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# In the frame of globalization and sustainability, process intensification, a path to the future of chemical and process engineering (molecules into money)

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## Abstract

In today's economy, chemical and process engineering must respond to the changing needs of the chemical processes and related industries in order to satisfy both the increasing market requirements for specific end-use properties of the product required by the customer, and the social, and the raw material and energy savings, and environmental constraints of the industrial-scale process. In such a context of globalization and sustainability and amongst several tracks, it is shown that process intensification is a path for the future of chemical and process engineering demands. Process intensification concerns the design of novel equipment based on scientific principles and new production methods and is obtained in using either multifunctional reactors, or new operating modes, or microengineering and microtechnology for both high throughput and formulation screening, and for chemical production. Thus process intensification leads to more or less complex technologies that replace large, expensive, energy-intensive equipment or processes with ones that are smaller, less costly, more efficient plants, minimizing environmental impact, increasing safety and improving remote control and automation, or that combine multiple operations into a single apparatus or into fewer devices. With the help of the multidisciplinary and multiscale approach of the chemical engineering applied from the scale of the microreaction technology up to the scale of multifunctional macroreactors or equipment, process intensification offers new opportunities for chemical engineering, e.g., in concurrent product/process or microprocess engineering which can offer strategic competitive advantage in speed to market, cost, and also production innovation. It is thus involved in the trend "molecules into money" which is based on the premise that chemical engineering drives today economy development and is fundamental to wealth creation.

*Keywords:* Future of chemical engineering; Process intensification; Multifunctional reactors; New operating modes of production; Microengineering; Microtechnologies

## 1. Introduction

To satisfy both the market requirements for specific end-use properties of the products manufactured in (bio) chemical reactors or catalytic reactors, and the social, and the raw material and energy savings, and environmental constraints of the industrial-scale processes and technologies, it has been shown that a necessary progress is coming via a multidisciplinary and time and length multiscale approach (the molecular processes, product, process engineering (3PE) approach) [1]. So organizing scales and complexity levels in chemical and process engineering is now necessary to understand and to describe the relationships between events at nano- and microscales to better convert molecules into useful products at the process scale in the plant-scale production site. For example Fig. 1 [1] presents schematically the different length scales concerned in organizing levels of complexity to translate molecular processes into phenomenological macroscopic laws in order to create and to control the end-use properties and functionality of products manufactured by a batch or continuous process.

In the frame of globalization and sustainability, the future of chemical engineering can be summarized in four main objectives [1]:

(a) Increase productivity and selectivity through intensification of intelligent operations and a multiscale approach to processes control (e.g., nano- or microtailoring of catalyst materials).

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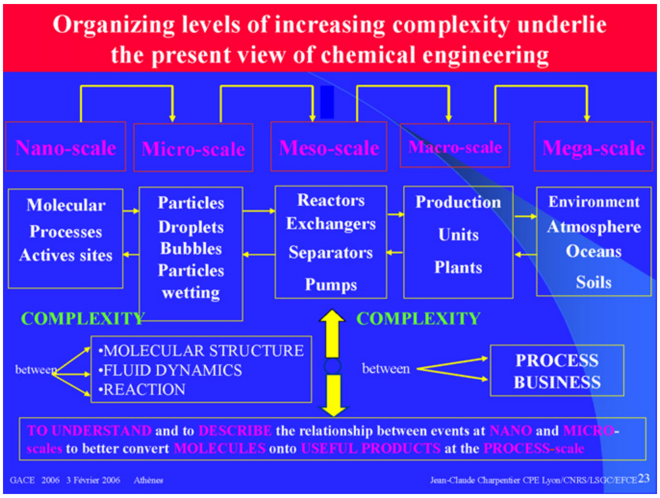

Organizing levels of increasing complexity underlie the present view of chemical engineering

Nano-scale
Micro-scale
Meso-scale
Macro-scale
Mega-scale

Molecular Processes Actives sites
Particles Droplets Bubbles Particles wetting
Reactors Exchangers Separators Pumps
Production Units Plants
Environment Atmosphere Oceans Soils

COMPLEXITY between
- MOLECULAR STRUCTURE
- FLUID DYNAMICS
- REACTION

COMPLEXITY between PROCESS BUSINESS

TO UNDERSTAND and to DESCRIBE the relationship between events at NANO and MICRO-scales to better convert MOLECULES onto USEFUL PRODUCTS at the PROCESS-scale

GACE 2006 3 Février 2006 Athènes
Jean-Claude Charpentier CPE Lyon/CNRS/LSGC/EFCE 23

Fig. 1. Organizing levels of increasing complexity underlie new view of chemical and process engineering [1].

(b) Design novel equipment based on scientific principles and new production methods: process intensification in using multifunctional reactors, microengineering and microtechnology.
(c) Extend chemical engineering methodology to product design and engineering using the "triplet molecular Processes-Product-Process Engineering (3PE)" approach to manufacture end-use properties.
(d) Implement multiscale application of computational chemical engineering modelling and simulation to real-life situations from the molecular scale to the production scale.

In this publication we shall emphasize only on process intensification due to the progress of basic research in chemical engineering.

Process intensification refers to more and less complex technologies that replace large, expensive, energy-intensive equipment or processes with ones that are smaller, less costly, more efficient plants, minimizing environmental impact, increasing safety and improving remote control and automation, or that combine multiple operations into a single apparatus or into fewer devices.

## 2. Process intensification using unit operation hybridisation

Such is the case with the "multifunctional" equipment that couples or uncouples elementary processes (transfer–reaction–separation) to increase productivity and/or selectivity with respect to the desired product and to facilitate the separation of undesired by-products. Extractive reaction processes involving single units that combine reaction and separation operations have received considerable attention as they offer major advantages over conventional processes due to the interaction of reaction, mass and energy transfer. Thermodynamic limitations, such as azeotrope, may be overcome and the yield of reactions increased.

