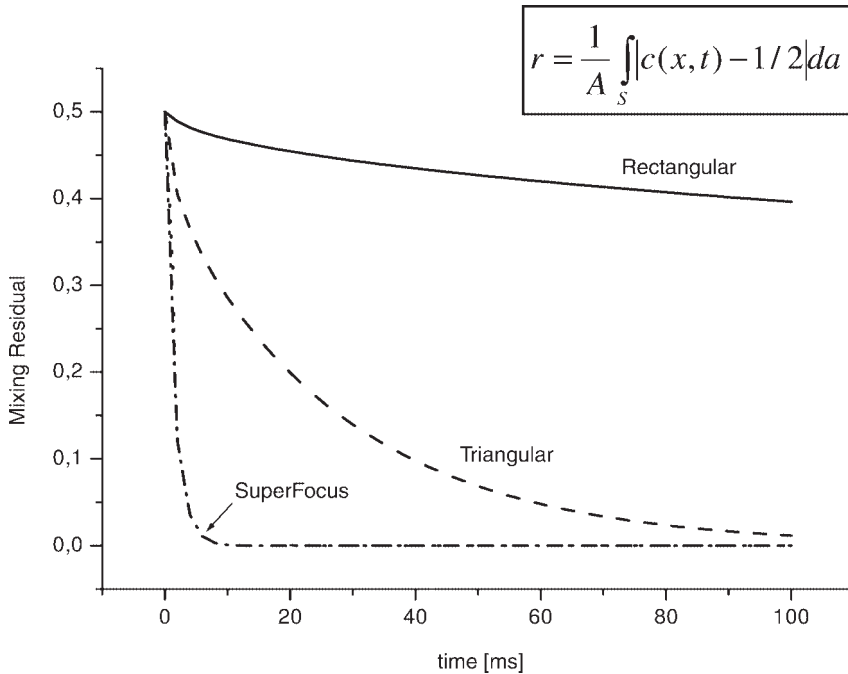
$$r = \frac{1}{A}\int_S |c(x,t) - 1/2| da$$

Figure 1.19 Semi-analytical calculation of the speed of mixing in an advanced interdigital micro mixer, named SuperFocus, and comparison with previously developed interdigital micro mixers [120].

ciency beyond the value found for two co-flowing, parallel lamellae [122]. Even in the laminar regime, chaotic flow patterns can be induced by superposing different vortex structures in channel flow. It has been shown that such chaotic micro mixers are very efficient at low Reynolds numbers [123]. Some micro-mixing principles have been proven to be much faster than the mixing observed in large-scale vessels or even in many specialized high-speed mixers (see, e.g., [3, 107, 124]).

Apart from this enhancement of mixing speed, a very uniform spatial distribution of mixing is typically achieved with micro mixers. Due to the laminar flow patterns, the flow field is uniquely determined in every part of the domain. As shown in Figure 1.20, a uniform mixing quality can be attained by multiply repeated flow geometries created by repetition of a unit flow cell. With suitable provisions taken, a very narrow mixing-time distribution is found in micro mixers. This stands in contrast to the turbulent flow characteristic of macroscopic equipment, accompanied by a chaotic velocity field with stochastic fluctuations. The turbulent vortices, the so-called eddies, occur on various length scales and with different intensity [125]. The eddies effect a stretching and folding of liquid volumes, finally creating very thin lamellae which mix by diffusion. Due to the stochastic nature of that process and variations of turbulence intensity, turbulent mixing is not uniform and displays a comparatively broad distribution of mixing times.
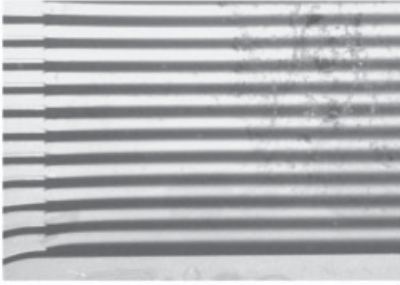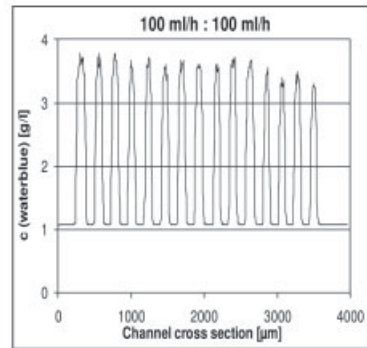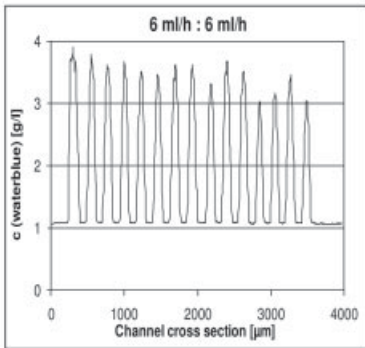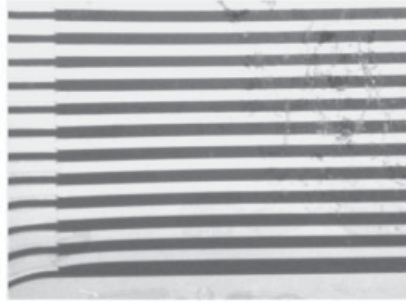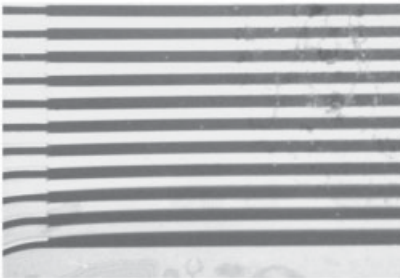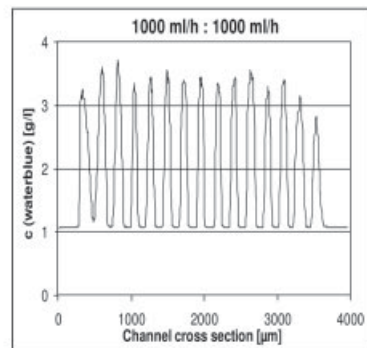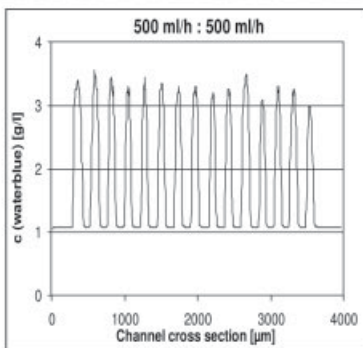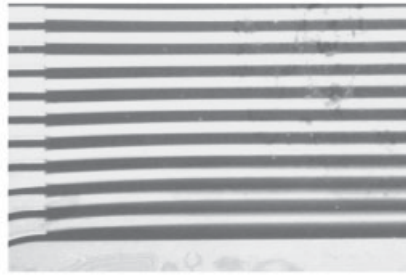
Figure 1.20 Periodic concentration profile of a regular multi-lamellar pattern in a rectangular interdigital micro mixer, determined by photometric-type analysis [119].

