Part I
Microreactor Systems Design and Scale-up

1
Structured Multi-scale Process Systems Design and Engineering – The Role of Microreactor Technology in Chemical Process Design

Michael Matlosz, Laurent Falk, and Jean-Marc Commenge

1.1
Introduction

Physical and chemical phenomena involved in chemical engineering processes are intrinsically multi-scale, since they operate at very different time and length scales [1]. The length scales range from the nanoscale, where molecular processes occur, up to the megascale, representing interactions between chemical plants and the environment. These length scales can be correlated with the time scales of the phenomena involved, ranging from less than 1 ns up to several years.

All of the scales affected by these processes have an impact on the global performance of a chemical production process [2]:

- At the submolecular scale, the thermochemical properties of the reactions are influenced by quantum mechanics.
- At the molecular scale, chemical interactions influence the selectivities of the reactions or catalysts, in addition to physical properties of the fluids.
- At the larger scales (up to tens of centimeters), physical phenomena govern hydrodynamics and heat and mass transfer.
- At the technical scales (up to several meters), physical plant equipment and devices such as reactors, mixers, exchangers and separators govern the performance of the complete process system.

The performance of the process can be influenced either positively or negatively by each of these scales, although phenomena only on certain scales were amenable to study in the past due to limitations on the available technical tools. Some scales have been known for a long time, such as the "reactor scale" or "unit-operation scale", employed for the development of the design principles of mixers and separators [3–5]. The concept of unit operations is now considered as the first paradigm for chemical engineering. The scales involved in unit operations have been available for study since the late eighteenth century, whereas direct investigation of phenomena on the molecular and submolecular scales became possible only in the twentieth century.

Some of the most important scales involved in chemical engineering processes are the scales related to transport phenomena, since those scales determine the efficiency of mixing and heat and mass transfer. Major advances in the comprehension of phenomena at these scales were made during the 1960s and the concept of "transport phenomena" developed at that time is considered as the underpinning scientific basis for the emergence of a second paradigm for chemical engineering [6].

Unfortunately, despite these advances in comprehension, technical tools to control transport phenomena at the appropriate scales were not systematically available at that time. The local operating conditions at the scales of interest could only be controlled by external actions applied at the reactor or unit-operation scale: flow rate, inlet or jacket temperature, pressure, mechanical energy provided to a stirrer, etc. The propagation of the consequences of these external actions from the unit-operation scale down to the transport-phenomenon scale could not be directly controlled and was only indirectly transmitted by non-selective dissipative hydrodynamics and physical processes.

Improved understanding of the important role of transport phenomena and of the major influence of heat, mass and momentum transfer on process performance very rapidly led to the emergence of new technologies designed to structure the intermediate scales between the equipment and unit-operation scales and the more fundamental scales of transport phenomena and molecular interactions. In the 1960s and 1970s, a number of developments were undertaken to address these issues, including the structured packings for multi-phase columns pioneered by Sulzer [7], static mixers such as the Kenics mixers and plate heat exchangers. The increased performance attained through the use of these technologies demonstrated the interest of geometric structuring in chemical engineering as a relevant strategy to control phenomena of interest. Nevertheless, the length scales available were still limited for technical reasons in most continuous chemical processes. Furthermore, no equivalent apparatus was available for low-tonnage production, leaving traditional stirred-tank reactors as the most widespread tool for a large number of processes, despite their well-known limitations.

Since the 1990s, the development of microfabrication technologies has permitted device structuring at the sub-millimeter and micrometer scales in a wide variety of chemically resistant materials, thereby creating new possibilities for local process control. The use of these new microstructured objects and devices in chemical engineering offers stimulating perspectives for the development of a new generation of highly original process components and systems for chemical and biochemical applications, capable of being exploited to improve significantly the quality, safety and effectiveness of industrial manufacturing.

Throughout the history of technological development, the application of miniaturization and precision engineering has led to numerous revolutionary changes in many industries and in society in general. For example, the revolution in portable watchmaking in the early seventeenth century radically changed the notion of time in society and contributed significantly to the birth of the industrial revolution in the eighteenth century. More recently, the miniaturization of silicon transistors led to

our current information society and it is therefore legitimate to ask whether a similar transformation can be expected from the use of precision engineering in chemical production.

Over the last 15 years, substantial research on small-scale structured devices for chemical applications has been undertaken and a host of academic studies have established a solid scientific basis for the fabrication of individual (generally unconnected) units. A number of reference books are now available [8, 9] as a substantial contribution to the already well-established general area of process intensification [10]. This research has demonstrated that miniaturized components can be exploited to act on the specific length scales (several tens to hundreds of micrometers) that are particularly relevant to chemical processing: boundary layers, transport processes, reaction and mixing zones.

Implementing these new technologies on the production scale, however, raises two important questions. The first relates to the flow rates that can be effectively employed in a microstructured system. Since many individual microstructured units can only operate with relatively low flow rates, using a large number of small-scale process units in parallel would appear to be a natural solution for production. This idea has led to the "numbering-up" concept that consists of connecting the process macroscale to the unit microscale through the design of a multi-scale distribution system. Biomimetic approaches inspired by vascular systems and lung structures, and the constructal theory developed by Bejan [11], led to the proposal of possible solutions to this connection problem. Nevertheless, the solutions proposed most often restrict the multi-scale design to a flow distribution problem, whereas the applications that have inspired the concept (vascular systems and lung structures) typically also involve mass-transfer phenomena.