The reduction in the number of equipment units leads to reduced investment costs and significant energy recovery or savings. Furthermore, improved product selectivity leads to a reduction in raw material consumption and hence, operating costs. Globally, process intensification through use of multifunctional reactors permits significant reductions in both investment and plant operating costs. Cost reductions between 10 and 20% are obtained by optimizing the process. In an era of limited profit margins, it allows chemical producers more leverage for competing in the global market place. Moreover in an increasingly commoditized market this may be also the determining factor for success.

A great number of reactive separation processes involving unit operation hybridization exist.

The concept of *reactive or catalytic distillation* has been successfully commercialized, both in petroleum processing, where packed bed catalytic distillation columns are used, and in the manufacture of chemicals where reactive distillation is often employed [2–4].

Catalytic distillation combines reaction and distillation in one vessel, using structured catalysts as the enabling element [5]. The combination results in a constant-pressure boiling system, ensuring precise temperature control in the catalyst zone. The heat of reaction directly vaporizes the reaction products for efficient energy utilization. By distilling the products from the reactants in the reactor, catalytic distillation breaks the reaction equilibrium barrier. It eliminates the need for additional fractionation and reaction stages, while increasing conversion and improving product quality. Both investment and operating costs are far lower than with conventional reaction followed by distillation [6].

The use of reactive distillation in the production of fuel ethers such as tertiary-amyl-methylether (TAME) or methyl-tertiary-butyl ether (MTBE) or methyl acetate, clearly demonstrates some of the benefits. Similar advantages have been realized for the production of high purity isobutene, for aromatic alkylation; for the reduction of benzene in gasoline and in reformate fractions; for the production of isopropyl alcohol by hydration of propylene; for the selective production of ethyleneglycol, which involves a great number of competitive reactions; and for the selective desulfurization of fluid catalytic cracker gasoline fractions; as well as for various selective hydrogenations. Extraction distillation is also used for the production of anhydrous ethanol. The next generation of commercial processes using catalytic distillation technology will be in the manufacture of oxygenates and fuel additives or in the synthesis of a range of fatty acid esters used in the manufacturing of cosmetics, detergents and surfactants [7], or in the recovering of lactic acid from fermentation broth [8].

Liquid maldistribution (large-scale and small-scale maldistribution) in packed columns distillation column is probably one of the most described effects influencing the efficiency of the column. A general trend is the emerging of multifunctional packings and their application in combined systems like catalytic distillation [9], or multiphase catalytic processes [10].

*Monolith* is an example of structured catalyst or reactor, the borders vanish for this catalyst application either as catalyst or as a functional reactor internal. The use of these structured reactors allow to decouple the chemistry, transport phenomena, and hydrodynamics and hence to tailor the reactor/catalyst independently to satisfy optimal operation conditions. Monoliths can be used both for co- and countercurrent operation in gas–liquid reactions [11]. They can combine the advantages of the slurry and trickle-bed reactor and eliminate the disadvantages such as discontinuous operation, stirring energy input and catalyst attrition or ineffective catalyst use, liquid maldistribution and local hot-spots that may develop and cause runaways. They can be contacted in virtually any desired way, opening up new processing routes [12,13]. Catalytic conversion can be combined, heat integration is possible, and lead to process intensification. In the laboratory monolithic structures provide a tool for scaling down catalyst testing units, with a wink to microreactor technology and combinatorial catalysis. It is expected that monoliths will be increasingly applied to chemical and biochemical conversion processes, from bulk and fine chemical production processes and in clean-up processes. Indeed the motivation of the use of monoliths (or capillary channels in other configurations), and the proof of concept has been established with great certainty, leading often to very accurate predictions of the performance [14,15].

Moreover one of the major aims of the researches on novel (micro-) structured reactor beds and catalytic support is process intensification, or herein, among others, a marked reduction of the size of the current reactor units is pursued. This involves monolith reactors, bead-string reactors, ceramic foam packings, composite structured packing reactors, three-levels of porosity reactors, etc. (see for example the global optimization analysis of a general class of perforated monolithic bed reactors for the case of an isothermal first-order reaction and for laminar flow conditions which is presented in Ref. [16]). The resulting design rules indicate how a given amount of catalyst material should best be perforated or distributed in space as a function of the available inlet pressure. It is shown that, in applying, the more advanced reactor designs involving beds with ultra-small flow-through pores, proposed in the past years, the productivity gain of these advanced concepts can even amount up to a factor of 100.

*An alternative reaction–separation unit is the chromatographic reactor*. It uses differences in the adsorptivity of the different components involved rather than differences in their volatility. It is especially interesting as an alternative to reactive distillation when the species involved exhibit small volatility differences, are non-volatile or are sensitive to temperature, as in the case of small fine chemical or pharmaceutical applications. There are several a class of reactions to which reactive chromatography is applied. The widest class of reactions is given by esterification reactions catalyzed by acidic ion-exchange resins or by immobilized enzymes, as the polarity difference between the two products (ester and water) makes their separation easy on many different adsorbents. Other applications include trans-esterifications, alkylation, etherification, (de)hydrogenations and reactions involving sugars. Reactive chromatography has also been used for methane oxidation. In all these applications, special care has to be devoted towards the choice of the solid phase for sorption selectivity, sorption capacity and catalytic activity. Typical adsorbents used are activated carbon, zeolites, alumina, ion-exchange resins and immobilized enzymes.

*Concerning the coupling of reaction and crystallization*, there exist myriads of basic chemicals, pharmaceuticals, agricultural products, ceramic powders and pigments produced by reactive crystallization-based processes: processes that combine crystallization with extraction to solution mine-salts. These separation processes are synthesized by bypassing the thermodynamic barriers imposed on the system by the chemical reactions, and the solubilities of the components in the mixture. By combining crystallizers with other unit operations, the stream compositions can be driven to regions within composition space where selective crystallization can occur. It is possible to selectively crystallize desired solid products after a reaction step and how to use compound formation to affect the separation of a mixture. A systematic method to synthesize flow sheets to separate binary mixtures by crystallizer–extractor hybrids has been presented [17] where the use of decanters, countercurrent extraction, and fractional countercurrent extraction is discussed for several phase behaviours including complex systems with multiple reactions.

*The complementary nature of crystallization and distillation is also explored*. Hybrids provide a route to bypass thermodynamic barriers in composition space that neither the distillation, which is blocked by azeotropes and hindered by tangent-pinches in vapour–liquid composition space, nor the selective crystallization, which is prevented by eutectics and hampered by solid solutions and temperature-insensitive solubility surfaces, can overcome when used separately [17]. Extractive and adductive crystallization are solvent-based techniques that require distillation columns. They are applied to high melting, close-boiling systems. Extractive crystallization uses a solvent to change the relative solubility of the solutes to affect separations. The distillation column is used to create solvent swings and to recycle the solvent. Commercial examples include solvent dewaxing, solvent deoiling and separation of sterols. Another advantage of such crystallization–distillation hybrid separation processes is that they do not require the addition of solvents, which may increase the process flows, create waste streams, propagate throughout a chemical plant and require costly separation and recycle equipment.

*Membrane technologies respond efficiently to the requirement of so-called process intensification* because they allow improvements in manufacturing and processing, substantially decreasing the equipment-size/production-capacity ratio, energy consumption, and/or waste production and resulting in cheaper, sustainable technical solutions. The papers [18,19] document the state-of-the-art and include progress and perspectives on integrated membrane operations for sustainable industrial growth.

The first studies on membrane reactors used membranes for distributing the feed of one of the reactants to a packed bed of catalyst. They were used in order to improve selectivity in partial oxidation reactions.

Other methods like the immobilization of biocatalysts on polymeric membranes have attempted selective removal of product from the reaction site in order to increase conversion of product-inhibited or thermodynamically unfavorable reactions. With such membrane bioreactors, provided that membranes of suitable molecular weight cut off are used, chemical reaction and physical separation of biocatalysts (and/or substrates) from the products can take place in the same unit. Substrate partition at the membrane/fluid interface can be used to improve the selectivity of the catalytic reaction toward the derived products with minimal side reactions. Bioreactors based on the hollow-fiber design are used to produce monoclonal antibodies for diagnostic tests, to mimic biological processes or to produce pure enantiomers, when a membrane separation is combined with an enantiospecific reaction. As for general membrane reactors, the result is a more compact system with higher conversion. This technology can respond to the increasing demand for food additives, feeds, flavors, fragrances, pharmaceuticals, and agrochemicals.

Phase-transfer catalysis can also be performed in membrane reactor configurations by immobilizing the appropriate catalysts in the microporous structure of the hydrophobic membrane. Catalytic membrane reactors are also proposed for selective product removal to remove equilibrium limitations, i.e., catalytic permselective or non-permselective membrane reactors, packed bed (catalytic) permselective membrane reactors, fluidized bed (catalytic) permselective membrane reactors. So the reaction step can be improved through the integration of a separation step, as for example in membrane reactors for dehydrogenation reactions where hydrogen in withdrawn from the reaction mixture using permselective Pd-membranes thereby shifting the reaction equilibrium to the desired products.

Alternatively, also the separation step can be improved due to the integration of a reaction step, as for instance in membrane reactors for the catalytic partial oxidation of methane using permselective dense perovskite membranes for the air separation, where the high consumption rate of oxygen at the permeate side helps increasing the chemical potential difference of oxygen across the membrane and hence the oxygen fluxes [20]. The development of such membrane reactors for high-temperature applications only became realistic in the last few years, with the development of high-temperature-resistant membranes (palladium membranes) mainly for dehydrogenation reactions, where the role of the membrane is simply hydrogen removal.

We should add that a new field of chemical and process engineering is now wide open with the coupling of supercritical fluids and membrane concepts to the design of very attractive and powerful processes, to improve transfer, reaction and handling of highly viscous liquids. This is the case for example of enzymatic membrane reactors where the use of supercritical fluid (low viscosity and high diffusivity—which result in faster reaction kinetics) improve several times the enzyme action respect to liquid conditions and additionally the enzyme membrane enhances its activity in many-fold by using a cross flow configuration in the reactor operation [21]. It should be also emphasized the recent design strategy aiming to provide concrete benefits in manufacturing and processing, which deals with the use of nanofiltration membrane for separating products of ionic liquid-mediated reactions from the ionic liquids used to enhance the reaction [22]. This major interest of all the processes thus created, is to safeguard the environment and the products. This is particularly essential when the processes are of a biological nature [23,24].

For more general applications, material scientists must solve the problem of providing inorganic membranes of perfect integrity, that have mechanical and thermal stability and that will allow large fluxes of desired species. Secondly, chemical engineers must resolve the heat transfer problem that now threatens successful scale-up. It might seem reasonable to expect membrane reactors, which combine oxygen transfer membranes with selective catalytic layers for partial oxidation of hydrocarbons. However, a continuous research effort in the dynamics of these processes and in the study of advanced control systems applied to integrated multi-membrane operations is now necessary.

Finally concerning the use of membranes for process intensification, it should be recommended the special issue of Chemical Engineering Research and Design, 2005, “Process Developments in Membrane Contactors and Reactors” [25]. This issue highlights the growing importance of membrane processes, the recent developments, and presents the important challenges in the topic at the same time as offering interesting prospects for process industries.

It should be mentioned that multifunctional reactors are not new to the chemical and process industries as they have been used since many decades for absorption or extraction with chemical reaction. But only recently reactors incorporating several “functions” in one reactor have been formally classified as being multifunctional and the great benefits obtained in integrating the progress of knowledge at different time and length scales have been acknowledged by the process industries.

This was illustrated by the first international symposium on multifunctional reactors in 1999 [26] with a presentation of research and development in the main domains of reaction and heat exchange, reaction and membrane separation, reaction and sorption, reaction and power generation, reactions and distillation, reaction and catalyst regeneration and the use of non-traditional structured packing. This was also illustrated by the second symposium on multifunctional reactors in 2002 [27] which shows that although two areas – reactive distillation and membrane reactors – still dominate the subject, several others, such as chromatographic reactors, are catching up rapidly and exotic newcomers, involving the electrochemical processes in fuel cells for example, are emerging. Then this was illustrated by the third International Symposium on multifunctional reactor held in Bath in 2003 [28] with contributions on reactive distillation, adsorptive reactors, membrane, reactors, autothermal reaction systems, and structured reactor configurations. And finally it was created on that topic in (2005) a Working Party of the European Federation of Chemical Engineering regrouping a great number of academic and industrial partners.

It should be mentioned that the use of hybrid technologies encountered in a great number of multifunctional reactors is still limited by the resulting problems with control and simulation. The interaction between simultaneous reaction and distillation introduces more complex behaviour, involving the existence of multiple steady states and output multiplicities corresponding to different conversions and product selectivity than those achieved in conventional reactors and ordinary distillation columns. This leads to interesting challenging problems in dynamic modeling, design, operation, and strong non-linear control [29,30]. Indeed, the response of a reactive separator with marginal changes in design parameters, such as feed position, feed flow, number of stages, height, type of packing or plates, etc. may be drastic and unforeseen and, consequently, the simulation of this hybrid equipment should be based on reliable models with high accuracy. Their control requires sophisticated model predictive control, robust control and adaptative control, where mathematical predictive control may have to run 50–500 times faster than real time.

There is also an increasing awareness that the full potential of multifunctional reactors may only be realized if the reaction and the unit operation integrated are properly harmonized and too much integration can even exert a negative influence, requiring detailed modeling of the underlying processes and careful selection of the chemical and physical system properties and operation conditions [31]. It is suggested that many of the potential benefits can be achieved by a partial approach to multifunctionality and that further integration has a low increment value [32].

## 3. Process intensification using new operating modes of production

The intensification of processes may be obtained by new modes of production that are also based on scientific principles. New operating modes have been studied in the laboratory and/or pilot stage: reversed flow for reaction–regeneration, unsteady operations, cyclic processes, extreme conditions, pultrusion, low-frequency vibrations to improve gas–liquid contacting in bubble columns, high temperature and high pressure technologies, and supercritical media and ionic liquids are now seriously considered for practical applications. Reactors can be operated advantageously with moving thermal fronts that are created by periodic flow reversal. Low-level contaminants or waste products such as volatile organic compounds can be efficiently removed in adiabatic fixed beds with periodic reversal by taking advantage of higher outlet temperatures generated in earlier cycles to accelerate exothermic reactions. Energy and cost savings are affected by this substitution of internal heat transfer for external exchange [33].

Some attractive options for improved catalytic reactor performance via novel modes of operation are periodic (symmetric) operation of packed beds with exothermic reaction, coupling of an exothermic and endothermic reaction in a periodically operated (asymmetric) packed-bed, and induced pulsing liquid flow in trickle beds to improve liquid–solid contacting at low liquid mass velocities in the cocurrent downflow mode [34,35]. Also such periodic operation with respect to liquid flow may help in getting process intensification for gas-limiting reactions or for petroleum applications where filtration and bed plugging are serious threats [36]. Moreover non-conventional research on magnetic-driven process intensification is worth noting for mini trickle-bed reactors especially in non-petroleum applications such as in fine and pharmaceuticals chemical processes. It has been shown that positive-gradient in homogeneous magnetic fields promote larger values of liquid holdup (and thus wetting efficiency in trickle flow regime) and two-phase pressure drop [37].

Also, when high conversions are required and the gaseous by-product of the reaction is known to inhibit the rate, as in hydrodesulfurization, or in selective hydrogenation, countercurrent flow operation of traditional trickle beds is now preferred [38], Also, improving the product selectivities in a parallel-series reaction by feeding one reactant through the reactor by stage wise reactant dosing will be applied [39] and it should be underlined the use of ultrasonic and microwave technologies to enhance the rates and improve the selectivities of catalytic reactions [40]. It should be also emphasized that in recent years, among non-conventional bioreaction media, supercritical fluids and ionic liquids have been appeared as interesting “green” alternatives to classical organic solvents to carry out enzymatic reactions for the preparation of valuable and active organic materials, opening the door for a clean chemical industry in the near future [41].

## 4. Process intensification using microengineering and microtechnology

Current production modes are increasingly challenged by decentralization, modularization and miniaturization. Microtechnologies developed, especially in Germany (i.e., IMM, Mains and Forschnungszentrum, Karlsruhe) and in USA (i.e., MIT and DuPont) lead to microreactors, micromixers, microseparators, micro-heat-exchangers and microanalyzers, making accurate control of reaction conditions possible with respect to mixing, quenching, and temperature profile. Microfabrication techniques and scale-up by replication have shown spectacular advances in the electronics industry, and, more recently, in microanalysis by biological and chemical applications. Microfabricated chemical systems are now expected to have a number of advantages for chemical kinetic studies, chemical synthesis, and more generally, for process development. Indeed the reduction in size and integration of multiple functions has the potential to produce structures with capabilities that exceed those of the conventional macroscopic systems and to add new functionality, while potentially making possible mass production at low cost.

Miniaturization of chemical analytic devices in micro-total-analysis-system ($\mu$TAS) represents a natural extension of microfabrication technology to biology and chemistry, with clear applications in combinatorial chemistry, high throughput screening, and portable analytical measurement devices. Also, the merging of $\mu$TAS techniques with microreaction technology promises to yield a wide range of novel devices for reaction kinetic and micromechanism studies, as well as on-line monitoring of production systems [42].

Microreaction technology is expected to have a number of advantages for chemical production [43,44]. The high heat and mass transfer rates possible in microfluidic systems allow reactions to be performed under more aggressive conditions with higher yields than conventional reactors. Also, new reaction pathways considered too difficult for application in conventional microscopic equipment, such as direct fluorination of aromatic compounds, could be pursued because if the microreactor fails, the small amount of chemicals released accidently could be easily contained. The presence of integrated sensor and control units could allow the failed microreactor to be isolated and replaced, while other parallel units continued production. In addition, these inherent safety characteristics could allow a production scale system of multiple microreactors, enabling a distributed point-of-use synthesis of chemicals with storage and shipping limitations, such as highly reactive and toxic intermediates like cyanides, peroxides, and azides.

Microchemical systems for combinatory synthesis and screening of small molecules and systems for nucleic acid synthesis and detection have already revolutionized drug discoveries in pharmaceutical companies [45]. Similarly rapid screening of small molecules and systems for nucleic acid synthesis pathways could lead to analogous productivity increases in chemical industry laboratories. Experimentation at the conventional bench-scale is limited by the high costs of reagents and safety concerns, which the small volumes and inherent safety characteristics of the microreactors could effectively eliminate [46,47].

Moreover, scale-up to production by replication of microreactors units used in the laboratory would eliminate costly redesign and pilot plant experiments, thereby shortening the development time from laboratory to commercial-scale production. This approach would be particularly advantageous for pharmaceutical and fine chemical industries where production amounts are often less than a few metric tonnes per year. Others more recently have begun to apply microchannel technology to larger scale applications such as methane steam reforming, gas to liquid, propylene oxide, hydrogen peroxide production, etc., some with industrial partnership, I.M.M., Degussa, UOP; FMC, Accentus, etc., as referred by Ref. [48].

Small reactors are already used for testing process chemistries, like catalyst testing. Chemical detection is the rate-limiting step in most techniques since detailed product information must be obtained using sequential screening. However, with the continual advances in μTAS and microfabrication techniques, these macroscopic test systems could be replaced by PC-card-sized microchemical systems consisting of integrated microfluidic, sensor, control, and reaction components requiring less space and utilities, and producing less waste. Moreover, the small dimensions imply laminar flow, making it feasible to fully characterize heat and mass transfer and extract chemical kinetic parameters from sensor data.

As an illustration it was proposed a new concept for high throughput screening (HTS) experiments for rapid catalyst screening based on dynamic sequential operations with a combination of pulse injections and micromachined elements [49]. The principle used for the test microreactor is a combination of pulse injections of the catalyst and the substrate, a static IMM micromixer with negligible volume and residence time less than $10^{-2}$ s mounted in a dynamic microactivity test, and a tubular stainless steel capillary reactor. The pulses mix perfectly in the micromixer and the liquids or the gas–liquid mixtures thereby emulsify and behave as a reacting segment, which then travels along the tubular microreactor. Collection and analysis at the outlet of the reactor provides the conversion and selective data. The catalyst library was then screened for two test reactions, a liquid–liquid isomerization of allylic alcohols and a gas–liquid asymmetric hydrogenation. The results of this technique lead to the selection of the best catalyst showing activity towards a large class of allylic alcohols and similar results obtained in a traditional well mixed batch reactor (40 $cm^3$) proves the validity of the microreactor concept. Indeed using these microreactors for HTS of fluid–liquid molecular catalysis offer considerable advantages over traditional parallel batch operations by ensuring good heat and mass transport in a small volume, reducing sample amounts (to microgram levels), a large range of operating conditions (temperature, pressure), fewer, simpler electro-mechanical moving parts and throughput testing frequencies of more than 500 per day. Complementary comparison of the performances with diverse reactors are presented in Ref. [50].

Moreover complementary data concerning a part of high throughput catalyst screening facility have been presented in a study which developed a microfluidic unit for sequencing fluid samples for composition analysis [51]. The novel feature is that the key components are the use of an array of microfluidic valves having no moving parts and operating at very low sample flow Reynolds numbers, typically below 100.

Another illustration is the design of a prototype miniature bioreactor for high throughput automated bioprocessing. Indeed a major challenge for drug discovery now is to elucidate the relationship between proteins produced by each gene, and disease. In this respect, advances in proteomics and automated HTS based on the shaken microwell plate system have provided the technology platform for a significant increase in the number of potential drug candidates that are likely to come forward. A related challenge is the need to define the conditions from the translation of results, from the microwell systems to conventional laboratory scale. Recently a new miniature gas–liquid bioreactor was described [52] which was designed to have the same diameter as that of a single well of a standard 24-well plate but is mechanically agitated and aerated with a microfabricated–bladed turbine impellor such that its operation mimicked the flow condition in a conventional mechanically stirred reactor. Experimental and theoretical analyses were used to establish its performance as a fermenter. Microfabricated fibre optic probes were used for in situ measurement of process parameters including dissolved oxygen, pH, temperature, and cell density. Volumetric oxygen transfer data were obtained for air–water and *Escherichia coli* fermentation under different operational conditions. The results were compared with data obtained from parallel experiments using a 20 l mechanically agitated fermenter with a working volume of 15 l and with predictions using Higbie's penetration model with the contact time obtained from the CFD simulations of the turbulent flow in the bioreactor. Predicted and measured volumetric mass transfer coefficients in the miniature bioreactor are in the range 100–400 $h^{-1}$, typical of those reported for large-scale fermentation which assessed its engineering performance as a fermenter.

Fig. 2. One vision of how a future plant employing process intensification may look (right) vs. a conventional plant (left) [57].

The examples reported here represent a small fraction of the many designs for microreactors being pursued or envisioned by different research groups. Microengineered reactors have some unique characteristics that create the potential for high performance chemicals and information processing on complex systems. They can provide significant advantages in information generation for high throughput experimentation and process development, and from difficulty to obtain operating regimes. In terms of chemical manufacture, they allow distributed, mobile and intensified processing [53]. However, when applying microengineered reactors, it should be suggested to conduct a fair comparison between microchannel reactors and their conventional counterparts. The new reactor type has to be tested against the best alternative reactor for the given application (kinetic measurements, catalyst screening, production, etc.) [54]. Moreover in developing microreaction technology for process intensification, it is essential to focus on systems where microfabrication can provide unique process advantages resulting from the small dimension, i.e., not only the high transport rates, but the forces associated with high surface area-to-volume ratio.

## 5. Conclusions: process intensification: a path to the future for chemical and process engineering (molecules into money?)

In summary for process intensification, it is shown that many new technologies are being developed in chemical industries motivated by improved chemistry, enhanced safety, improved processing energy and environment benefits, low inventories, capital cost reduction, enhance corporate image, novel or enhanced products and value to customers [55,56]. In Ref. [57] a vision of how a future plant employing process intensification involving both microtechnology and unit operation hybridization is proposed and compared to a conventional plant (see Fig. 2). These improvements in the design of modern petrochemical plants are actually already obtained to day in certain cases (see Fig. 3 showing a TAMOIL plant located in Switzerland, including a Fluid Catalytic Cracking unit for the valorization of heavy crude oil charges).

But several important barriers must be overcome before process intensification is widely adapted, such as the maturity and economic competitiveness of the new technologies compared to the conventional technologies. The conservatism of plant owners using batch processes means will not easily accept continuous processing solutions.

Anyway it has to be underlined that today's microreaction technology contributes substantially to the fields of chemistry, chemical engineering and energy generation, to name but a few. It is seen that this technology, which on the reaction level already shows a broad variety of facets concerning different applications, has now reached the field of downstream processing to influence industrial pilot and also production processing. Indeed one of the main advantages of microstructured reactor technology is that a lot of industrial batch processes can be run continuously by using this new technology which provides more flexibility compared to traditional plants. The integration of microstructured reactors within existing plants is thus facilitated. For illustration we could mention the industrial use of recent microstructured mixers operating with typical maximum throughputs barrier lifted to several tens of cubic meters per hour flow rate domain. These micromixers are applied to carry out advanced syntheses of fine chemicals or pharmaceuticals, as well as for the generation of dispersions, foams, creams and emulsions [58]. Moreover the availability of complete plants with microstructured reactors has

Fig. 3. A vision of a modern petrochemical plant located in Switzerland (rendering courtesy of IFP).

also led to commercial interest and certainly reaction classes where microchannel architecture appears to be advantageous include dehydrogenation, oxidation, alkylation and others. Furthermore it should be underlined that the current impact of microreaction technology on chemical and process engineering is reflected in the fact that two consecutives issues of Chemical Engineering and Technology journal in 2005 [59] have been dedicated to this topic, showing both breathtaking scientific results and their process application.

And it is clear that there exists now a current trend which can be called *from microreactor design to microreactor process design*. This is illustrated by the today existence of at least 30 production plants operating with microstructured reactors. And it should be also mentioned and underlined the recent publication of favourable and hopeful cost analysis on the use of microprocess engineering for the fine chemistries, thus being obtained in detailing the plant engineering cost [60]. It should be added that the IMPULSE European consortium recently created develops concerted research actions between industrial and academic institutions encouraging the development of the necessary methodological tools required for future industrial implantation of the approach [61].

More generally this shows clearly that with the help of the integrated multidisciplinary and multiscale approach of the chemical engineering, as schematically presented in Fig. 1 and applied from the structured microtechnology up to multifunctional macroequipment scales, process intensification is totally involved in the trend “Molecules into Money” which is based on the premise that chemical and process engineering drive today economic development and are fundamental to wealth creation. And in using process intensification which is actually a path to the future for the chemical engineering demands in the frame of globalization and sustainability, there are today new opportunities for chemical engineering, in product and microprocess design for structured product formulation. These opportunities are both in process analysis of product end use, and in concurrent product/process or microprocess design, the last one can offer strategic competitive advantage in speed to market, cost, and also product innovation.

## References

[1] J.C. Charpentier, Four main objectives for the future of chemical and process engineering mainly concerned by the science and technologies of new material production, Chem. Eng. J. 107 (2005) 3–17.

[2] M.F. Malone, M.F. Doherty, Reactive distillation, Ind. Eng. Chem. Res. 39 (2000) 3953.

[3] R. Taylor, R. Krishna, Modelling reactive distillation, Chem. Eng. Sci. 55 (2000) 5183–5229.

[4] Z. Guo, J.W. Lee, Feasible products in batch reactive extraction distillation, AICHE J. 50 (7) (2004) 1751–1762.

[5] A. Gorak, A. Hoffmann, Catalytic distillation in structured packings: methylacetate synthesis, AICHE J. 47 (5) (2001) 1067–1076.

[6] Y. Xu, T. Chuang, A.R. Sanger, Design of a process for production of isopropyl alcohol by hydration of propylene in a catalytic distillation column, Chem. Eng. Res. Des. 80 (2002) 686–694.

[7] F. Omota, A. Dimian, A. Bliek, Fatty acid esterification by reactive distillation. Part 1. Equilibrium based design, Chem. Eng. Sci. 58 (2003) 3159–3174; Part 2. Kinetic based design for sulphate zirconia catalysts, Chem. Eng. Sci. 58 (2003) 3175–3185.

[8] J. Choi, W.H. Hong, Recovery of lactic acid by batch distillation with chemical reaction using ion exchange resin, J. Chem. Eng. Jpn. 32 (1999) 184–189.

[9] L. Spiegel, W. Meier, Distillation columns with structured packing in the next decade, Chem. Eng. Res. Des. 81 (2003) 22–34.

[10] F. Kapteijn, J.A. Moulijn, Structured catalysts: potent alternatives for multiphase catalytic processes, in: Proceedings of the XVIIIth Croatian Meeting of Chemists and Chemical Engineers, Zagreb, February 16–19, 2003.

[11] A.K. Heibel, W. Liu, M. Morse, Structured catalysts and processes for gas–liquid reactions. World Patent WO03/041852 A1.

[12] R. Shaibal, T. Bauer, M. Al-Dahhan, P. Lehner, T. Turek, Monoliths as multiphase reactors: a review, AICHE J. 50 (2004) 2918–2938.

[13] T. Boger, A. Heibel, C.M. Sorensen, Monolithic catalysts for the chemical industry, Ind. Eng. Chem. Res. 43 (2004) 4602–4611.

[14] M.T. Kreutzer, F. Kapteijn, J.A. Moulijn, I.J. Heiszwolf, Multiphase monolith reactors: chemical reaction engineering of segmented flow in microchannel, Chem. Eng. Sci. 60 (2005) 5895–5916.

[15] T. Bauer, R. Guettel, S. Roy, M. Schubert, M. Al-Dahhan, R. Lange, Modelling and simulation of the monolithic reactor for gas–liquid reactions, Chem. Eng. Res. Des. 59 (2005) 811–819.

[16] G. Desmet, H. De Greef, H. Verelst, G.V. Baron, Performance limits of isothermal packed bed and perforated monolithic bed reactors operated under laminar flow conditions. Part 1. General optimization analysis, Chem. Eng. Sci. 58 (2003) 3187–3202; Part 2. Performance comparison and design considerations, Chem. Eng. Sci. 58 (2003) 3203–3214.

[17] (a) D.A. Berry, K.M. Ng, Synthesis of reactive crystallization processes, AICHE J. 43 (1997) 1737–1750;
(b) D.A. Berry, K.M. Ng, Synthesis of crystallization in distillation hybrid separation processes, AICHE J. 43 (1997) 1751–1762.

[18] E. Drioli, M. Romano, Progress and new perspectives on integrated membrane operations for sustainable industrial growth, Ind. Eng. Chem. Res. 40 (2001) 1277–1300.

[19] E. Drioli, E. Curcio, G. Di Profio, State of the art and recent progresses in membrane contactors, Chem. Eng. Res. Des. 83 (2005) 223–233.

[20] M.U. Van Sint Annaland, S.A.R.K. Deshmukh, J. Smit, J.A.M. Kuipers, Development and modelling of membrane reactors, in: Proceedings of the XVIth International Conference on Chemical Reactors, Abstracts PL 3, Berlin, December 1–5, 2003, pp. 10–14.

[21] D. Paolucci-Jeanjean, M.P. Belleville, G.M. Rios, Biomolecule applications for membrane-based phase contacting systems—distribution, separation and reaction—a first state of the art, Chem. Eng. Res. Des. 83 (2005) 302–308.

[22] S. Han, H.T. Wong, A.G. Livingston, Application of organic solvent nanofiltration to separation of ionic liquids and products from ionic liquid mediated reactions, Chem. Eng. Res. Des. 83 (2005) 309–316.

[23] S. Sarrade, C. Guizard, G.M. Rios, Membrane technologies and super critical fluids: chemical engineering for coupled processes, Desalination 144 (2002) 137–142.

[24] Z. Knez, M. Habulin, M. Primozic, Hydrolases in supercritical $CO_2$ and their use in a high pressure membrane reactor, Bioprocess Biosyst. Eng. 25 (2003) 279–284.

[25] Process developments in membrane contactors, Eds. M. Nyström, G.M. Rios, Chem. Eng. Res. Des. 83 (special issue) (2005) 221–330.

[26] J.A. Moulijn, A.I. Stanckiewicz, First international symposium on multifunctional reactors, Chem. Eng. Sci. 54 (special issue) (1999) 1297.

[27] D.W. Agar, Second international symposium on multifunctional reactors, Chem. Eng. Sci. 57 (special issue) (2002) 1489.

[28] L. Kershenbaum, Third international symposium on multifunctional reactors, Chem. Eng. Res. Des. 82 (special issue) (2004) 127–301.

[29] S.B. Hung, M.J. Lee, Control of different distillation configurations, AICHE J. 52 (2006) 1423–1440.

[30] K. Sundmacher, A. Kienle, Reactive Distillation: Status and Future Direction, Wiley–VCH, Weinheim, Germany, 2003.

[31] E.H. Stitt, Reactive distillation for toluene disproportionation: a technical and economic evaluation, Chem. Eng. Sci. 57 (2002) 1537–1543.

[32] E.H. Stitt, Multifunctional reactor? “up to a point Lord Copper”, Chem. Eng. Res. Des. 82 (2004) 129–139.

[33] F.M. Dautzenberg, M. Mukherjee, Process intensification using multifunctional reactors, Chem. Eng. Sci. 56 (2001) 251–267.
[34] P.L. Silvestone, J. Hanika, Periodic operation of 3-phase catalytic reactors, Can. J. Chem. Eng. 82 (2004) 1105–1142.
[35] K.D.P. Nigam, F. Larachi, Process intensification in trickle bed reactors, Chem. Eng. Sci. 60 (2005) 5880–5894.
[36] I. Iliuta, F. Larachi, Mitigating fines plugging in high pressure/temperature hydrotreaters using an induced-pulsing trickle-bed filtration approach, Chem. Eng. Sci. 60 (2005) 6217–6225.
[37] I. Iliuta, F. Larachi, Theory of trickle-bed magnetohydrodynamics under magnetic-field gradients, AICHE J. 49 (2003) 1525.
[38] C. Julcour, R. Jaganathan, R.V. Chaudary, A.M. Wilhem, H. Delmas, Selective hydrogenation of 1,5,9,-cyclododecatriene in upflow and downflow fixed bed reactors: experimental observations and modelling, Chem. Eng. Sci. 56 (2001) 557–564.
[39] M. Morbidelle, A. Gavriidilis, A. Varma, Catalyst Design: Optimal Distribution of Catalyst in Pellets Reactors and Membranes, University Press, Cambridge, 2001.
[40] J.P. Mikkola, J. Kuusists, J. Aumo, T. Salmi, Studies on the ultrasonic enhancement of the catalytic activity in the hydrogenation of citral, in: E.G. Derouane, et al. (Eds.), Principles and Methods for Accelerated Catalyst Design and Tasting, Kluwer Academic Publishers, 2002, pp. 333–335.
[41] C.G. Laudani, M. Paljevac, M. Habulin, Z. Knez, Biosynthesis by lipase–ionic liquid systems in supercritical carbon dioxide, in: Proceedings of the Slovenian Chemical Days 2005, Maribor, September 22–23, 2005, p. 127.
[42] K.F. Jensen, Microreaction engineering—is small better? Chem. Eng. Sci. 56 (2001) 293–303.
[43] V. Hessel, St Hardt, H. Löwe, Chemical Micro Process Engineering: Basic and Fundamentals, Wiley–VCH, Germany, 2004.
[44] V. Hessel, H. Löwe, A. Müller, G. Kolb, Chemical Micro Process Engineering: Processes and Applications, Wiley–VCH, Germany, 2005.
[45] S. Borman, Combinatorial chemistry: refining the scientific method, Chem. Eng. News 78 (2000) 53–65.
[46] D.C. Hendershot, Process minimization: making plants safer, Chem. Eng. Prog. (2000) 23.
[47] R. Jachuck, Process intensification for responsive processing, Chem. Eng. Res. Des. 80 (2002) 233–238.
[48] A. Tonkovich, D. Kuhlmann, A. Rogers, J. Mc Daniel, S. Fizgerald, R. Arora, T. Yuschak, Microchannel technology scale-up to commercial capacity, Chem. Eng. Res. Des. 83 (2005) 634–639.
[49] C. de Bellefon, C. Tanchoux, S. Caravieilhes, P. Grenouillet, V. Hessel, Microreactors for dynamic, high throughput screening of fluid/liquid molecular catalysis, Angew. Chem. Int. Ed. 39 (19) (2000) 3442–3445.
[50] C. de Bellefon, R. Abdallah, T. Lamouille, N. Pestre, S. Caravieilhes, P. Grenouillet, Chimia 56 (2002) 621.
[51] V. Tesar, J.R. Tippetts, Y.Y. Low, R.W.K. Allen, Development of a microfluidic unit for sequencing fluid samples for composition analysis, Chem. Eng. Res. Des. 82 (2004) 708–718.
[52] S.R. Lamping, H. Zhang, B. Allen, P. Ayari Shamlou, Design of a prototype miniature bioreactor for high throughput automated bioprocessing, Chem. Eng. Sci. 58 (2003) 747–758.
[53] A. Gaviilidis, P. Angeli, E. Cao, K.K. Yeong, Y.S.S. Wan, Technology and applications of microengineered reactors, Chem. Eng. Res. Des. 80 (2002) 3–30.
[54] S. Walter, S. Malmberg, B. Schmidt, M.A. Liauw, Comparison of microchannel and fixed bed reactors for selective oxidation reactions, Chem. Eng. Res. Des. 83 (2005) 1009–1018.
[55] C. Tsouris, J.V. Porcelli, Process intensification—has it time finally come? Chem. Eng. Prog. 10 (2003) 50–55.
[56] A.I. Stanckiewicz, J.A. Moulijn, Reengineering the chemical process plant: process intensification, Marcel Dekker, New York, 2004.
[57] A.I. Stankiewicz, J.A. Moulijn, Process intensification: transforming chemical engineering, Chem. Eng. Prog. 96 (2000) 22–34.
[58] B. Werner, V. Hessel, P. Löb, Mixers with microstructured foils for chemical production purposes, Chem. Eng. Technol. 28 (2005) 401–407.
[59] Microreaction Engineering, Ed. V. Hessel, special issues, Chem. Eng. Technol. 28 (2005) 243–527.
[60] V. Hessel, Process intensification and exploring novel processing routes by micro structured reactors, in: Proceedings of the CPAP Satellite Meeting, University of Washington Rome Centre, Rome, Italy, March 20–22, 2006.
[61] T. Bayer, J. Jenck, M. Matlosz, IMPULSE—a new approach to process design, Chem. Eng. Technol. 28 (2005) 431–438.