The spatio-temporal variations of the concentration field in turbulent mixing processes are associated with very different conditions for chemical reactions in different parts of a reactor. This scenario usually has a detrimental effect on the selectivity of reactions when the reaction time-scale is small compared with the mixing time-scale. Under the same conditions (slow mixing), the process times are increased considerably. Due to mass transfer inhibitions, the true kinetics of a reaction does not show up; instead, the mixing determines the time-scale of a process. This effect is known as mixing masking of reactions [126].

Mixing-masked reactions should develop differently when processed by conventional and micro mixers, for reasons of both global mixing speed and associated spatio-temporal concentration evolution. For instance, different solvent environments may be generated for a short period, impacting on the reactant strength, e.g. on the nucleophilicity or base strength of nucleophiles or on the electron distribution of aromatics. This will affect side reactions or even the nature of the product itself, e.g. by determining the position of reaction at a multi-functional target molecule or the atom moiety that actually attacks a bivalent reactant (for instance, by attack of the C or N moiety for CN^- anions, giving either nitriles or isonitriles) [126].

Mixing masking, i.e. influences of micro mixing on the reaction course, has been determined for a number of reactions, including azo coupling as a prominent process [126]. Since the selectivity of organometallic reactions is known to be particularly sensitive to the feed ratio of the reactants, a deliberate variation of global feed ratios was performed using micro mixers in an industrial study. It was found that the contribution of side reactions increased steeply on moving away from the ideal reactant ratio [11].

Speed-up of mixing is known not only for mixing of miscible liquids, but also for multi-phase systems the mass-transfer efficiency can be improved. As an example, for a gas/liquid micro reactor, a mini packed-bed, values of the mass-transfer coefficient $K_L a$ were determined to be 5–15 s^{-1} [2]. This is two orders of magnitude larger than for typical conventional reactors having $K_L a$ of 0.01–0.08 s^{-1}. Using the same reactor filled with 50 μm catalyst particles for gas/liquid/solid reactions, a 100-fold increase in the surface-to-volume ratio compared with the dimensions of laboratory trickle-bed catalyst particles (4–8 mm) is found.

1.4.4.2 Heat Transfer

The increase in heat transfer by micro-channel processing is frequently cited in the literature [5]. A number of authors cite overall heat-transfer coefficients, which serve to underline the high efficiency of heat transfer in micro-channel devices. The highest one measured so far was reported by Brandner et al. using micro-fin heat exchangers, amounting to 56 000 W m^{-2} K^{-1} using water as test fluid [23]. Heating rates may be another figure of merit to make evident the high thermal performance of micro devices. A heating rate of 680 000 K s^{-1} was reported for gas streams heated to 850 °C [23].

One of the most often cited advantages of micro reactors is their prevention of hot spots by strongly enhanced heat dissipation. Hence higher dosing of reactants, i.e. higher reactant concentration and/or higher catalyst loading, may be possible

Table 1.7 Numerical example illustrating the increased heat transfer on miniaturization of industrial reactors [110].

Scale of reactor	Typical volume/typical internal dimension	Normalized specific surface
Production	30 m^3	1
Laboratory	1 l = 10^{-3} m^3	30
Micro	30 μm	3000

when dealing with exothermic reactions [124], thereby enhancing productivity. Also for endothermic reactions, improved heating may be advantageous, since thermal ramping can be achieved faster, reducing the pre-heating time to a minimum and avoiding overshoots. In contrast, the slower heating for conventional equipment can lead to undesired side products [124]. For a methane chlorination reaction, the origin of this is seen in a more undefined radical formation during the slower thermal ramping, having in addition a thermal overshoot [127].

For oxidative propane dehydrogenation in a fixed bed, hot spots ranging from 3 to 100 K were detected [128, 129]. Even when using diluted gases, the hot spots were as large as 20 K. Using the micro-channel reactor, isothermal processing was achievable for nearly all conditions applied, giving a maximum temperature increase of 2 K [128, 129].

Wörz et al. give a numerical example to illustrate the much better heat transfer in micro reactors [110–112]. Their treatment referred to the increase in surface area per unit volume, i.e. the specific surface area, which was accompanied by miniaturization. The specific surface area drops by a factor of 30 on changing from a 1 l laboratory reactor to a 30 m^3 stirred vessel (Table 1.7). In contrast, this quantity increases by a factor of 3000 if a 30 μm micro channel is used instead. The change in specific surface area is 100 times higher compared with the first example, which refers to a typical change of scale from laboratory to production.

Wörz et al. stress the possibility of carrying out very fast reactions with large reaction heat in micro reactors [110]. They often use the terms 'isothermal operation' or 'isothermicity' to describe adequately the carrying out of a reaction with a heat that is taken out of the processing volume immediately upon release. In practice, they often refer to a temperature increase of 1–2 °C as a limit for fulfilling the criterion of isothermal operation.

1.4.4.3 Microfluidics

The key attribute of flows in micro devices is their laminar character, which stands in contrast to the mostly turbulent flows in macroscopic process equipment. Owing to this feature, micro flows are *a priori* much more accessible to a model description than macro flows and can be described by first-principle approaches without any further assumptions. In contrast, for the simulation of turbulent flows usually a number of semi-heuristic models are applied, and in many situations it is not clear which description is most adequate for the problem under investigation. As a result, it stands to reason to assume that a rational design of micro reactors

based on simulation approaches is in some sense more realistic than for their macroscopic counterparts.

Apart from obvious features such as laminarity, there are speculations that flows in micro channels exhibit a behavior deviating from predictions of macroscopic continuum theory. In the case of gas flows, these deviations, manifesting themselves as, e.g., velocity slip at solid surfaces, are comparatively well understood (for an overview, see [130]). However, for liquid flows on a length scale above 1 µm, there is no clear theoretical foundation for deviations from continuum behavior. Nevertheless, various unexpected phenomena such as friction factors deviating from the continuum prediction [131–133] have been reported. A more detailed discussion of this still unsettled matter is given in Section 2.2. At any rate, one has to be careful here since it may be that measurements in small systems lack precision, essentially because of the incompatibility of analysis in a confined space and with large measuring equipment.

1.4.5
Fouling

Wegeng et al. mentioned fouling as a major problem, decreasing micro-fluidic system reliability [1]. Active control over fouling was demanded in their review, but no strategies to overcome it were given.

Hessel and Löwe state that fouling is a term which is only said in a whisper among 'micro chemical engineers' [9, 10]. Nonetheless, there is no denying of the fact that it is a frequent experience during handling of microfluidic components. The impact of fouling in micro reactors is over- and underestimated concurrently, this statement not being contradiction as it includes the opinions of different parties. Fouling still attracts too little attention in the technical–scientific exploration of micro systems. It is observed mainly when processing is not sufficiently adapted to the needs of fluid operation in micro channels. By choice of proper parameters, laboratory operation (i.e. from several tens of minutes to hours) of micro reactors becomes possible in many cases and hence usually does not pose a problem. For selected, albeit so far only a few, processes, considerably longer operation times have been achieved up to processing times that are demanded for chemical production.