The second question relates to the identification of what is truly original and novel in these recently developed microstructured systems. One might argue that these systems are not new, since the micrometer length scales involved have been exploited for a long time in equipment such as fixed-bed reactors and chromatographic columns. It should be noted, however, that columns containing natural or structured packings generally address only one particular phenomenon, such as mass transfer. Although effective for enhancing certain aspects of mass transfer, fixed-bed reactors are well known to exhibit poor heat-transfer characteristics, thereby making them unsuitable for highly exothermic reactions. Precision-engineered systems, in contrast, are capable of acting simultaneously on several phenomena by providing geometric and topological characteristics that combine enhanced performance and selectively on several phenomena (and their corresponding length scales) in the same device. As with vascular systems, the multi-scale approach of precision-engineered devices deals not only with the geometric scales of the hydraulic connections but also with the characteristic scales of the transport phenomena involved. In contrast to the possibilities offered to chemical engineers during the 1960s, when only external actions were available, multi-scale design with novel microstructured devices opens up new perspectives by matching the reactors and process equipment closely to the needs of the chemical systems [12].

Since numerous competitive phenomena may influence process performance (heat transfer versus mass transfer, heat transfer versus reaction rate, separation rate versus reaction rate, etc.), the applications of multi-scale design cover a wide variety of situations. The potential advantages are substantial. Appropriate control of operating conditions for exothermic reactions, for example, not only improves process selectivity and safety but also contributes to the objectives of green chemistry and sustainable development. Selective intensification of phenomena permits the design of miniaturized processes that lower operating costs, improve process control and offer perspectives for new business models, such as distributed or delocalized production. Conversion of batch processes to continuous flow using intensified reactors can also reduce operating costs, simplify production procedures and improve operational safety [13].

For all of these reasons, the structured multi-scale chemical devices envisioned here offer the perspective of significant innovation through the use of microfabrication in the chemical process industries. To illustrate these possibilities, the following sections demonstrate how multi-scale structuring can provide a new degree of freedom for process intensification/miniaturization and contribute to the satisfaction of criteria for sustainability. In conclusion, a critical comparison of scale-up, numbering-up and multi-scale design is proposed.

1.2
Multi-scale Structuring for Sustainable Intensification/Miniaturization

Sustainable intensification/miniaturization is a design strategy aimed at increasing the capacity/volume ratio of reactors and plants while satisfying simultaneously criteria for sustainability. To attain these objectives, the design strategy must either (a) reduce the volume of an existing plant or process while maintaining its production rate or (b) increase the production rate of an existing plant or process of a given volume. From a technical and economic perspective, the second strategy appears more attractive, since only limited additional investment should be necessary. Nevertheless, one might ask if it is truly possible to increase the production rate of an existing reactor or process solely by modifying the operating conditions, while at the same time satisfying criteria for sustainability.

To answer this question, one can compare the global performance of two common types of reactors:

- a fed-batch system, composed of a stirred tank
- a continuous-flow system, composed of a tubular reactor.

To make this analysis shorter, a rapid exothermic reaction is considered, similar to the analysis performed by Lomel *et al.* [14]. While this analysis intends to increase the productivity of these reactors, the sustainability criterion retained involves the mechanical energy, ε [W kg^{-1}], dissipated in these systems either by stirring or by friction. Due to the exothermicity of the reaction, Lomel *et al.* [14] demonstrated that the process productivities of both the fed-batch reactor and the tubular reactor are

proportional to the ratio of the reactor volume V to the characteristic heat-transfer time t_{heat}:

$$P \approx \frac{V}{t_{heat}} \tag{1.1}$$

As a result, a two-fold increase in the reactor productivity requires either a two-fold increase in the reactor volume or a two-fold decrease in the heat-transfer time. Since an increase in reactor volume is not compatible with the intensification objectives, only the second option (two-fold decrease in heat-transfer time) will be examined here. The following analysis is intended to quantify the variation in the mechanical energy dissipated in these reactors that would be required to accelerate heat transfer by a factor of two.

To ease readability, Section 1.2.1 only describes the results of the reactor comparison whereas Section 1.2.2 presents a more detailed comparison.

1.2.1
Multi-scale Design that Reconciles Intensification with Sustainability

The detailed analysis presented in Section 1.2.2 demonstrates that heat transfer for a given chemical system in a given reactor, either batch or continuous, cannot be increased without dissipating more mechanical energy in the system. The intensification goal of the present analysis, aimed at accelerating heat transfer by a factor of 2, systematically implies an increase in the specific mechanical energy by at least a factor of 8. This suggests that increasing the capacity/volume ratio of existing reactors without modifying the chemical conditions implies a drop in reactor sustainability, which is contradictory to the objectives of sustainable process intensification.

Multi-scale design, by providing an additional degree of freedom, can open up new paths to true sustainability. In the case examined here, analysis of friction losses in tubular reactors provides a solution capable of intensifying heat-transfer performance without additional energy dissipation. The multi-scale design solution consists of subdividing the main reactant flow in order to apply the intensified conditions to each sub-flow in the system.

To demonstrate the viability of these multi-scale solutions, the multi-scale reactor is first considered as a bundle of parallel tubes or channels, corresponding to the sub-flows, with a channel diameter D, a length L and a total number of channels N. The heat-transfer characteristic time, the reactor volume and the specific mechanical energy can be expressed as a function of these independent geometric parameters. Moreover, the ratio of the specific energy of a reactor after intensification (subscript 2) and before intensification (subscript 1) can be related to the features of interest as follows:

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{N_1}{N_2}\right)^a \left(\frac{V_2}{V_1}\right)^b \left(\frac{t_1}{t_2}\right)^c \tag{1.2}$$

where V_i denotes the reactor volume [m^3] and t_i the heat-transfer time [s]. It should be noted that using $N_1 = 1$ and $N_2 > 1$ enables comparison of a multi-scale reactor with a

tubular reactor. Furthermore, it should be noted that the three ratios on the right are independent since the time ratio depends only on the channel diameter, whereas the volume ratio depends on the channel length.

