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From Process Miniaturization to Structured Multiscale Design: The Innovative, High-Performance Chemical Reactors of Tomorrow

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Abstract: The increasing use in recent years of microstructured components and devices for chemical analysis and laboratory applications has led to the development of a large number of miniaturized reactor systems of proven performance and interest for the chemical industries. The primary objective of these small-scale devices has been to generate chemical information, and for such applications 'smaller' is very often 'better' since smaller devices allow for use of smaller reactant volumes. Contrary to chemical information, however, chemical production (even for mini-plants) implies the use of significant volumes of reactants, and the motivations for employing microstructured systems in such cases require therefore closer examination. Upon reflection, one concludes that the potential advantages of microstructured devices and components are not limited solely to process miniaturization. On the contrary, incorporation of appropriately designed and targeted microstructured components within large-scale macrodevices can provide novel, innovative design concepts for performance enhancement, resulting in safer, cleaner and more efficient reactors and process units for production plants of all sizes.

Keywords: Microreaction engineering · Multiscale design · Process innovation · Process intensification

In the last 15 years, the international engineering-science community has witnessed a veritable revolution in the application of microfabrication technology in the industrial economy. Previously limited solely to microelectronics, miniaturized microdevices are now largely present in an ever growing number of diversified industrial sectors, due in particular to the exponential development of low-cost MEMS (micro electromechanical devices) and MOEMS (micro opto-electro-mechanical devices) of increasing complexity and integration.

In chemistry and biology as well, totally new areas of application for miniaturized and/or microstructured devices and components are now coming to light. The essential driving forces for these new applications are two-fold. On the one hand, 'technology push' due to the development of novel microfabrication methods, on the other hand, 'market pull' resulting from ever-increasing demands for chemical and biological information, improved product quality and faster time-to-market for new products and processes.

Modern microfabrication technology now enables production of miniaturized microstructured components and devices at highly competitive prices. For chemical and biological applications, a very important feature of the new microfabrication methods is their ability to produce precision machined structures in a wide variety of chemically resistant and/or biologically compatible materials. Early development of MEMS and MOEMS, and still much of contemporary work, has been largely limited to silicon processing. Silicon micromachining is highly accurate and reliable, and can produce microstructures of spectacular complexity. Nevertheless, for many chemical and biological applications, other materials are required. The recent developments in microstructure fabrication in plastics, metals, alloys, glasses and ceramics open up totally new possibilities that would be extremely difficult, if not impossible, to imagine with standard silicon processing.

Technological development in microfabrication, resulting in lower cost and greater diversity of materials is clearly a leading factor in the drive for miniaturization. Such a 'technology push' cannot be solely responsible, however, for the development of a multi-million-dollar industry. 'Supply' alone cannot create innovation: there must also exist (explicitly or implicitly) some unfulfilled society or market 'demand'.

A striking example of 'society demands' having a particularly strong impact on industrial behavior can be found in the biosciences. The demand for faster and more reliable DNA analysis for medical diagnosis, for criminal investigations, and for genetic research has led to extremely rapid development of new miniaturized analysis tools such as DNA-chips and micro total analysis systems (microTAS). The recent extension of research on DNA (genomics) to include the more general case of cellular proteins (proteomics) will require an enormous increase in the speed and reliability of miniaturized analyzers and should create even greater driving forces for innovation in microstructured devices and systems in the future.

In the chemical and pharmaceutical sectors, the rapid development of new products

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and synthesis routes has been a key 'demand driver' for microtechnology. In particular, the use of miniaturized, microstructured devices and components has been a major factor in the development of combinatorial chemistry for identification of new reaction routes for chemical and pharmaceutical synthesis. Microstructured systems can enable testing of many hundreds or even thousands of possible syntheses or pharmacological assays in a short time and with only very small quantities of reactants, thereby offering potential order-of-magnitude reductions in time-to-market for new chemical products.

Process Miniaturization: Chemical Information *vs.* Chemical Production

It is important to realize that the essential objectives of most miniaturized processes for microTAS, combinatorial chemistry and related applications concern primarily chemical and/or biological information. When analyzing perspectives for process integration and miniaturization, a clear distinction must be made between such applications and a fundamentally different class of applications for which the primary objective involves chemical (or biological) production.

In the case of chemical information, the extensive quantity involved ('amount of information') can be decoupled to a large extent from the amount of chemical product employed. It would appear, therefore, by analogy with microelectronics, that 'smaller' should (almost) always be 'better'. Performance objectives such as higher speed, higher throughput and smaller sample volumes should promote development of devices with exceptional degrees of process integration and intensification. In the extreme case, the only 'theoretical limit' to size reduction in devices and systems would be the requirement of guaranteeing (statistically) the presence of at least one molecule of a desired substance or element in the original sample volume!

Ultimate size reduction and 'ultra' miniaturization are of course not the only performance criteria involved. In addition to size reduction, other performance imperatives such as accuracy and facilities for sample handling must be taken into account, as well as technological limits for the design and construction of small-scale devices and components. Miniaturized 'microreactors' both for applications involving chemical information and chemical production have been the subject of considerable research over the last ten years, and the journal reviews by Jensen [1][2] as well as the recently published book of Ehrfeld, Hessel and Löwe [3] provide extensive summaries of the research literature in the specific area of miniaturized devices for applications in chemistry.

Although the basic physical laws of nature are generally not significantly altered on the microreactor scale for applications in chemistry (several tens to hundreds of microns for the smallest spatial dimension in most cases), the small sizes of internal structures of the devices can lead to operating regimes that are often radically different from those of more traditional devices. Small-scale 'microreactors' are characterized, for example, by the predominance of surface phenomena, such as capillary forces and heterogeneous reactions, in contrast to classical 'macroreactors' for which volumetric phenomena, such as gravitational forces and homogeneous reactions, generally play a major role. As a result, fluid flow in 'micro' devices tends to take place in a laminar regime, and surface-driven fluid movement (*e.g.* electro-osmotic pumping) is frequently employed, whereas in 'macro' devices, turbulent flow is frequently desirable (and attainable!) and fluid movement is practically always pressure-driven. Among the factors limiting 'ultra' miniaturization of microdevices, plugging, contamination, viscous flow, gas–liquid mixing (and/or separation) and mass transfer in confined volumes are important elements that will require considerable efforts in research, in particular in the newly developing area of 'microfluidics'.

In contrast to applications involving chemical information, for which the objective of 'maximum' miniaturization is very often desirable (although in practice limited by numerous physical and chemical factors), the situation for applications of miniaturization in chemical production is radically different. For chemical production, it is clear that the extensive quantities involved ('amount of material transformed', 'amount of energy generated', *etc.*) differ fundamentally from 'amount of information'. Whereas the amount of 'information' can be largely decoupled from the amount of chemical product involved, this is clearly impossible for chemical production, since the amount of chemical product involved is in itself an objective of the operation!

Although seemingly trivial at first glance, this simple distinction (information *vs.* production) alters significantly the analysis of the relative advantages and disadvantages of miniaturized chemical devices in practice and suggests that the specific features of miniaturization for chemical production should be addressed separately from those involved in applications for chemical information.

Since the distinction between these two application areas has not always been explicitly addressed in the research literature in the area of 'microreactors', research results have on some occasions led to confusing and/or apparently contradictory conclusions.

Miniaturization in Chemical Production: The Paradox

In some ways, it is rather surprising even to be discussing miniaturized production devices, since standard chemical engineering experience over the last century has confirmed time and again the validity of economies of scale in the chemical process industries. The 'Chilton rule', indicating that the cost of a chemical plant only increases to the 0.7 power of the plant size, suggests that bigger plant capacities should lead to lower production costs per unit of product generated and therefore to more competitive prices. This is in fact the case for many high-volume products, for which plant sizes world-wide over the last 15 years have continued to increase, with a corresponding decrease in the number of production sites [4].

It should be noted, however, that the cost of production on site at the plant is only one element in the total production chain from raw materials to consumer use. Many other factors, including transportation costs, suggest that distributed smaller-scale production may be of interest in certain cases. In this connection, the concept of 'mini-plants' for distributed production has been a subject of debate for the last 10 years [5]. In addition to reduced transportation costs, several other potential advantages have been explored including on-site production of hazardous intermediates. The presence on a given site of smaller quantities of potentially dangerous substances should offer advantages for process safety. It must be realized, however, that distributed production will necessarily lead to the presence of significant (albeit smaller) quantities of hazardous substances on a greater number of sites. One may therefore legitimately wonder whether the risk has been truly 'reduced' or whether on the contrary the risk has not simply been 'distributed'. In the latter case, the relative advantages and disadvantages for process safety will depend also on human factors such as the level of training of operators dealing with a larger variety of products on a larger number of delocalized sites.

Contrary to fixed production activities, for which distributed *versus* centralized operation is still open to discussion, miniaturized devices for chemical production and energy transformation for portable applications are clearly necessary, useful and in demand. Such applications include portable energy sources such as miniaturized fuel cells for lap-top computers and mobile phones, as well as biomedical devices such as artificial organs. In these areas, miniaturized components and devices respond to true society and market demands and are likely to continue to experience significant development in the future requiring increased process integration and intensification.

A related area of recent interest concerns the impact of miniaturized production devices on the relationship between suppliers and customers. The wide-spread availability of miniaturized production systems offers perspectives for new 'business models' in some industrial sectors, including the concept of 'selling the process' rather than 'selling the product'.

In conclusion, it is clear that despite the apparent paradox regarding economies of scale, additional qualitative considerations such as safety and portability will lead to significant demand for miniaturized production devices. The subject is therefore worthy of investigation, and should represent an important issue in industrial competitiveness for the future of the process industries.

Microstructured 'Macro' Devices: Intrinsically Multiscale

The design of miniaturized chemical devices such as mini-plants requires integration of numerous unit operations (heat transfer, mass transfer, separations, *etc*.) in compact, confined volumes. The corresponding process intensification involved in such systems will clearly require internal microstructuring, but equally important will be the design of the necessary connectors and interfaces to the external 'macro' world. Miniaturized production devices are therefore intrinsically multiscale and require therefore a multiscale approach for their chemical engineering design.

Although the initial driving force for such multiscale designs has come from the area of process miniaturization, upon reflection one realizes that the use of internal microstructures in macrodevices need not be limited solely to mini-plants. In fact, all production equipment should be able to benefit to a greater or lesser extent from internal microstructuring. Microstructured devices and components can provide extremely interesting and attractive possibilities capable of improving process performance in virtually all production systems. The internal dimensions of chemical 'microreactors' (typically several tens to hundreds of microns) are comparable to heat and mass-transfer boundary layers in chemical systems. Microstructuring can be used, therefore, to enhance heat- and mass-transfer performance in many devices (and not only in mini-plants).

The key objective in production applications, in contrast to information applications, will therefore NOT be the use of the smallest possible structuring but rather the smallest structuring necessary for a given performance enhancement. In addition, one will not try to miniaturize an entire plant, but rather apply small-scale structured devices and components solely at those points in the process where they are truly necessary. This hybrid, multiscale approach has recently been demonstrated by integrating a battery of micromixers into a macroprocess for production of polyacrylates [6]. Since enhanced micromixing is only required for contacting of the initial reactants, only the initial mixing elements were replaced by their microstructured counterparts, the remaining process units being left unstructured.

Future Perspectives: Structured Multiscale Design and Local Process Control

For the case of integrated micromixers, the mixing elements themselves are static devices, providing improved performance by means of a microstructured internal geometry. Future innovative process designs may wish to go further by incorporating directly small-scale sensors and actuators within the structured chemical production device. Such incorporation of active elements opens the way to true ' local process control'. Rather than fixing the operating conditions solely at the boundaries of a process (inlet flowrate, reactor wall temperature, *etc*.), integrated miniaturized sensors and actuators can be used to impose desired operating conditions locally point-by-point within the device itself. This concept has been suggested and tested for an electrochemical synthesis cell for which the internal actuators are particularly simple, since they involve directly the feed of the desired electrical current [7][8]. Electronic current is not the only control variable possible, however, and similar approaches of local process control for thermally-activated reactors can be envisioned by incorporation of heating and cooling elements, or for photochemical processes, by incorporation of optical fiber elements. Such 'smart' process units offer exciting perspectives for dramatic improvement in process performance and for safer, cleaner, and more competitive production systems [10].

In conclusion, microstructured reactors and process units are no longer limited solely to process miniaturization. Appropriate, targeted integration of specific microstructured components, when needed, into large-scale macroproduction devices offers promising perspectives for enhanced performance in the chemical plants of the future. For such innovative approaches to become reality, however, collaborative research between industrial and academic partners on an international level will be needed, not only to test these new concepts and ideas, but also to train the chemical engineers of tomorrow to adopt a structured multi-scale approach for their future process designs.

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