In some cases, a simple increase in characteristic dimensions is sufficient to suppress micro-channel plugging [9, 10]. In the first euphoria about the new technical capabilities, miniaturization of processing equipment was possibly flogged to death. The motto therefore is: *as small as (beneficially) needed, but not as small as possible*.

As a kind of specialty solutions for the real 'hard' cases where fouling is intense and unavoidable, IMM first proposed ideas to develop special micro mixers for fouling-intense reactions and conducted feasibility tests, among them very fast organic reactions with spontaneous precipitation such as the amidation of acetyl chloride in THF [134]. The Forschungszentrum Karlsruhe developed special anti-fouling coatings in cooperation with partners [135].

1.5
Impact on Process Engineering

1.5.1
Laboratory-scale Processing

1.5.1.1   Provision of a Multitude of Innovative Reactor Designs

Jensen stresses the great flexibility in reactor design that can be achieved by means of microfabrication, in particular when parallel, MEMS-based mask processes are followed, having a multitude of miniature designs on one mask [75]. This should '... invigorate the innovative nature of reactor design ...' and allow one to overcome '... the tedium of stirred tanks, and tubular and trickle bed reactors'. Micro-chemical engineering as such an approach will probably not only provide many more reactors of different, distinct designs, but will also facilitate their testing and to modeling. If this can be put in an optimization loop, it stands to reason that much better performing reactor designs than we know now will become available. How this may be achieved was also shown by Jensen et al., who have provided an idea of an advanced test station where many micro reactors can be tested in parallel [19].

1.5.1.2   Quality of Information – More Accurate and In-depth

Another implication of micro reactors for chemical-process engineering involves the provision of accurate, in-depth and reliable experimentation data. This is exemplarily discussed for high-throughput screening.

   Micro reactors permit high-throughput screening of process chemistries under controlled conditions, unlike most conventional macroscopic systems [2]. In addition, extraction of kinetic parameters from sensor data is possible, as heat and mass transfer can be fully characterized due to the laminar-flow conditions applied. More uniform thermal conditions can also be utilized. Further, reactor designs can be developed in this way that have specific research and development functions.

1.5.1.3   Quantity of Information – Speed of Experimentation

Besides quality of information, quantity of data still is a decisive factor in laboratory-scale development.

   Following in the footprints of screening for drug discovery, the smallness of micro reactors recommends their use for high-throughput testing [2]. Today's laboratory testing suffers from high costs of reactants and safety concerns. In addition, the introduction of new ideas is hindered by the risk and high capital costs of scale-up, once a lead candidate has been found by laboratory testing. Micro reactors have the potential to overcome pilot-scale testing and redesign. This should be of particular advantage if only small quantities are produced, such as for the pharmaceutical industry. This allows scheduled, gradual investment in new chemical production facilities.

1.5.1.4 **Shrinkage of Total System**

One implication of micro reactors on chemical-process engineering concerns the shrinkage of the total system. This is exemplarily discussed for catalyst testing.

For catalyst testing, conventional small tubular reactors are commonly employed today [2]. However, although the reactors are small, this is not the case for their environment. Large panels of complex fluidic handling manifolds, containment vessels, and extended analytical equipment encompass the tube reactors. Detection is often the bottleneck, since it is still performed in a serial fashion. To overcome this situation, there is the vision, ultimately, to develop PC-card-sized chip systems with integrated microfluidic, sensor, control, and reaction components [2]. The advantages are less space, reduced waste, and fewer utilities.

1.5.1.5 **Integratability of Sensing and Other Functions**

Jensen highlights the potential of integrating multiple functions in one small micro reactor. In this context, he suggests that micro-reactor engineering must go beyond exploiting high transport rates due to their small dimensions, and rather integrate sensing and separation functions [75]. He points out, 'It was the integrated circuit that created the microelectronics revolution, not the transistor itself". With increased integration, packaging rather than only microstructuring becomes the issue.

Concerning function integration, for example, micro-flow membrane reactors can exhibit similar process intensification, as shown already for their large-scale counterparts [75]. Separation columns for proteomics, immobilizing enzymes, utilize the large surface-to-volume ratios. Surface tension differences can guide and transport liquids selectively.

To realize micro reactors with sensing and surface-control structures, the underlying fabrication methods have to go beyond MEMS and classical micro machining [75]. Plastic and glass manufacture and also novel innovative methods such as soft lithography have to be developed further and applied.

Hessel and Löwe agree on the need of future micro-sensor development, but in a kind of state-of-the-art analysis also discuss today's solutions for monitoring of micro-channel flow [9, 10]. The integration of appropriate conventional sensing, e.g. for temperature monitoring, is a non-ideal but practical, simple solution. The simple transition from a non-transparent to a glass material allows visual inspection of the processing for the operator. A multitude of information is supplied by this smart change without a newly integrated sensing function.

As an alternative to both classical sensing and integration of micro sensors, they also provide examples of contact-free in-line measurements of temperature or concentration, e.g. to characterize transport processes in micro reactors, using advanced, conventional apparatus (Figure 1.21) [9, 10]. Having this in mind, Hessel and Löwe argue in favor of caution when dealing with sensing/monitoring solutions. They come to the conclusion that new developments are definitely desired, albeit we do not need them for every problem. There is no reason why pressure determination, for example, could not still be done in a classical way. The advantages of micro-sensor-based pressure measurements are, at least, not obvious.
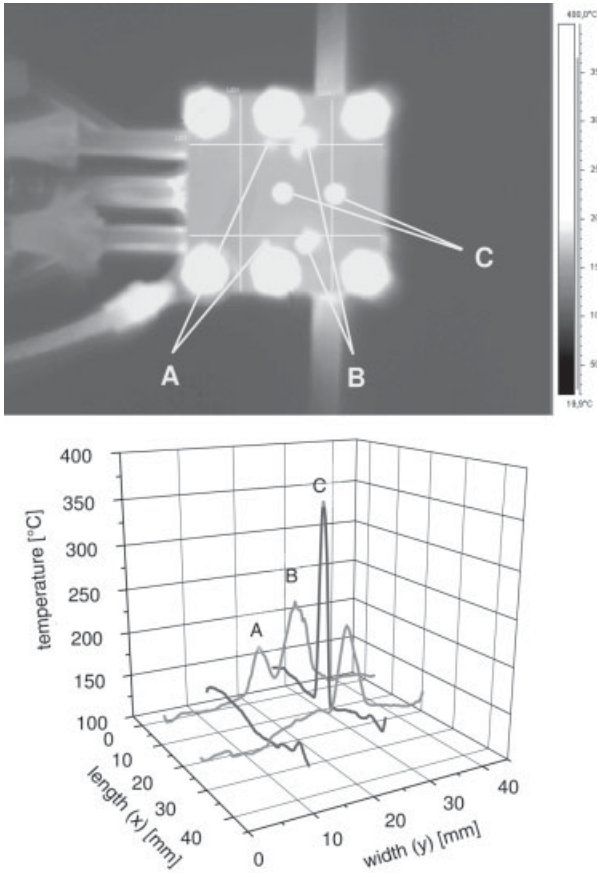
Figure 1.21 Thermographic image taken during heating-up of a gas-phase reactor (top). A multitude of information is supplied on the spatio-temporal temperature evolution at the outside of the reactor housing and via conduits even within the micro reactor (bottom) [15].