This equation includes the four ratios of interest to quantify the potential of multi-scale systems to reach the objectives of sustainable intensification:

- The ratio of specific mechanical energy describes the gain in sustainability. A value lower than unity indicates that the multi-scale design (subscript 2) requires less energy.
- The ratio of channel numbers describes the multi-scale aspect.
- The volume ratio quantifies reactor miniaturization which is one objective of process intensification. A value lower than unity indicates effective miniaturization.
- The ratio of heat-transfer characteristic times describes the second interpretation of process intensification consisting of accelerating the phenomena involved. A value larger than unity indicates accelerated heat transfer in the multi-scale reactor.

The exponents a, b and c exhibit different values depending on the flow regime in the channels (see the next section), but typical values can be considered as follows:

$$2 < a < 2.75 \quad 0 < b < 1.5 \quad 3 < c < 4.5$$

These values confirm what has been observed previously in a single tubular reactor: using $N_1 = N_2$ and $V_1 = V_2$ demonstrates that heat-transfer acceleration ($t_1 > t_2$) implies an increase in the required specific energy ($\varepsilon_2 > \varepsilon_1$). This effect is still observed with multi-scale reactors, since the exponent c is always positive. Nevertheless, this increase can be counter-balanced by adapting the multi-scale design with an appropriate value of the ratio of channel numbers.

Figure 1.1 illustrates this possibility by presenting the variation of the specific energy ratio ($\varepsilon_2/\varepsilon_1$) as a function of the characteristic time ratio (t_1/t_2) for values of the channel number ratio (N_2/N_1) equal to 1, 2 and 10 at fixed reactor volume ($V_1 = V_2$) using values of the exponents a, b and c equal to 2.5, 1 and 3.5, respectively. If the flow rates entering both reactors are equal, maintaining a constant volume requires maintaining the space time, which implies (for a homogeneous reaction) operation at equal conversions. Whereas the specific energy is always larger than unity when the channel number is unchanged (full line), this ratio can be lower than unity when the number of channels is increased, indicating that less energy is required (dashed line). Moreover, using 10 times more channels of smaller diameter allows acceleration of the heat transfer by a factor of 5 without requiring any additional energy (dotted line).

Whereas the previous equation allows the multi-scale design to be related to criteria of interest, it should be noted that additional constraints should be included depending on the design objectives retained. For instance, considering a slightly exothermic homogeneous reaction, reactor miniaturization is not possible by geometric structuring [15]. In such cases, miniaturization requires acceleration of the reaction rate, which is made possible by increasing the operating temperature or reactant concentration. This chemical acceleration creates a higher rate of heat generation, which must be controlled by a simultaneous increase in heat transfer. As
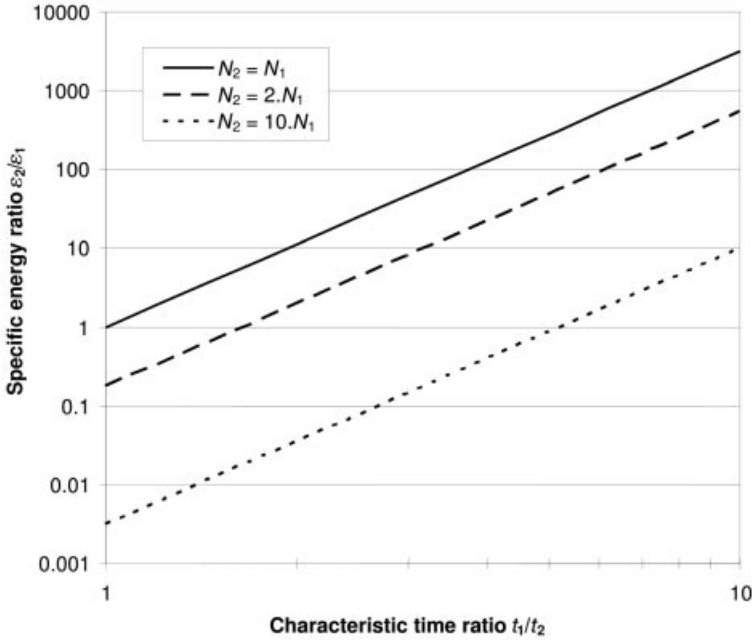
Figure 1.1 Variation of the specific energy ratio as a function of the characteristic time ratio for values of the channel number ratio equal to 1, 2 and 10, at fixed reactor volume. Average values of the exponents are $a = 2.5$, $b = 1$ and $c = 3.5$.

a result, miniaturization of such a reaction requires two time ratios to be maintained constant:

- the ratio of the space time to the reaction time to maintain sufficient conversion
- the ratio of the space time to heat-transfer time to maintain efficient heat transfer.

Including these additional constraints in the general equation and using the intermediate values of exponents a, b and c yield the following relation:

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{N_1}{N_2}\right)^{2.5} \left(\frac{V_2}{V_1}\right)^{-2.5} \tag{1.3}$$

The relation demonstrates that reactor miniaturization ($V_2 < V_1$) requires an increase in the dissipated energy ($\varepsilon_2 > \varepsilon_1$) if multi-scale design is not considered. Figure 1.2 presents the variation of the specific energy ratio as a function of the volume ratio for values of the channel number ratio of 1, 2 and 10. Here again, taking into account the multi-scale design of the reactor demonstrates that miniaturization by a factor of 10 can be considered without requiring additional mechanical energy.