The integration of sensing and other functions in a micro-flow system requires either monolithic, on-chip or hybrid, multi-scale approaches. Concerning the latter, Hessel and Löwe discuss the lack of compatibility of today's fluidic interfaces and report on a German project team developing a standard for micro-reactor interconnection [9, 10].

1.5.2
Industrial Process Development and Optimization

1.5.2.1 Information on Industrial Large-scale Chemical Manufacture: Time to Market

There is common agreement that with the aid of micro reactors, process development can be speeded up considerably [5]. First industrial examples on the implementation of micro-reaction technology for pilot-scale and production seem to con-

firm this assumption [11, 21, 110, 136]. Besides providing the mere facts on the specific process developments made, the descriptions of Wörz et al. give vivid examples of the value of micro reactors for process development from an industrial perspective [110].

Felcht reports that the testing of industrial-scale processes can be performed with low expenditure by using micro reactors, since this should result in a faster time to market of the development [137]. He also sees uses for micro reactors at the laboratory scale as a means of high-throughput screening and model examinations such as fast determination of reaction kinetics.

1.5.2.2 Pharmaceutical and Organic Synthesis Process Development

The organizational format in current industrial chemistry impacts on the choice of process development and the respective tools. In a contrasting scenario, a new tool with much improved performance could impact the way of approaching chemical synthesis (Figure 1.22). In this context, Schwalbe et al. describe how micro reactors can change current trends in organizing industry's chemistry development [81]. Whereas the established process is made in several steps by several groups, comprising discovery, functional chemistry, chemical development, and process development until market entry, the micro-reactor process ideally should have only
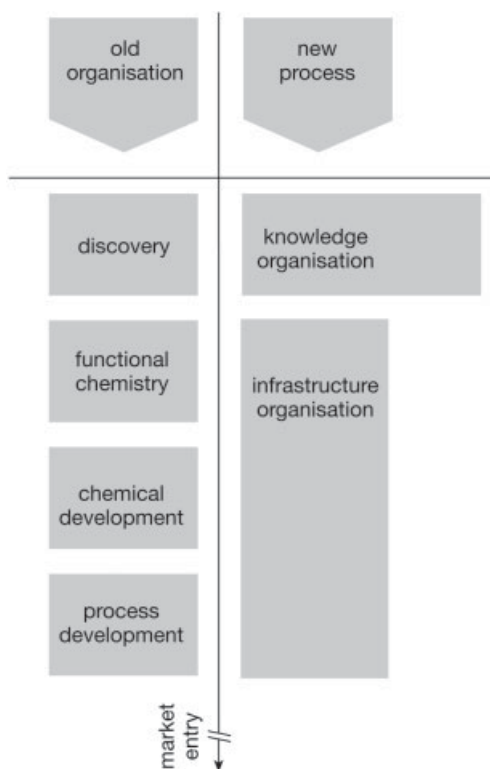

Figure 1.22 Organizational format in current industrial chemistry and proposal for a change in the future which may be induced by use of micro reactors [81].

two steps, termed knowledge and infrastructure organization (see [81] for an explanation). As a result, faster total development and faster market entry are claimed to be achievable.

1.5.2.3 Approval by Public Authorities

According to an older German study, the time-to-market of new chemical products, besides optimizing the internal research and development as outlined above, could profit from faster administrative approval by the public authorities [138]. For example, the phase of getting the concession has a share of about 20% of the overall time for process development, amounting on average to 7.5 years in Germany. Process development in other countries is faster, e.g. 5.0 and 5.7 years in Japan and the USA, respectively.

Although it is unclear at present how the public authorities would react if micro reactors were largely employed for production purposes, it stands to reason that in principle faster approval could be achieved in this way. Approval is often connected with assigning the equipment under consideration to certain reactor categories which typically are defined, among other features, by the reactor internal volume. Due to their small internal volumes and their large fraction of construction material, micro reactors, as a general rule, do not fall into the categories usually considered for tedious and thorough approval. In addition, considering their safety features and new ways of environmental protection (e.g. complete encapsulation [139]), faster approval can certainly be realized. However, one should not be too starry-eyed. Approval processes in the chemical industry have a long tradition and have previously never been faced with an abrupt, quasi-revolutionary change in processing apparatus. Therefore, they will not be changed overnight, but more likely in an evolutionary way.

1.5.3
Pilot-stage Processing and Centralized Production

1.5.3.1 Production as a Challenge for Micro Reactors

There is essentially no other question which more vigorously splits the micro reactor and even the chemical community into groups of complete stances. There are even commentators who consider the proof of production feasibility of micro reactors as the central issue to be solved, like a *'conditio sine qua non'*. As an extreme view, they claim to see no other *raison d'être* for micro reactors or at least none of similar importance.

Among the chemical community, three groups can be identified. One group of experts strongly doubt that micro reactors can be used at all for production. While this is most of all the point of view of those engaged in chemical producing manufacture (maybe for reasons of not waking up competitors), micro reactor researchers themselves are torn between conservative skepticism and optimistic views, the latter saying it is not practiced now, but will come anyway.

The chemical manufacturers defend their negative view by referring to the scaling law, which predicts that processing equipment becomes more cost-efficient

the larger it is, referring to the 'seven tenths law' [139]. However, an opposite position can be taken as well, saying that the economy of scale is now applied to plant manufacture (through production of large numbers of small units) rather than to plant operation itself [139]. In addition, the chemical manufacturers raise objections if fouling problems can be solved and if generally reliability can be set to a level acceptable for automated industrial processing.

Wörz et al. give an 'in principle, yes' answer, but point at the serious problems to be encountered [110–112]. They say that production in micro reactors will be the exception rather than the rule. In view of the background of the authors coming from a large-base chemical provider, they assume that production has to occur in hundreds or even millions of separate parallel streams. Accordingly, they refer to the problems of uniformly splitting one main stream into a multitude of streams and also then regard fouling as a major problem. Cleaning procedures after shutdown of the system, common for laboratory equipment, are said to be 'inconceivable' for industrial production.

1.5.3.2 Micro Reactors as Information Tools for Large-scale Production

One of the most interesting theorems of Wörz et al. is that they see a serious potential for micro reactors to permit small-scale production of some different sort [110–112]. Micro channels serve as an ultra-precise measuring tool, whereas production is done in channels about 10 to 100 times larger, i.e. millimeter-sized channels. The limit of tube diameter of industrial production reactors is reported to be 2 cm; hence any new reactor of smaller characteristic dimensions bears some potential for improvement. Wörz et al. conclude with the remark that the above strategy 'could be the most important result' of their studies [110–112].

Jensen is of the same opinion, pointing out that replication of micro reactors used in the laboratory avoids costly redesign and pilot-plant experiments, shortening the development time from laboratory to commercial production [75]. He sees particular uses of that for the fine-chemical and pharmaceutical industries with production of a few metric tons per year. A peculiar feature of such a numbering-up approach is that it allows for '... scheduled, gradual investment in new chemical production facilities without committing to a large-scale manufacturing facility from the outset' [75]. Accordingly, mass fabrication of individual micro-reactor components and subsequent integration could challenge the traditional centralized economy of scale practiced in the chemical industry. This manufacturing-based approach, albeit not implemented so far for micro-reaction technology, is today's practice in the electronics and automotive industries.

1.5.3.3 Micro reactors for Specialty-chemicals Production

Felcht reports on Degussa's activities in cooperation with partners from academia and industry to develop innovative industrial-scale micro-structured reactors for making large-tonnage products by liquid- and gas-phase reactions [137]. The aim is to make the potential of micro reactors more widely available for a larger variety of processes, naturally with focus on Degussa's fine and specialty chemical productions. Also, the aim is to circumvent traditional problems of scale-up.
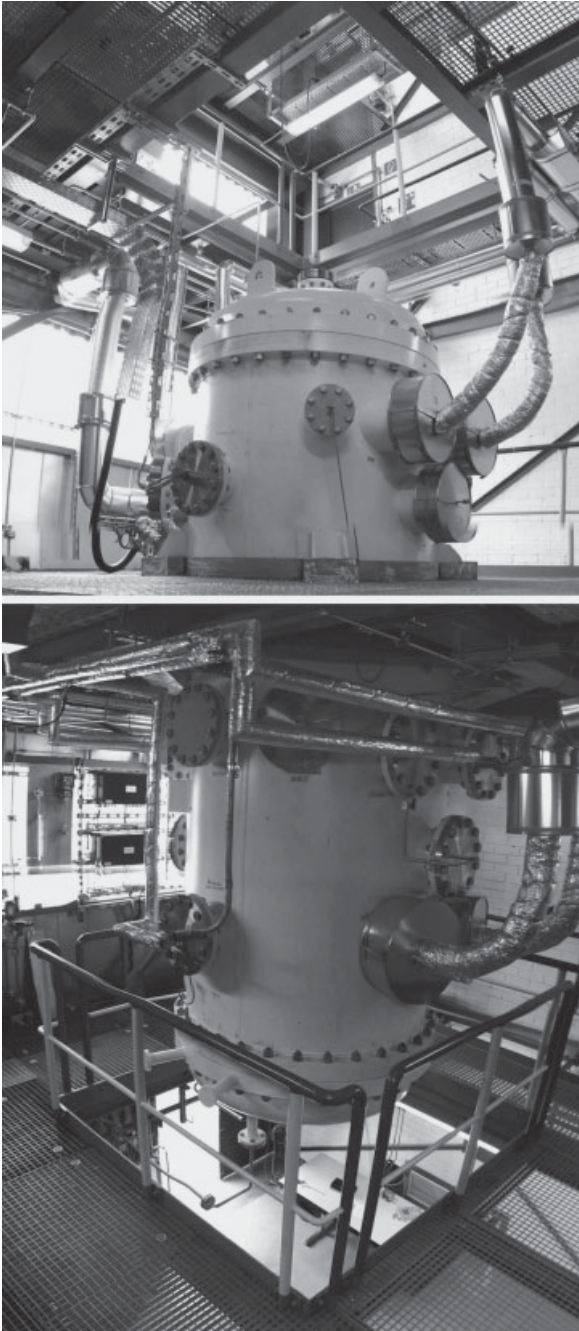
Figure 1.23 Large-scale reactor with microstructured internals tested at the industrial site of Degussa and developed jointly by a project team of several partners [137].

One of the reactors that Degussa and the plant manufacturer Krupp-Uhde are currently investigating in the framework of a government-funded project has re-markably large outer dimensions and is being tested for pilot-scale feasibility (see Figure 1.23).

1.5.3.4 Intensification of Transport – Reduction of Equipment Size

Many publications refer to the use of micro reactors for process intensification, with all the implications related to this definition – safety, cost reduction, high productivity rate, environmental friendliness, energy efficiency and so on [5, 25, 104]. A particular feature of interest is the reduction of the equipment size (see also Section 1.4.3.5 for a systematic top-down description of this topic).

Calculations predict that improved heat transfer for reacting systems in micro-channel heat-exchanger reactors could lead to considerable size reduction of the equipment, by enhancing the degree of product formation per micro channel (see Figure 1.24) [140, 141]. This was exemplarily shown for a fast, high-temperature
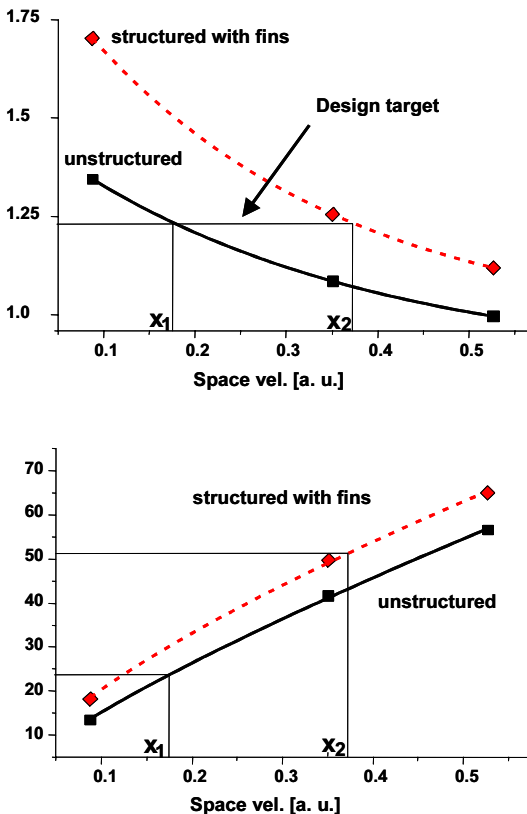

Figure 1.24 Outlet concentration and specific molar flux of product (P1) in arbitrary units as a function of the space velocity of a feed component.

gas-phase industrial reaction, the nature of which was not disclosed, with a hypothetical catalyst. For thick (e.g. 100 µm) catalyst layers, mass-transfer limits in the porous structure are observed, reducing catalyst effectiveness. Accordingly, for the same performance, the catalyst mass can be reduced when using micro reactors as compared with standard fixed-bed technology. This comes together with a reduction in the total device size; for the application investigated this was an order-of-magnitude reduction. Concerning heat transfer, the use of micro fins gave improvements, i.e. an increase in Nusselt number by a factor of five. Similar findings of heat-transfer enhancement with fin-type microstructures have been reported [14, 23, 142, 143].

Substantial heat-transfer intensification was also described for a special micro heat exchanger reactor [104]. By appropriate distribution of the gas-coolant stream, the axial temperature gradient can be decreased considerably, even under conditions corresponding to very large adiabatic temperature rises, e.g. of about 1400 °C.

A detailed characterization of micro mixing and reaction performance (combined mixing and heat transfer) for various small-scale compact heat exchanger chemical reactors has been reported [27]. The superior performance, i.e. the process intensification, of these devices is evidenced and the devices themselves are benchmarked to each other.