In conclusion, despite the simplicity of the sustainability criterion retained, the analysis shows how multi-scale design enables various aspects of process miniaturization and intensification to be reconciled. By including a new design parameter, this strategy makes it possible to reconcile the rapid transfer characteristics offered by
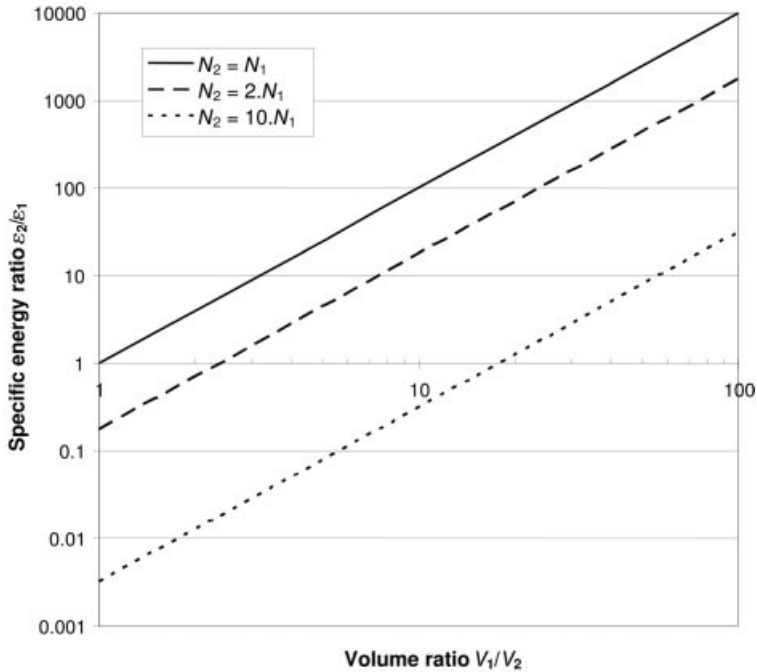
Figure 1.2 Variation of the specific energy ratio as a function of
the volume ratio for values of the channel number ratio equal to
1, 2 and 10, at fixed space time to reaction time ratio and
space time to heat-transfer time ratio.

microstructured dimensions and large production flow rates without a prohibitive
increase in energy requirements. Extensions of this analysis to more elaborate
criteria such as the Specific Operation Cost in Mechanical Energy (SOCME) [16]
can also be performed, but fall outside the scope of the present chapter. Nevertheless,
whereas many improvements can be expected from this analysis, the detailed design
of multi-scale reactors is far from complete and the difficulties in more widespread
development and use of the concept are discussed in Section 1.3.

1.2.2
Detailed Comparison

1.2.2.1 Fed-batch Reactor
In stirred-tank reactors, the characteristic time for heat transfer can be related to
geometric parameters and fluid properties as follows:

$$t_{\text{heat}} = \frac{\rho V C_p}{hA} \tag{1.4}$$

where ρ denotes the liquid density [kg m^{-3}], V the tank volume [m^3], C_p the liquid
specific heat [J kg^{-1} K^{-1}], h the global heat-transfer coefficient [W m^{-2} K^{-1}] and A the
heat-transfer area [m^2].

In order to divide this heat-transfer time by a factor of 2, the only possibility is an increase in the heat-transfer coefficient *h*. Indeed, since we use the same reactor, the reactor volume *V* and heat-transfer area *A* remain unchanged. Furthermore, we only analyze here the intensification possibilities offered by modifying operating parameters, which implies that the fluid properties ρ and C_p are the same. As a result, only the heat-transfer coefficient can be modified. Assuming a process-side heat-transfer limitation, this coefficient is related to the stirring Reynolds number as follows:

$$Nu = \frac{h D_{\text{vessel}}}{\lambda} \approx Re^{0.8} \tag{1.5}$$

where *Nu* denotes the Nusselt number [−], D_{vessel} the vessel diameter [m], λ the fluid thermal conductivity [W m^{-1} K^{-1}] and *Re* the stirring Reynolds number, defined as:

$$Re = \frac{\rho N D_{\text{stir}}^2}{\mu} \tag{1.6}$$

where *N* denotes the stirring speed [s^{-1}], D_{stir} the stirrer diameter [m] and μ the fluid viscosity [Pa s].

For similar reasons to those indicated above considering fluid properties and existing equipment, an increase in the heat-transfer coefficient requires an increase in the stirring speed *N*. As a result, the specific mechanical power dissipated in the system, ε [W kg^{-1}], can be expressed as follows:

$$\varepsilon = \frac{P}{\rho V} = \frac{Np N^3 D_{\text{stir}}^5}{V} \tag{1.7}$$

where *P* denotes the total mechanical power [W], *Np* the power number [−] and *V* the vessel volume [m^3].

To quantify the variation of dissipated mechanical power, the "intensified" reactor (subscript 2) operating at higher stirring speed is compared with the original reactor (subscript 1). The ratio of the characteristic heat-transfer times can then be expressed as follows:

$$\frac{t_1}{t_2} = \frac{h_2}{h_1} = \frac{Nu_2}{Nu_1} = \left(\frac{Re_2}{Re_1}\right)^{0.8} = \left(\frac{N_2}{N_1}\right)^{0.8} \tag{1.8}$$

Assuming a turbulent flow regime in the vessel for both operating modes, the power number *Np* can be considered constant, which enables the specific dissipated powers to be related to the stirring speeds as follows:

$$\frac{\varepsilon_1}{\varepsilon_2} = \frac{P_1}{P_2} = \left(\frac{N_1}{N_2}\right)^3 \tag{1.9}$$

Combining these equations yields

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{t_1}{t_2}\right)^{3.76} \tag{1.10}$$

The equation demonstrates that an intensification of the heat transfer, which implies a decrease in the heat-transfer characteristic time ($t_2 < t_1$), necessarily implies an

increase in the specific dissipated power ($\varepsilon_2 > \varepsilon_1$). For the present analysis, a two-fold increase in the reactor productivity requires an increase in the dissipated power by a factor of 13.5.