1.5.4
Distributed, On-Site Production

1.5.4.1 An Existing Distributed Small-scale Plant for Phosgene Synthesis
When discussing distributed small-scale production of hazardous materials, one should be aware that such plants already exist, albeit not using micro-channel technology. The Ciba-Geigy phosgene plant produces phosgene on demand [144]. It is said to be a very safe apparatus, as phosgene is neither liquefied nor stored. The plant contains only about 10 kg of gaseous phosgene and is encapsulated by a double mantle. On-line monitoring of phosgene is applied. In case of an incident, a two-fold washing equipment is provided, able to quench the whole phosgene content. The rated output can be varied from 10 to 100%. Product selectivity exceeds 97.5%. A 5–10 min start-up time is needed. As waste, only sodium chloride and sodium carbonate are produced. Waste water in an amount of only 3 m^3 per month is generated for an annual production of 5000 t of phosgene.

1.5.4.2 Distributed Manufacturing – A Conceptual Study of Future Scenarios
Concerning process-engineering impacts of micro reactors, many authors argue for distributed production owing to size and weight advantages of these devices and to their modularity and hence flexibility for multi-purpose syntheses [1, 5, 104]. Felcht outlines the potential of external numbering-up of micro-reactor devices for adjusting the capacity to the quantity needed at decentralized sites, albeit saying that this refers to a limited number of devices [137].

As a possible chemical process for distributed manufacture, the production of toxic feedstock gases is claimed [1, 139]. Benson and Ponton were among the first
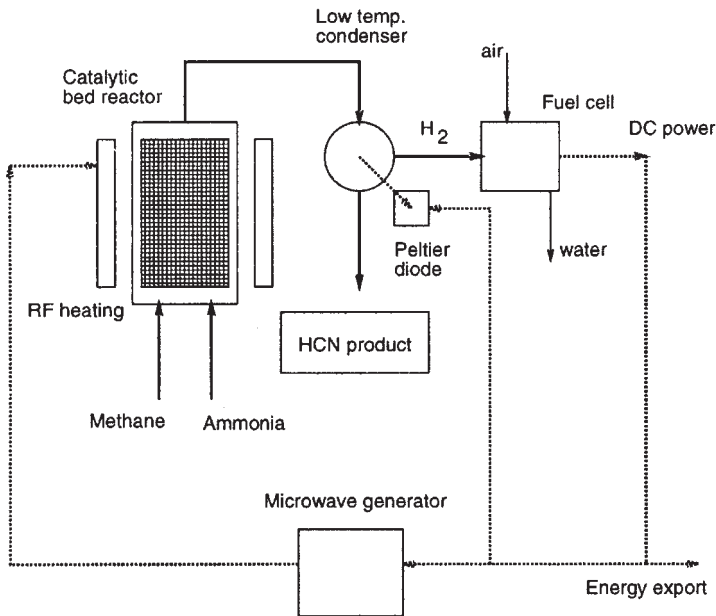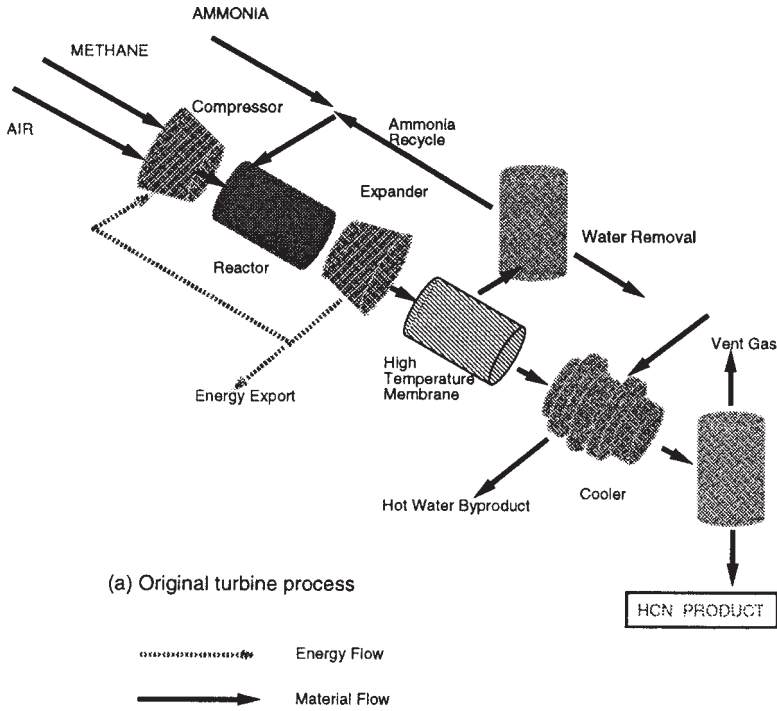
AMMONIA

METHANE

AIR

Compressor

Ammonia
Recycle

Expander

Reactor

Water Removal

Water Removal

Water Removal

Vent Gas

High
Temperature
Membrane

Energy Export

Hot Water Byproduct

Cooler

(a) Original turbine process

HCN PRODUCT

⊙⊙⊙⊙⊙⊙⊙⊙⊙⊙◀⊶   Energy Flow

➤   Material Flow

Low temp.
condenser

air

Catalytic
bed reactor

Fuel cell

H_2

DC power

RF heating

Peltier
diode

water

HCN product

Methane   Ammonia

Microwave generator

Energy export

Figure 1.25 Explosion drawing and schematic of a future plant for distributed chemical manufacturing [139].

to figure out some details of a concept of distributed manufacturing [139] (see [145] for the comments of trade press), which will be referred to in detail in Volume 2 of this book series (more information is also provided in this volume; see Section 1.7.3). Basically, they refer to small, transportable plants which are fed with reactants 'over the fence', hence using only non-hazardous, generally available materials by normal piping or standard transport (Figure 1.25).

The authors provide selection criteria, by which the suitability of a process for a distributed production can be assessed [139]. These are explicitly given for the categories of feedstock, processes, customer products, and waste products. This is completed by a list of suitable device types for distributed production such as plate heat exchangers, pressure and temperature swing units, electrostatic dispersers, and membrane units. The various operations often rely on the use of electricity and therefore are said to be particularly suited for operation at the mini scale.

1.5.4.3 Central Role of Control Systems and Process Models

Control systems will play a key role in future distributed plants [139, 145]. As a rule of thumb, plants will be smaller and simpler, but the control systems will be much more advanced, of a standard not known today. Plant personnel for operation and managing will ultimately no longer be required, except for start-up, shutdown, and services. This is a shift from a regulatory to a 'servo' role, supported by a sophisticated sequence control. Control is needed for safety issues, operability, and product quality control. Sensors have a central role to provide the information needed for control and modeling and simulation is needed for process models.

Although 'active' safety is provided by the control systems mentioned above, 'passive' safety is an additional important feature of a distributed plant. Due to the low inventory, even a total release of the reaction volume or an explosion would create no significant impact on the environment [139]. To prevent such scenarios, a total containment of the plant is envisaged; it needs to be 'sealed for life'. Hydrogen cyanide synthesis and chlorine 'point-of-sale' manufacture are two examples for safety-sensitive distributed syntheses.