1.2.2.2 Tubular Reactor

Here, the analysis considers a tubular reactor of diameter D and length L. To simplify the analysis, a thermally developing laminar flow regime is considered. Under these conditions, an increase in productivity also requires an increase in the heat-transfer coefficient, which is related to the Reynolds number as

$$Nu = \frac{hD}{\lambda} = 1.86 \left(\frac{RePrD}{L} \right)^{0.33} \approx Re^{0.33} \approx \left(\frac{\rho u D}{\mu} \right)^{0.33} \approx u^{0.33} \tag{1.11}$$

where Pr denotes the Prandtl number [$-$] and u the mean fluid velocity [m s^{-1}]. As a consequence, an increase in the heat-transfer coefficient requires an increase in the fluid velocity.

In continuous-flow systems, the specific dissipated power ε [W kg^{-1}] can be expressed as follows:

$$\varepsilon = \frac{Q \Delta P}{\rho V} \tag{1.12}$$

The pressure drop in a fully developed laminar flow can be calculated from the Poiseuille law, which yields

$$\varepsilon = \frac{Q \Delta P}{\rho V} = \left(\frac{\frac{\pi}{4} D^2 u}{\rho V} \right) \left(32 \frac{\mu u L}{D^2} \right) \approx u^2 \tag{1.13}$$

Combining these equations to relate the ratio of heat-transfer times to the ratio of the specific dissipated powers yields

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{t_1}{t_2} \right)^6 \tag{1.14}$$

A similar analysis performed by assuming turbulent flow conditions yields a power of 3 instead of 6, which again demonstrates that intensification in traditional equipment requires an increase in the mechanical dissipated power. Moreover, the previous analysis of a continuous reactor did not take into account the fact that increasing the velocity in a given device reduces the space time and may prevent reactions from reaching satisfactory conversion. Indeed, the operating conditions (temperature, pressure, concentration) determine the reaction time as a function of which the space time must be adapted to reach a desired conversion. Including this constraint of a fixed space time in the analysis reveals that the exponent over the time ratio can be as high as 9, instead of 6.

In conclusion, in addition to the lack of flexibility of continuous reactors for rapid intensification, these reactors also create a large increase in dissipated power.

1.2.2.3 Comparison of Continuous and Fed-batch Reactors

In both reactors, the variation in dissipated power can be related to the time ratio as follows:

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{t_1}{t_2}\right)^n \tag{1.15}$$

where n ranges from 3 to 9 depending on the reactor and transfer regimes.

Since this analysis aims at intensifying heat transfer in the reactor, these values of the exponent indicate that a two-fold decrease in the heat-transfer time implies at least an eight-fold increase in the required mechanical power. As a result, the desired intensification of an existing reactor cannot be attained without an increase in the required mechanical power, which is not compatible with the objectives of sustainable intensification. An additional analysis is therefore required to combine heat-transfer intensification and sustainability criteria, while maintaining reactor flexibility.

1.2.2.4 A Possible Solution: Multi-scale Design

One of the key features demonstrated by the previous sections is the role of the characteristic time. In this case, the intensification requires the reduction of the heat-transfer time, which can only be attained (for a given chemical system) by reducing the characteristic dimension of the reactor. It seems clear that intensification of a batch process cannot be attained by reduction of the size of the batch vessel but requires conversion of the process to a continuous-flow regime.

Furthermore, the previous analysis of the tubular reactor highlighted the necessity to make the distinction between two characteristic dimensions:

- the diameter D that appears in the Nusselt number and allows intensification of the heat transfer (a decrease in the diameter strongly increases the heat transfer coefficient and reduces the heat-transfer time);
- the length L that must be adapted to the space time required by the reaction rate.

In order to find flexible and effective solutions for process intensification, the major problem identified previously concerns the pressure drop in small channels. This pressure drop under laminar flow conditions can be related to the production flow rate and geometric dimensions as follows:

$$\frac{\Delta P}{L} \approx \frac{Q}{D^4} \tag{1.16}$$

As explained above, intensification requires a decrease in the diameter D. The length L cannot be considered as an independent parameter for the design of the apparatus since it must be adapted to the required space time with respect to the diameter D. As a result, the only parameter that can be adjusted to maintain the pressure drop in a satisfactory range is the production flow rate. The production flow rate must therefore be decreased. That does not mean, however, that the productivity will be decreased but that the flow rate "in contact" with the characteristic dimension D will be decreased. This implies that the total flow rate must be divided into sub-flows. Each of these sub-flows can then be put in contact with the dimension D, the intensified conditions being then applied to each of these sub-flows.

The appropriate type of reactor therefore includes multi-scale geometry, at least in the sense of its internal flow, since the macroscopic inlet flow must be divided into numerous sub-flows. This multi-scale feature, which might be interpreted at first sight as a design constraint, in fact represents a new degree of freedom. This can be explained by comparing two multi-scale structures and relating their characteristics of interest for process intensification. To facilitate this comparison, the multi-scale reactors will be assimilated to a bundle of N_i identical parallel channels of diameter D_i and length L_i. The subscript $i = 1$ is used for the reference reactor, which could be a single tube, whereas subscript 2 concerns the higher-degree multi-scale reactor.