1.5.4.4 Off-shore Gas Liquefaction

Off-shore gas liquefaction of natural gas on oil platforms is often mentioned as an example of on-site production [5]. Natural gas today is flared as its transportation is not economic. Conversion on-site by conventional reactors suffers from the large weight of the equipment. Gavriilidis et al. state that 5 kg of support are needed to support 1 kg of equipment on an oil platform [5]. Light-weight micro reactors have the potential to use the precious area of the platforms better (Figure 1.26).

1.5.4.5 Energy Generation and Environmental Restoration

Wegeng and Drost give five examples for distributed processing applications, which relate to the fields of energy generation and environmental restoration [106]. The first example concerns distributed heat pumps, designed for military purposes. A lightweight, portable unit serves for cooling in airtight, protective clothing under bio-hazardous conditions. Compared with industrial absorption-cycle heat pumps,
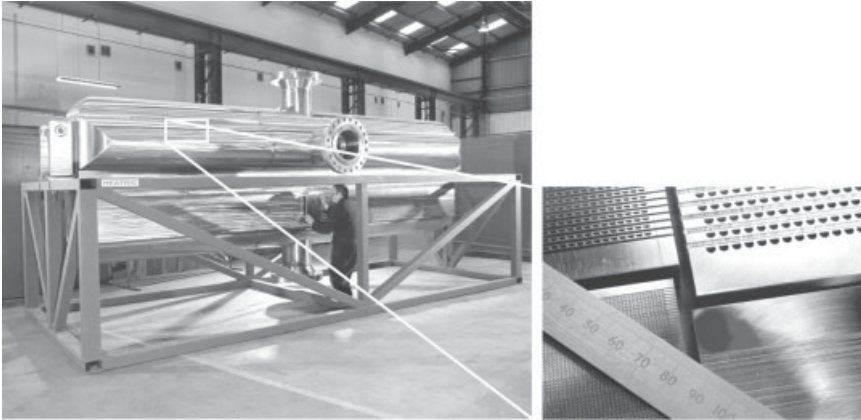
Figure 1.26 Large-capacity heat exchanger, e.g. for use on oil platforms, constructed from diffusion-bonded plate stacks comprising a vast number of millimeter-sized channels. This apparatus was manufactured by Heatric (Poole, UK).

the volume is said to be reduced by a factor of about 60 when relying on micro-channel-based heat-transfer performance.

The second example describes distributed, mobile and portable power-generation systems for proton-exchange membrane (PEM) fuel cells [106]. A main application is fuel processing units for fuel cell-powered automobiles; it is hoped that such processing units may be achieved with a volume of less than 8 l.

The third example is compact cleanup units for waste treatment, mainly in consideration of the numerous radioactive sites, stemming from cold-war military developments [106]. The Hanford, Washington, USA, site with a multitude of seriously contaminated tank wastes is among them. Due to the unknown character of most polluting species, the installation of a central waste-treatment facility is said to be not the best and most inexpensive solution. Rather, small modular units, able to be individually adapted to various separation tasks, which are inserted into the tanks and perform cleanup on site, are seen as the proper solution.

The fourth example, the use of chemical processing on Mars for producing a propellant, is presented in Section 1.9.7 [106]. The fifth and last example describes the use of distributed systems for global carbon dioxide management, aiming at reducing the greenhouse effect [106]. The main issue here is the installation of gas-absorption equipment for CO_2 capture at central, fossil-fuel power plants.

1.5.4.6 Desk-top Pharmacies, Home Factories and More

Other suggestions on distributed processing reach beyond the capabilities of today's micro reactors, and hence are of more visionary character [5]. These include desktop pharmacies, home-recycle factories, mobile factories, house-water treatment plants, processing cereal crops at the combine, purification of blood in the body, recycling of plastics in the collection vehicle and more [5].

1.5.4.7 **Production of Chemical Weapons?**

One (at least theoretical) variant of distributed processing by micro reactors, although by no means useful or desirable, is to use them for making chemical weapons at various sites. This possibility for the use of micro reactors has been discussed [83], particularly with respect to their employment as tools for terrorist attacks and to facilitate the clandestine manufacture of chemical agents. At the moment, highly skilled personnel are still needed for micro-reactor fabrication. However, the emerging worldwide capabilities of microfabrication techniques will render future processing in micro reactors no longer unique or proprietary. One day they will be available in regular workshops. Thus, it cannot be ruled out completely that people with allegiance to a terrorist organization could misuse micro-reactor technology by construction at their site or simply by purchasing these devices.

Among the hazardous chemical weapons scheduled class 1–3, methyl isocyanate becoming more and more important as a precursor [83]. This is just one among a number of substances which could be made via micro-reactor synthesis. Especially in the case of so-called binary weapons, where two relatively harmless substances are mixed to give a weapon, on-site mixing is demanded; this can be accomplished with high performance by micro reactors. Pocket-sized miniature plants can neither be monitored nor detected.

1.5.4.8 **Standardization**

Standardization is seen as advantageous for distributive production by micro reactors, as it is supposed to decrease development times and to provide higher flexibility by modularity [5]. Hessel and Löwe discuss the current lack of compatibility of suitable fluidic interfaces for hybrid, multi-scale micro-reactor construction (see Section 1.1.7) and report on a German project team developing a standard for micro-reactor interconnection (Figure 1.27) [9, 10].

1.5.5
The Shape of Future Plants/Plant Construction

1.5.5.1 **The Outer Shape of Future Chemical Manufacture Plants**

Many authors have addressed this important topic. The visions extend from shoe box-sized construction-kit plants, back bone-based micro-device assemblies, to much larger pilot and production plants of a shape not too different from now. Most authors follow the last path. In the end, as a consequence of process intensification, the equipment of the plants will become smaller in addition to the plant itself. A nice drawing of how such plant with process-intensification equipment may look is given in [25] as a future plant vision (Figure 1.28). Since one type of equipment will be replaced after another, it may take some time until we see a noticeable change in the external shape of a plant. As a governing principle of plant construction, this implies inserting micro-channel reactors in an existing plant environment. This is termed a hybrid [9, 10] or multi-scale approach (see Section 1.1.7). Naturally, micro devices with larger throughputs, hence larger internal components and so larger external dimensions, will be the first to be chosen.
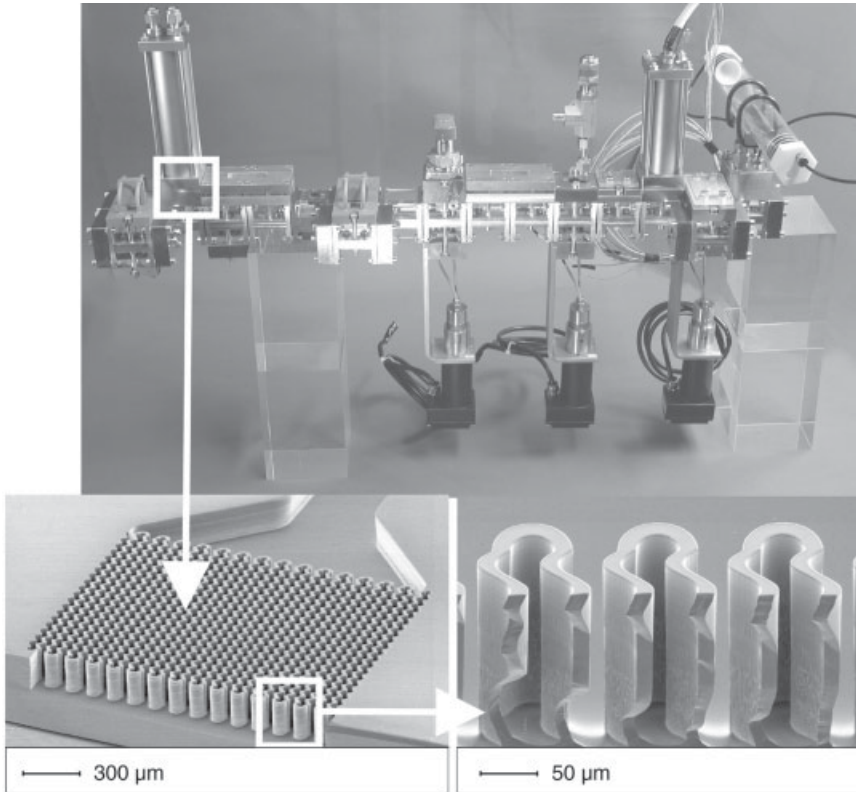
Figure 1.27 Standardized fluidic backbone for connecting micro-reactor components from different suppliers, yielding a small, compact 'micro-plant' with multiple functions. This backbone not only has a fluidic path, but also contains an electric bus system.