The specific mechanical power dissipated by friction in such a reactor (assuming isothermal laminar flow) is the following:

$$\varepsilon_i = \frac{Q_{\text{tot},i} \cdot \Delta P_i}{\rho V_i} = \frac{Q_{\text{tot},i}}{\rho V_i} \cdot \left(32 \frac{\mu \cdot u_i \cdot L_i}{D_i^2} \right) \tag{1.17}$$

If both reactors are operated with equal flow rates, Q_{tot}, the ratio of the specific dissipated powers is as follows:

$$\frac{\varepsilon_2}{\varepsilon_1} = \frac{u_2}{u_1} \cdot \frac{L_2}{L_1} \cdot \left(\frac{D_1}{D_2} \right)^4 \tag{1.18}$$

Since the inlet flow rates are divided into sub-flows, the mean fluid velocity in the channels depends on the channel number and diameter, as follows:

$$u_i = \frac{4Q_{\text{tot}}}{\pi N_i D_i^2} \quad \text{and} \quad \frac{u_2}{u_1} = \frac{N_1}{N_2} \left(\frac{D_1}{D_2} \right)^2 \tag{1.19}$$

Rearranging these equations yields

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{N_1}{N_2} \right)^2 \left(\frac{D_1}{D_2} \right)^3 \tag{1.20}$$

In order to quantify the interest of these multi-scale structures with respect to process intensification, the equation that describes the gain in sustainability of the system must also include both aspects of process intensification:

- the acceleration of fundamental phenomena through the ratio of characteristic times
- the miniaturization of the reactor volume through the ratio of the volumes of the reactors.

As stated previously, if heat transfer is the phenomenon of interest, the ratio of characteristic times is the following:

$$\begin{aligned}
\frac{t_2}{t_1} &= \frac{D_2}{D_1} \frac{h_1}{h_2} = \left(\frac{D_2}{D_1} \right)^2 \frac{Nu_1}{Nu_2} = \left(\frac{D_2}{D_1} \right)^2 \left(\frac{Re_1}{Re_2} \right)^{0.33} \left(\frac{D_1}{D_2} \right)^{0.33} \left(\frac{L_2}{L_1} \right)^{0.33} \\
&= \left(\frac{N_2}{N_1} \right)^{0.33} \left(\frac{L_2}{L_1} \right)^{0.33} \left(\frac{D_2}{D_1} \right)^2
\end{aligned} \tag{1.21}$$

The ratio of reactor volumes is as follows:

$$\frac{V_1}{V_2} = \frac{N_1}{N_2}\frac{L_1}{L_2}\left(\frac{D_1}{D_2}\right)^2 \tag{1.22}$$

Finally, recombining these equations to emphasize the variables of interest yields

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{N_1}{N_2}\right)^2 \left(\frac{V_2}{V_1}\right)^{2.5} \left(\frac{t_1}{t_2}\right)^{4.5} \tag{1.23}$$

If the Reynolds number in the channels is low enough that the Nusselt number can be considered constant, the power dependencies of this equation change to

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{N_1}{N_2}\right)^2 \left(\frac{t_1}{t_2}\right)^3 \tag{1.24}$$

In contrast, if the Reynolds number is large enough that a Blasius regime must be considered, then the powers are

$$\frac{\varepsilon_2}{\varepsilon_1} = \left(\frac{N_1}{N_2}\right)^{2.75} \left(\frac{V_2}{V_1}\right)^{1.5} \left(\frac{t_1}{t_2}\right)^{3.12} \tag{1.25}$$

These last three equations can be generalized and discussed with respect to the various parameters involved. This discussion is presented in Section 1.2.1.

1.3
Multi-scale Design: Requirements and Developments

Given the very significant advances indicated previously on individual small-scale structured devices on the laboratory scale, the major challenge facing the chemical industry in order to perform sustainable process intensification is not the further development of individual locally structured units but rather the effective integration of those units into complete production systems, exhibiting the required multi-scale features described above.

In this connection, it should be noted that the seductively simple ideas of direct "numbering-up" or "scale-out" of microreactor systems initially envisioned in the 1990s are now being brought into question [17, 18]. It now appears clear that the principle of numbering-up through direct interconnection of individual small-scale units into large-scale production systems does not really solve the scale-up problem as initially intended. On the contrary, numbering-up displaces a well-known chemical engineering problem of process scale-up to an unsolved problem of multi-scale process interconnection.

In order to comprehend fully the promises and difficulties of the structured multi-scale approach proposed here, it is of interest to compare the design methodology of multi-scale assembly with other alternative design solutions. Two contrasting and in many ways complementary approaches to industrial process design are worthy of consideration:

- traditional scale-up, based on mathematical modeling of large-scale systems

- recently proposed numbering-up, based on replication of small-scale systems and an analysis of their fundamental basis leading to the new, hybrid approach proposed here:
- multi-scale design, characterized by construction of large-scale systems with small-scale inner structuring.

1.3.1
Scale-up by Modeling

The conventional approach to industrialization of chemical processes is generally called "scale-up". Although in the past scale-up was frequently performed by empirical trial and error, the development of process engineering has led to tremendous improvements through the use of numerical simulation and computer-aided design of production devices in view of their optimization. For scale-up, the large-scale production system is mathematically broken down for calculation into a large number of smaller "finite elements" or "finite volumes", but the industrial system itself remains a large-scale device. Optimization is global, based on the mathematical analysis of local physical and chemical phenomena, but without any true attempt to control local operating conditions within the large-scale device. In the ideal case, scale-up using this approach includes the following steps:

- measurement of reaction kinetics and physico-chemical properties in laboratory devices in order to obtain information on rate laws, temperature dependencies, etc.;
- calculation of fluid flow, temperature and concentration fields in reactor devices;
- choice of optimal conditions taking into account the variations in operating conditions throughout the device, calculated by using the precise kinetic information from the laboratory studies and using calculation methods for the large-scale device.

The clear advantage of this approach is that detailed kinetic information and accurate modeling of large-scale devices offer the possibility to design processes with high performance in standard industrial equipment. It should be noted that if "microreactors" can be used to provide some quantitative information, they can be used in laboratory studies to shorten time and improve knowledge for the scale-up of existing equipment.

There are nevertheless disadvantages for rapid development with this approach. The most obvious disadvantage is that detailed kinetic and physico-chemical property information is required over a large range of operating conditions for accurate modeling, which is difficult to obtain rapidly in laboratory devices. Moreover, significant quantities of reactants are required and detailed studies to obtain rate expressions are time consuming.

Furthermore, local operating conditions throughout traditional large-scale devices are difficult to control and a compromise must be found between external operating parameters (reactor wall temperature, inlet flow rate, etc.) and process performance.

Variations in local operating conditions are not imposed within the device but rather "accepted" from spontaneous distributions within the large-scale system.

1.3.2
Numbering-up by Replication

The alternative to traditional scale-up, proposed in the context of microreaction technology and coined "scale-out" or "numbering-up", has attracted considerable academic interest. With this approach, the system of interest is studied only on a small scale in so-called "microreactors" and the final reactor design is simply a multiplication of interconnected small-scale devices. No attempt is made at large-scale optimization. Instead, the optimal functioning point is found for a small-scale device by empirical laboratory studies and then is simply reproduced by "replication" into the large interconnected structure.

The obvious advantages of this approach are that empirical measurements of qualitative performance can be used directly without recourse to the precise mechanisms necessary for the detailed modeling of the scale-up approach. The industrial user seeks optimal conditions for running the reactor using microreactors which can be obtained with small quantities of reactants in a relatively short time. It has even been claimed that scale-up disappears using this approach since the macro-device can be obtained by simple multiplication of the laboratory microreactors: by interconnecting a large number of them, the macro-production device should be achievable by running each microunit under the same optimum conditions as those found in the laboratory device.

In reality, although this approach may avoid reactor scale-up in the traditional sense, it does not solve the scale-up problem but simply changes the nature of the problem. In the numbering-up approach, the true problem results from the difficulty of optimal design for the numerous interconnections between reactors and for the essential connections of the "microreactor assembly" to the "macro-structure" necessary to feed the system.

Upon reflection, one concludes that it is rather unlikely that individual laboratory microreactors will be connected in this way in industrial designs. More likely is that large-scale macro-devices will be created with internal microstructuring and it is not evident that such devices will truly operate under identical conditions at all points in the interconnected structure. Numbering-up is therefore not the complete answer to the scale-up problem, but it does provide a stimulating model for a totally new way to design and construct reactor devices.

In addition to these technical aspects, economic aspects should also be taken into account: whereas the capital cost of a plant designed by scale-up generally increases with respect to the production to the power of approximately 0.7, the capital cost of plants designed by numbering-up is expected to be proportional to their capacity [13, 19]. This implies that numbering-up should be intrinsically more appropriate for variable production systems not exceeding a given maximum production level and for which the overall value depends on the complexity of the system. Since the various unit operations involved in a system require more or less complex microunits

to be intensified or miniaturized, some parts of a process may benefit from a numbering-up design whereas some others may only be cost-effective through traditional scale-up. A combination of both strategies therefore appears as a necessity for structured processes, resulting in a pragmatic hybrid approach.

1.3.3
Structured Multi-scale Design: a New Hybrid Approach

With the multi-scale assembly approach, diverse interacting small-scale units can be integrated into a large-scale device that is globally optimized with respect to standard industrial performance criteria. The strategy and rationale of the approach are to move from optimization of individual equipment units, which is the basis of numbering-up, to whole process design, which is the principle of scale-up. To respond to this challenge, design of such systems will involve integration and interconnection of diverse, small-scale structured components into large-scale macro-production devices. This approach should provide intensification locally only in those parts of a process where it is truly needed and then adapt interconnection of the locally intensified structures into a global macro-device.

The approach is not limited to any particular scale; on the contrary, it includes a variety of scales. In addition to the scales that the chemical engineer is used to controlling, the advances in microfabrication on the sub-millimeter scale and the fact that many important transport and transfer phenomena occur on length scales on the order of several tens to hundreds of micrometers indicate that the time is ripe to look into new design methodologies that can also benefit from the control of the phenomena at those scales. To reach that goal, not only microstructured channels should be included for transfer intensification, but local sensors and actuators can also be included to permit local process control of operating conditions (that may vary with position and time) throughout the reactor unit.

Basic design principles for process layout and process performance evaluation are clearly needed and these issues will require substantial research efforts in view of the development of a truly generic multi-scale design methodology. As a complement to the detailed research and development efforts, it should be noted that sophisticated methodology for detailed equipment design, interconnection and layout is only of use for industrial application once an initial, preliminary decision has been made to explore new technological options. The availability of approximate, short-cut methods and principles, derived from the more complete, rigorous research results, is an additional challenge for emerging innovation that cannot be ignored.

Examination of the state-of-the-art reveals that for a thorough evaluation of true technological opportunities for the use of small-scale structured components in chemical production, a comprehensive and systematic protocol is required as an aid to decision-making and for ultimate design and exploitation. Whether for retrofit of structured components into existing plant or for new design of future plant facilities, a new methodological approach is an urgent need and a clear contribution to future industrial competitiveness in chemical production technologies. Comparable to a Pinch Analysis for heat integration or to HAZOP for safety issues, the

structured multi-scale design methodology should be developed in such as way as to permit reliable qualitative and quantitative techno-economic evaluation of structured multi-scale process systems for both existing and potential production processes.

To attain acceptance in industrial practice, it is necessary to provide a number of validated business cases for true commercial processes of industrial interest, in the framework of a multidisciplinary R&D program. Overall results should include:

- proof of principle in several major industrial supply-chain sectors
- validated business models, including techno-economic analysis for each case
- generic design and optimization rules and software tools for their implementation
- decision criteria for appropriate choices of multi-scale approaches in practice.

1.4
Conclusion

The principle of geometric structuring emerged as a chemical engineering tool in the 1960s as a natural consequence of the concept of unit operations and of the comprehension of the importance of transport phenomena. With the rapid development of microfabrication technologies in the 1990s, integration and direct control of submillimeter scales in chemical processes now appear possible and particularly relevant as a contribution to the design of more sustainable processes. Combination of the advances in microfabrication with the development of multi-scale process design yields optimized process devices that resemble in some ways the highly evolved multi-scale biological structures observed in nature.

From an engineering point of view, microstructured devices and process components set the stage for a true paradigm shift in the principles of chemical process engineering. Rather than adapting the operating conditions and chemistry to available equipment, the process structure, architecture and equipment can now be adapted to the physico-chemical transformation. Production units can be created by integration and interconnection of diverse, small-scale structured units into large-scale macro-production devices. A key feature of the resulting structured chemical devices is local process control (through integrated sensors and actuators), leading to enhanced global process performance.

These devices could be helpful to realize production on demand (avoid transportation of hazardous chemicals, elimination or reduction of ecological risks) and to speed-up time-to-market for new production processes. The local, targeted intensification should enhance process performance by

- facilitating conversion from batch to continuous-flow processing
- increasing safety due to a lower holdup of hazardous components
- providing improved, more reliable and more reproducible quality
- permitting higher yield and selectivity
- reducing resource consumption (energy, reagents, water, solvents)

- offering access to new synthesis routes and to on-site on-demand manufacture, while at the same time remaining competitive, cost-effective and reliable.

The methodology for structured multi-scale chemical process design is an extremely promising area of scientific and technological investigation, rich in theoretical and experimental research and with significant potential for industrial competitiveness. In addition, the new approach should have a lasting impact on the teaching of chemical engineering and industrial chemistry and should also contribute to the attractiveness and acceptability of the chemical process industries.

Although relatively easy to imagine in principle, true industrial development and use of the concepts of structured multi-scale devices require further progress in research, combined with corresponding advances in the microfabrication methods required for the construction of the devices themselves. Targeted laboratory- and pilot-scale demonstrator units are an urgent necessity in this regard, along with critical techno-economic analysis of potential practical applications. Despite the difficulties, prospects and potential uses for these new chemical devices and production systems are considerable and concerted research actions between industrial and academic institutions should lead to rapid advances and significant perspectives for their development in the near future.

References

1 J. Villermaux, in *Proceedings of the Fifth World Congress of Chemical Engineering*, San Diego, CA, July 14–18, **1996**, pp. 16–23.

2 J. J. Lerou, K. M. Ng, *Chem. Eng. Sci.* **1996**, *51*, 1595–1614.

3 G. Agricola, *De Re Metallica Libri XII*, Froben & Episopius, Basel, **1556**.

4 G. E. Davis, *A Handbook of Chemical Engineering*, Davis Bros., Manchester, **1904**.

5 A. D. Little, *Professional Papers*, A. D. Little Inc., Cambridge, MA, **1908**.

6 R. B. Bird, W. E. Stewart, E. N. Lightfoot, *Transport Phenomena*, John Wiley & Sons, Inc., New York, NY, **1960**.

7 L. Spiegel, W. Meier, *Chem. Eng. Res. Des.* **2003**, *81*, 39–47.

8 M. Matlosz, W. Ehrfeld, J. P. Baselt, *Microreacction Technology: Proceedings of the Fifth International Conference*, Springer, Berlin, **2002**.

9 V. Hessel, S. Hardt, H. Loewe, *Chemical Micro Process Engineering: Fundamentals,* *Modeling and Reactions*, Wiley-VCH Verlag GmbH, Weinheim, **2004**.

10 A. I. Stankiewicz, J. A. Moulijn, *Re-engineering the Chemical Processing Plant: Process Intensification*, Marcel Dekker, New York, **2004**.

11 A. Bejan, *Shape and Structure – from Engineering to Nature*, Cambridge University Press, Cambridge, **2000**.

12 P. N. Sharratt, M. Matlosz, T. Bayer, *Proceedings of the 17th International Congress of Chemical and Process Engineering*, CHISA, Prague, August 27–31, **2006**.

13 L. Falk, *9th International Conference on Microreaction Technology, IMRET 9*, Potsdam, September 6–8, **2006**.

14 S. Lomel, L. Falk, J. M. Commenge, J. L. Houzelot, K. Ramdani, *Trans. IChemE, Part A* **2006**, *84*, 363–369.

15 J. M. Commenge, L. Falk, J. P. Corriou, M. Matlosz, *Chem. Eng. Technol.* **2005**, *28*, 446–458.

16 P. Le Goff, *Chem. Eng. Sci.* **1980**, *35*, 2029–2063.

17 K. F. Jensen, *Chem. Eng. Sci.* **2001**, *56*, 293–303.

18 M. Matlosz, J. M. Commenge, *Chimia* **2002**, *56*, 654–656.

19 A. R. Oroskar, K. VandenBusche, G. Towler, in *Proceedings of Microtec 2000, World Micro-technologies Congress*, 25–27 September, VDE-Verlag, Hannover, **2000**, pp. 385–392.