Figure 1.28 Illustration of a future plant using process-intensification equipment, aiming at giving the corresponding shape or perception. Compared with today's plants, a reduction in size is predicted [25].
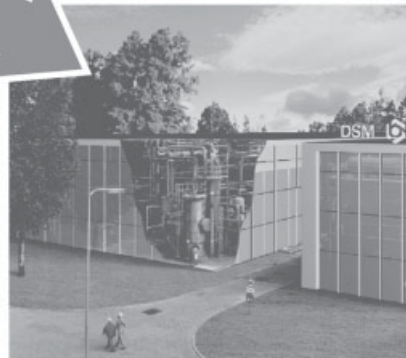
1.5.5.2 **Today's Shape of Micro-reactor Bench-scale Plants:**
         Monolith vs. Hybrid/Multi-scale? Specialty vs. Multi-purpose?

The realization of complete bench-scale micro reactor set-ups is certainly still in its infancy. Nevertheless, the first investigations and proposals point at different generic concepts. First, this stems from the choice of the constructing elements for such set-ups. Either microfluidic components can be exclusively employed (the so-called monolithic concept) or mixed with conventional components (the so-called hybrid or multi-scale concept). Secondly, differences concerning the task of a micro-reactor plant exist. The design can be tailor-made for a specific reaction or process (specialty plant) or be designated for various processing tasks (multi-purpose plant).

Hessel and Löwe provide examples of hybrid, i.e. multi-scale, approaches, including the first commercial systems (see Section 1.1.7) [9, 10]. Such approaches are currently most often favored for micro-reactor construction, simply for practical time and cost reasons. In addition, such an approach allows one to fit micro reactors in existing industrial and academic environments for production and measurement. The micro reactor is only used where it is really needed, and in this way costs of changing the processing are kept to a minimum.

A micro reactor concept proposed by MIT and DuPont on the basis of electronic circuits is the most prominent among the examples listed for the hybrid approach [19, 101]. The so-called *turnkey multiple micro-reactor test station* relies on the use of standard components originating from the semiconductor industry for microchemical processing, the construction being oriented at the concept of *printed circuit boards*.

Micro mixer-tube reactor set-ups also belong to the hybrid category. Institutes such as the Forschungszentrum Karlsruhe [146] and IMM [147] have presented both monolithic and hybrid concepts, giving many variants of the latter option. These set-ups are often highly specialized, often only developed for one specific purpose. Commercial suppliers such as mgt mikroglas technik (see [148]) or CPC (see Figure 1.29 and [81]) developed hybrid concepts which usually target a broader range of applications (<www.mikroglas.de>; <www.cpc-net.com>, [113]).
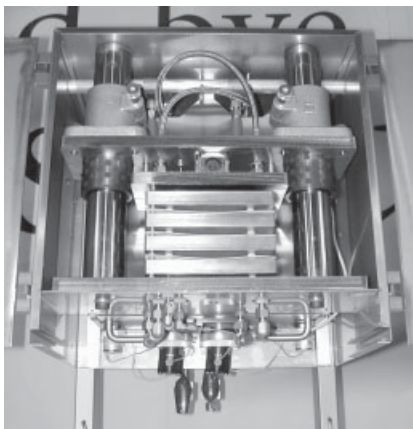

Figure 1.29 CPC micro-reaction system CYTOS [9].

The hybrid approach seems to be the more pragmatic procedure and its time has come already. It allows one to analyze the advantages of micro reactors without delay, especially facing today's industrial time demands. The impressive results gathered so far, especially on the industrial side, substantiate that this – and so far only this – concept is not lacking in innovative character besides pragmatism [11, 28]. Set-ups with many micro-reactor components, pointing to a monolithic concept, will find use when each of these components on their own or the interplay between all of them gives advantages. This needs more time for development, but can be built on the progress achieved so far.

1.5.5.3 Methodology of Micro/Mini-plant Conception

Rinard dedicated his research to a detailed analysis of methodological aspects of a micro-reactor plant concept which he also termed mini-plant production [85] (see also [4, 9, 10] for a commented, short description). Important criteria in this concept are JIT (*just-in-t*ime) production, zero holdup, inherent safety, modularity and the KISS (*k*eep *i*t *s*imple, *s*tupid) principle. Based on this conceptual definition, Rinard describes different phases in plant development. Essential for his entire work is the pragmatic way of finding process solutions, truly of hybrid character [149] (miniaturization only where really needed). Recent investigations are concerned with the scalability of hybrid micro-reactor plants and the limits thereof [149]. Explicitly he recommends jointly using micro- and meso-scale components.

1.5.5.4 Highly Integrated Systems

Jensen emphasizes the potential of system integration to combine many functions on one chip [101] (see Section 1.5.1.5). Chemical detection is often the rate-limiting step in many chemistry investigations for gathering product information. Macroscopic test systems may be replaced by PC card-sized micro-chemical systems consisting of integrated microfluidic, sensor, control, and reaction components. The advantages are obvious: namely less space requirements, less utilities, and less waste production. This is seen as the step towards high-throughput screening of process chemistries under controlled conditions.

Jensen gives several examples for his present highly integrated chip systems [101], including a gas-phase reactor, a liquid-phase reactor, a catalyst-testing reactor, and a packed-bed multi-phase reactor. In addition, he provides the vision of a multiple micro-reactor test station (see Section 1.5.5.2).

1.6
Impact on Process Results

1.6.1
Selection Criteria for Chemical Reactions for Micro Reactors

Lerou et al. mention the following criteria that render reactions suitable for investigations in micro reactors [74]: