

# Intensified Reaction and Separation Systems

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## Keywords

process intensification, reactive separations, hybrid separations, structured reactors, alternative energy forms, multifunctionality

## Abstract

Process intensification follows four main goals: to maximize the effectiveness of intra- and intermolecular events, to give each molecule the same processing experience, to optimize the driving forces/maximize specific interfacial areas, and to maximize the synergistic effects of partial processes. This paper shows how these goals can be reached in reaction and separation systems at all relevant time and length scales and is focused on the structuring of reactors and separation units, on the use of different energy forms to improve the reaction and separation, on combining and superimposing of different phenomena in one integrated unit or reactor, and on the application of oscillations for intensification of reaction and separation processes.

## INTRODUCTION: PROCESS INTENSIFICATION AND ITS FUNDAMENTAL APPROACH

Process intensification (PI) is commonly mentioned as one of the most promising development paths for the chemical processing industry and one of the most important progress areas for chemical engineering research. Originating from the high-gravity distillation concepts developed in the early 1980s (1), for more than two decades, PI has been considered as a kind of technological “toolbox” containing some spectacular examples of process improvement. This view of PI as a toolbox has led to more in-depth discussions and interpretations. Numerous, diverse definitions and interpretations of PI have been proposed. In 2009, van Gerven & Stankiewicz (2) undertook the first attempt to define the fundamentals of PI. They distinguished four generic principles (goals) of PI (shown in **Table 1**).

In realization of the above-mentioned principles, the multiscale application of fundamental PI approaches involves four domains: spatial, thermodynamic, functional, and temporal. **Table 2** summarizes the main PI approaches in those domains and the motivation behind each.

Here, we follow these PI approaches and critically review their application in intensified reaction and separation systems. In doing so, we examine each of the four domains separately, moving across all relevant time and length scales, from molecules to the processing-unit plant.

### SPATIAL DOMAIN: STRUCTURE INSTEAD OF RANDOMNESS

#### Structures on the Molecular Scale

On the molecular scale, the effectiveness of a reaction event can be improved by structural measures. Here, a structure is used to influence the mutual orientation of molecules at the moment of their collision. This usually consists of immobilizing the molecules for the duration of the reaction in confined nanospaces by imposing “hard walls” of structures or of other molecules. In doing so, the reacting molecules are forced either to assume certain positions inside the offered structure or not to react. A wide range of the molecular reactors, such as cyclodextrins, are being studied (3, 4). Shape-selective catalysts, e.g., zeolites (5, 6) and molecularly imprinted systems (**Figure 1**) (7, 8), also belong to this category. Liquid crystals have also been investigated as a structured environment to control molecular orientation (9).

#### Structured Reactors

Structured reactors greatly improve the uniformity of the processing experience of the molecules while significantly enhancing the transfer rates. Various types of structured reactors have been developed thus far, including monoliths, gauzes, and foams (10).

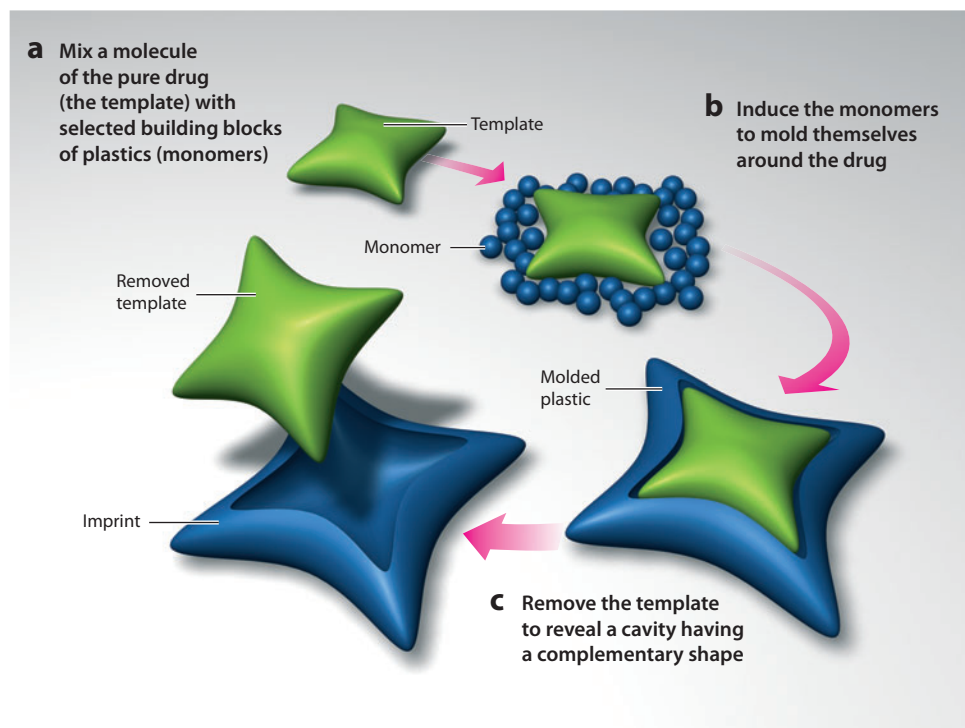
In the past decade, an explosive growth in the development and application of microstructured reactors has been observed. The common structures in these reactors are platelets with a multitude of straight fluidic ducts (microchannels, approximately 50–300  $\mu\text{m}$  in diameter) stacked into

**Table 1** Generic principles of process intensification (2)

Principle (goal)	Focus issues related to the principle
Maximize the effectiveness of intra- and intermolecular events	Control of spatial orientation and energy in molecular collisions
Give each molecule the same processing experience	Residence time and thermal uniformity
Optimize the driving forces at every scale and maximize the specific surface area to which these forces apply	Transport across interfaces
Maximize the synergistic effects from partial processes	Combining functions

**Table 2 Four fundamental domains and main approaches of process intensification (PI)**

Domain	Main PI approach	Motivation
Spatial	Structured environment	<ul style="list-style-type: none"> <li>■ Well-defined geometry</li> <li>■ Creation of maximum specific surface area at minimum energy expenses</li> <li>■ Creation of high mass and heat transfer rates</li> <li>■ Precise mathematical description</li> <li>■ Easy understanding, simple scale-up</li> </ul>
Thermodynamic	Alternative forms and transfer mechanisms of energy	<ul style="list-style-type: none"> <li>■ Manipulation of molecular orientation</li> <li>■ Activating/moving targeted molecules</li> <li>■ Selective, gradientless, and local energy supply</li> </ul>
Functional	Integration of functions/steps	<ul style="list-style-type: none"> <li>■ Synergistic effects</li> <li>■ Better energy management</li> <li>■ Increase of overall efficiency</li> <li>■ More compact equipment</li> </ul>
Temporal	Timing of the events, introducing dynamics (pulsing)	<ul style="list-style-type: none"> <li>■ Controlled energy input</li> <li>■ Influencing hydrodynamic behavior</li> <li>■ Increased energy efficiency</li> <li>■ Minimization of unwanted phenomena, such as fouling</li> </ul>



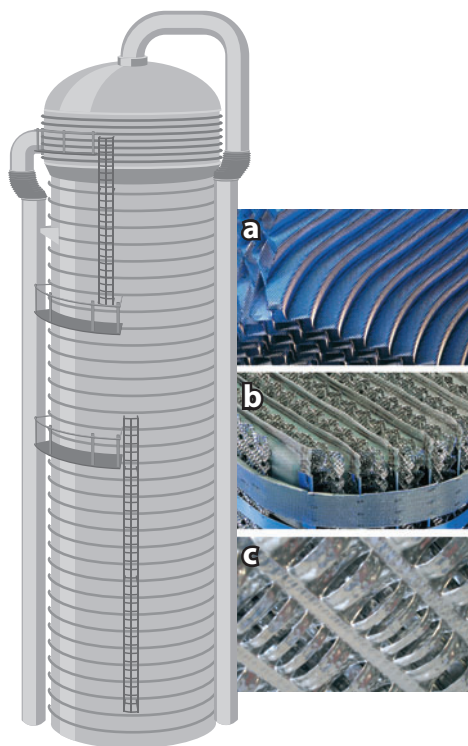
**Figure 1**

The process of making an imprint.

functional layers (premixing, preheating, reaction, cooling, etc.). Excellent heat transfer efficiency is the most important advantage of the microchannel structures; heat transfer coefficients exceeding  $20 \text{ kW m}^{-2} \text{ K}^{-1}$  and specific heat transfer areas exceeding  $30,000 \text{ m}^2 \text{ m}^{-3}$  have been reported. As a result, even very fast and highly exothermic processes can be carried out in microreactors under full temperature control. Current industrial applications of microreactors include primarily pharmaceutical and fine-chemical processes, where spectacular intensification effects are reported. An example here is a specialty product technology at DSM Linz, where the application of a microreactor resulted in a reduction of the reactor volume for the same production capacity by a factor of more than 3,000 (11). Extremely small channel dimensions in microreactors limit their applicability in processes where fouling or clogging by solids may occur. For such cases, and also for large-scale processes with intensive heat exchange, so-called millireactors are developed with channel diameters in the millimeter range. Most of these reactors are based on similar constructional principles as plate heat exchangers and are often called heat exchanger (HEX) reactors.

### Structured Internals for Mass Transfer Operations

At present, structured column internals (**Figure 2**) are commonly used in different technologies for separating mixtures into components such as distillation, absorption, or extraction if a low-pressure drop, high capacity, or high specific surface area is needed.



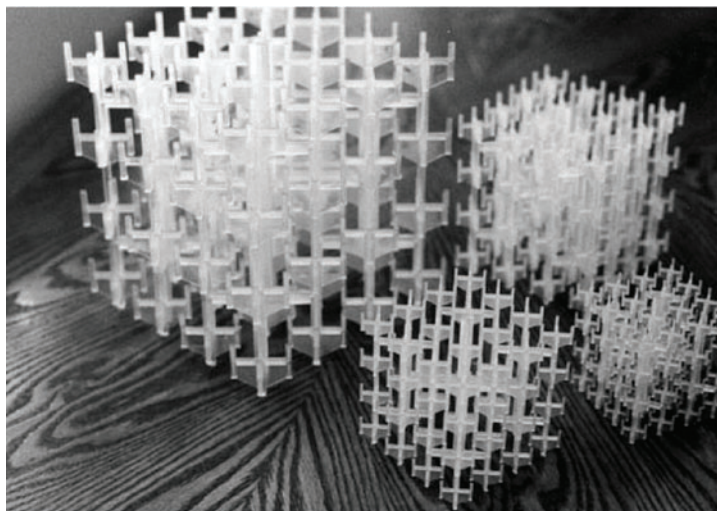
**Figure 2**

Different types of novel structured packings: (a) Montz-Pak B1-250M (copyright © Julius Montz GmbH), (b) Katapak SP-12 (copyright © Sulzer Chemtech), and (c) Raschig Super-Pak (copyright © Raschig GmbH).

Structured internals were first applied in the 1960s, when Sulzer BX gauze packing was used for the separation of heat-sensitive products in high-vacuum distillation (12). Over the years, the gauze packings were improved and new corrugated sheet metal-structured packings such as Montz-B1, Sulzer Mellapak, Koch-Glitsch Flexipac were introduced into the market. These are primarily made of stainless steel, though other materials such as ceramics or plastics are used for special applications. Current research and development of structured internals focus mainly on corrugation and surface design. An important development was a change in the flow-channel configuration. A smooth bend was added at either the lower end or both ends of the packing to reduce the pressure drop significantly and allow a capacity increase (13–15). Other innovations are the perforation of the packing sheets, which also allows higher capacities in comparison to unperforated packing sheets (16–18), and a more open packing structure (19). The idea of spatial ordering of traffic flow within the column was also applied in catalytic structured packings used for catalytic distillation. Two types of catalytic structured packings are available on the market. In packings such as Katamax (20) or Katapak-S (21), the catalyst is immobilized in the gauze structure of the packing. The other type, such as Katapak-SP, has a hybrid structure (22) with alternating catalytic and separation layers (23).

Another application for spatial structuring is in the use of foams made from metal or ceramics. Their high voidage (up to 97%) and small pore sizes lead to a combination of relatively high specific surface area (up to  $40 \text{ m}^2 \text{ g}^{-1}$ ) with low pressure drop per height. Good gas-liquid mass transfer performance, low flooding behavior, and corrosion resistance of structurally customized foams allow for intensified separation (18). Additionally, open-cell foams show high liquid residence times, which make foams coated with catalytic materials applicable to reactive distillation (RD) processes despite their relatively low capacity (24).

Fractal structures need to be discussed separately. Fractals are obtained by progressively adding copies of the basic structure at increasingly smaller scales. Numerous systems found in nature, e.g., lungs, have a fractal structure. Fractal concepts can be used in chemical engineering to transport and distribute fluids. Fractal distributors (**Figure 3**) provide a uniform fluid distribution, enable reliable scale-up, and exhibit a very low sensitivity to changes in feed flow rate (25).



**Figure 3**

Three-dimensional fractal fluid distributors by Amalgamated Research, Inc. (26).

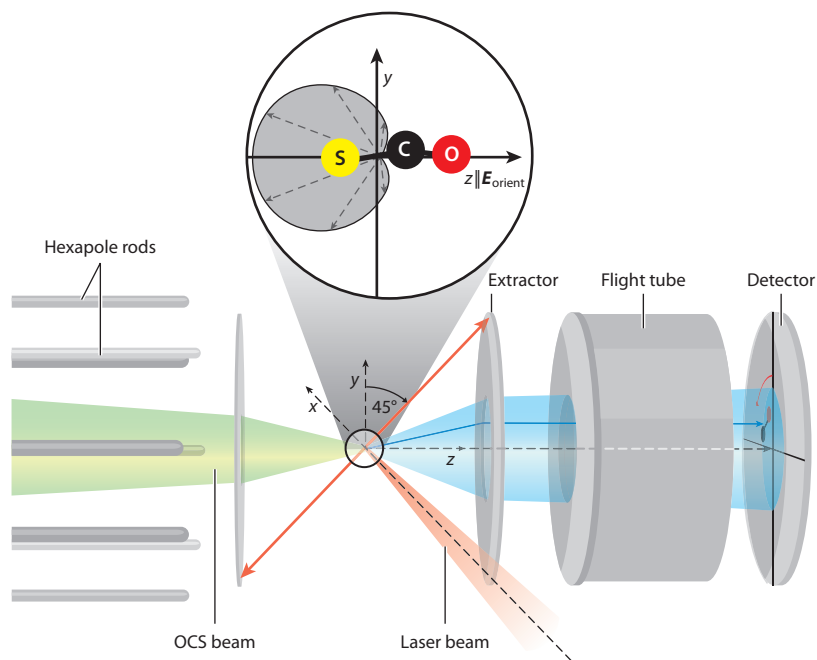
## THERMODYNAMIC DOMAIN: ENERGY ISSUES

### Energy in Chemical Reactors

Energy management on the molecular scale presents a fundamental issue in the control of chemical reactions. A perfect chemical reactor is one in which the geometry of molecular collision is fully controlled while energy is transferred selectively from the source to the required molecules under the required conditions of form, amount, time, and position.

Energy can be used both to align and orient molecules as well as to activate them selectively. The forced-alignment methods include the electric, magnetic, or optical field-based methods. The electric field-based methods that organize the Stark effect are the oldest examples, as they date back to the early 1960s (27, 28). The brute-force techniques work on polar molecules with a permanent electric dipole moment or paramagnetic molecules, which respectively align with the homogeneous static electric or magnetic field (29–33).

The optical methods for molecular-orientation control are based on strong nonresonant laser pulses (34, 35). Laser fields also present a method that is fundamentally proven to (selectively) activate molecules by addressing individual bonds. Zare and coworkers (36, 37) used a laser field for the excitation and “stretching” of the C–H bond in a methane molecule, which increased the rate of its chlorination by a factor of more than 100. This clearly proves that a targeted introduction of an alternative energy can enable getting far beyond the limits of “conventional inherent kinetics,” which are based on the macroscopic temperature, pressure, and concentrations. Another example of the use of lasers to break chemical bonds is shown in **Figure 4**: Carbonyl sulfide



**Figure 4**

Orientation of a molecular beam of OCS molecules moving along the  $z$ -axis under the influence of a hexapole electric field (left), followed by their dissociation by a laser beam acting along the  $x$ -axis. (Inset) Probability plot of the molecular orientation of the OCS molecule; length of dotted arrows are proportional to the orientation probability of the OCS dipole moment along each direction.

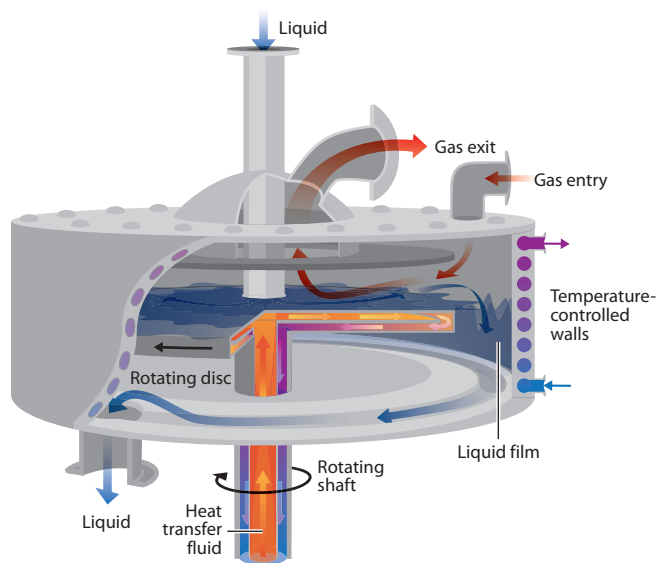
molecules are first aligned and oriented in an electric field, before being dissociated by a laser beam (38).

Other forms of electromagnetic fields, including microwaves and UV or visible light, can also be applied to activate molecules. The discussion about how the highly polarizing radiation of microwaves promotes and accelerates chemical reactions continues. As of late, however, authors increasingly agree that the effects of microwaves are purely thermal in character (39). Dramatic effects of microwave irradiation have been reported in heterogeneous catalysis. Microwaves selectively and preferentially heat metal catalyst nanoparticles, resulting in, among other things, reactions that can be carried out at lower bulk temperatures when compared with conventional conductive heating (40).

Photochemical reactions are activated by the energy from light. Because of this specific form of activation, the selectivity of photochemical reactions can reach 100%. To date, numerous designs of photocatalytic reactors have been proposed (41). The most important hurdle for photocatalytic reactors is their low energetic efficiency due to light absorption and dissipation between the source and the catalytic site. One way to solve this problem would be in situ nanoillumination to generate the light directly in the catalyst.

The exposure of a liquid system to ultrasound results in formation, growth, and subsequent collapse of microbubbles (microcavities), occurring in an extremely short period of time (milliseconds). The microimplosions are accompanied by an energy release with very high energy densities, which leads to local generation of extremely high temperatures and pressures. Free radicals are also released. Similarly to microwaves, the use of ultrasound can dramatically accelerate chemical reactions and increase the product yield (42). Acoustic irradiation also intensifies the mass transfer processes in multiphase systems, where an increase of up to 20-fold in mass transfer coefficients has been reported (43, 44).

The energy of high-gravity fields generated by centrifugal operation also dramatically improves the heat and mass transport in chemical reactors. In the spinning disc reactor (SDR) (**Figure 5**), a



**Figure 5**

Spinning disc reactor.

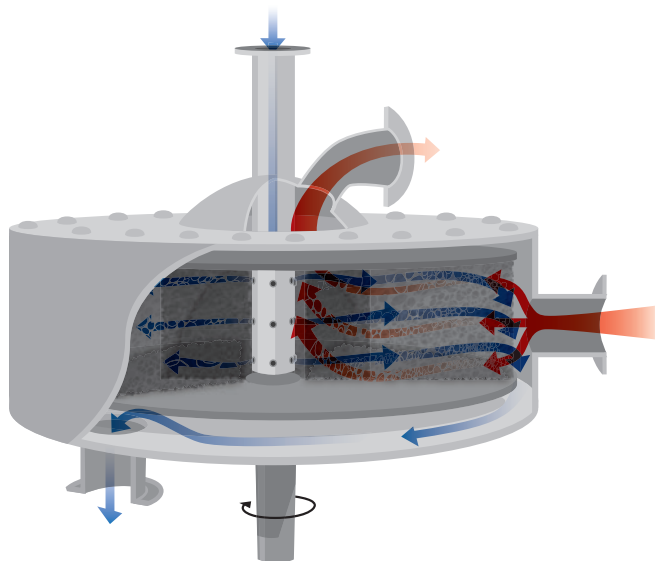
highly sheared liquid film flow occurs on the rotating surface of the disc. In particular, heat transfer performance of the SDR is impressive as heat transfer coefficients reach local values of  $20 \text{ kW m}^{-2} \text{ K}^{-1}$  or more (45). The SDR is, therefore, particularly suitable for fast, very exothermic processes that involve viscous liquids (e.g., polymerizations). An example of such a process is a phase-transfer-catalyzed Darzen's reaction for preparing a drug intermediate, where SDR allowed for a 99.9% reduction in reaction time, 99% reduction of inventory, and 93% reduction of impurities level (46).

### Energy in Separation Systems

PI in the energy domain results either from superimposition of the chemical potential driving force and different forms of an energy supply (electric fields, acoustic fields and microwaves, high gravity) or from the combination of heat and mass transfer driving forces within one apparatus (internal heat integration, divided wall column).

Rotating packed beds (RPB) can be applied to mass transfer operations, in which centrifugal forces create a high-gravity environment (100 to 500 times gravity). A toroidal-shaped, high-specific area packing made of foam, mesh, wire, or spheres with a specific surface area of 150 to 5,000  $\text{m}^2 \text{ m}^{-3}$  is mounted on a shaft inside a casing. The liquid is injected into the eye of the rotor. It then flows radially outward and spreads into thin films, rivulets, or flying droplets. The gas is introduced into the casing and flows countercurrently inward (see **Figure 6**). Thereby, micromixing and mass transfer are significantly intensified by one to three orders of magnitude, whereas the volume and weight of the unit are decreased by two to three orders of magnitude (47, 48). Countercurrent RPBs are used mainly for applications with gas-liquid contact (degassing of liquids, absorption), whereas cocurrent and cross-flow RPBs are applied for liquid systems (liquid-liquid extraction) (47).

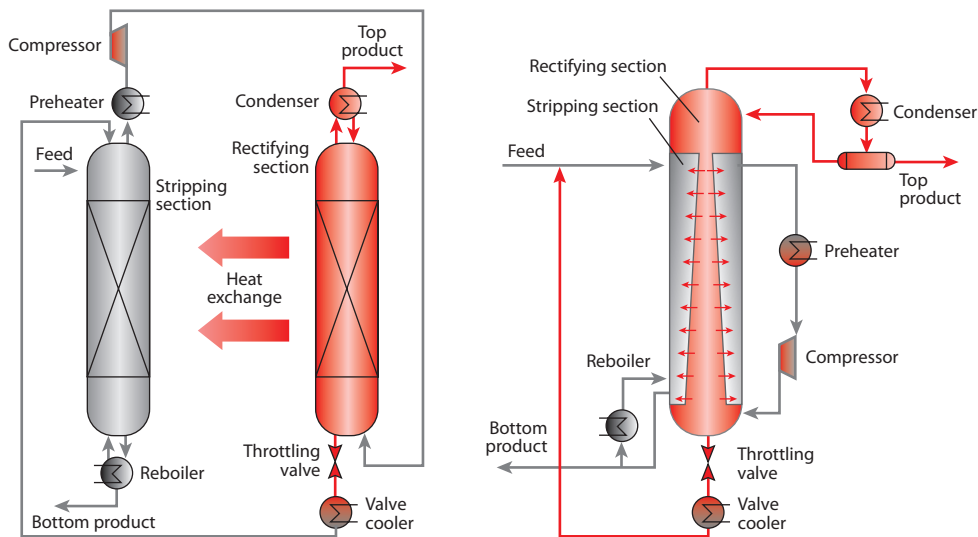
Successful commercial applications are reported for seawater deaeration, degassing of liquids, and production of hypochlorous acid by reactive stripping (48). Furthermore, lab-scale exploration



**Figure 6**

Principles of a countercurrent rotating packed bed.





**Figure 7**  
Principles of a heat-integrated distillation column system (*left*) and schematic drawing of a pilot plant (*right*).

has been done in absorption, stripping, distillation, heat transfer, adsorption, extraction, and crystallization (47).

Within an internally heat-integrated distillation column (HIDiC), an energy reduction of approximately 60% can be achieved. HIDiC is especially suitable for close-boiling mixtures and can be applied to large industrial-scale distillation columns (16). The concept of the general process was introduced by Mah et al. (49) in the 1970s; however, it has not yet been commercialized owing to high investment costs, complex design, and process-control problems (50). HIDiC can be seen as an improvement in heat-pump-assisted distillation and combines vapor recompression and adiabatic operation (16, 51). The principle of an HIDiC system is illustrated in **Figure 7** (52). The stripping and rectifying sections operate at different pressure levels to allow for heat transfer.

The dividing wall column (DWC) is an attractive concept for the separation of mixtures with three or more components in one column. This industrially proven technology requires less space and energy consumption; additionally, capital costs can be reduced by up to 30% compared with those of conventional distillation columns (16, 53). DWCs are equipped with one or more vertical partitions inside the column shell, and separating a multicomponent mixture into its pure fractions in one apparatus is possible (54). Although further research activities must be conducted and should be focused on reactive DWC (55), it can already be seen as a success story for PI (53).

Electric fields can be applied in extraction processes to enhance heat and mass transfer across the interface. In contrast to mechanical energy, an electrical field interacts selectively with the interface, and less energy is dissipated in the bulk (56). Consequently, reduction of energy consumption by 2 to 4 orders of magnitude and increases in mass transfer rates by a factor of 2 to 20 in electric field extractions are possible.

Ultrasound can be used to induce nucleation in liquids by evoking acoustic cavitations and, therefore, may be a powerful tool to control and improve crystallization processes. Strong effects on growth, secondary nucleation, and agglomeration in ultrasound crystallization have been reported (57). Nucleation can be induced at a lower supersaturation because the metastable bandwidth is

reduced. Additionally, product properties such as particle size and shape can be influenced to allow the production of nanostructured materials.

Microwaves can be used to introduce energy directly into a particle. Thus, energy does not need to be conducted from the surface to the inside (58). Microwave dryers are applied in the food industry to lower bacteria counts and to reduce drying time and dryer dimensions. For example, conventional drying of pasta using hot air takes 10–20 h; with a 60-kW microwave, drying needs only 15 min (59). Coss et al. (60) investigated desorption using microwaves to remove organic solvents from activated carbon. Neither surface area nor adsorption capacity of the activated carbon was influenced by microwave radiation.

## FUNCTIONAL DOMAIN: REALIZING SYNERGIES

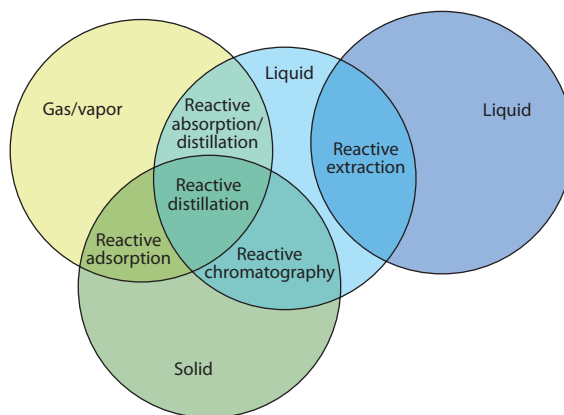
### Combining Functions on the Nanoscale in Catalysis

On the molecular scale, the catalytic function can be combined with a secondary or even tertiary function, such as an additional catalytic function (61) or adsorption (62). Combining the catalytic and the membrane functions by coating the catalytic nanoparticles with membrane layers (e.g., carbon molecular sieves or silicate-1) allows the realization of a controlled and selective feed to the active sites or a controlled product removal (63).

### Reactive and Hybrid Separations

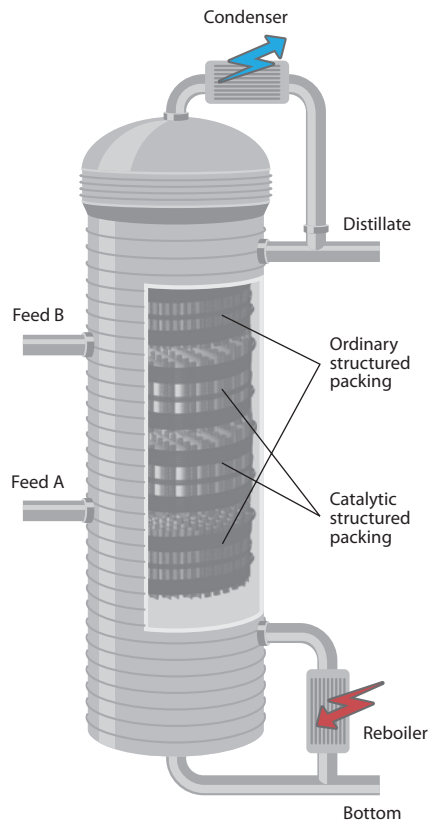
PI in the chemical industry can be carried out either by integrating separation and reaction in one single device or by combining different separation units in a hybrid process (64, 65). Reactive separations are the combined processes in which the separation and reaction occur simultaneously within the combined unit (**Figure 8**) (66–68). Hybrid separations consist of combination of at least two physical separation units, which achieve the separation effect better than each of the unit alone. This integration may result in smaller, cheaper, cleaner, and safer technologies. In the following section, an overview of successful and promising reactive and hybrid separations is given.

**Reactive separations.** RD, in which reaction and distillation are integrated into a single device (**Figure 9**), is one of the best-known examples of reactive separations. This integration offers



**Figure 8**

Definition of reactive separations.



**Figure 9**

Scheme for a reactive distillation column.

several advantages, such as reduction of investment and operating costs, improvement of conversion and selectivity for equilibrium-limited reactions, heat integration, and avoidance of azeotropes. However, the feasible operating window of RD is one of the limiting factors for further applications (69). Despite this drawback, there are currently more than 150 RD columns in commercial operation around the world, most of which are licensed by CDTECH and Sulzer Chemtech (70). Potential industrial applications and perspectives of RD processes are discussed in the reviews by Hiwale et al. (71) and Sundmacher et al. (72). Etherification, esterification, hydrolysis, and hydrogenation reactions are suitable systems for the application of RD. Additionally, both homogeneous- and heterogeneous-catalyzed RD can be distinguished. No separation of the catalyst is necessary if the solid phase is immobilized in the reaction zone, which is advantageous when compared with a homogeneously catalyzed RD (73).

In recent years, extensive investigation has been carried out to identify the criteria of applicability to new processes (74). Published models of different complexity can be found in the open literature to describe RD processes, and in most cases, a rate-based model is recommended (75, 76). However, suitable correlations for the description of mass transfer and the hydrodynamic behavior of column internals are required. One of the main challenges is scale-up because the geometry of the catalytic packings and, in some cases, the reaction mechanism can differ from lab scale to industrial scale (77, 78). Current investigations in the field of RD focus on the development

of new packings (79), scale-up procedures, biofuels production (80), hybrid processes [RD with pervaporation or a decanter (81)] and fully thermally coupled RD columns (82).

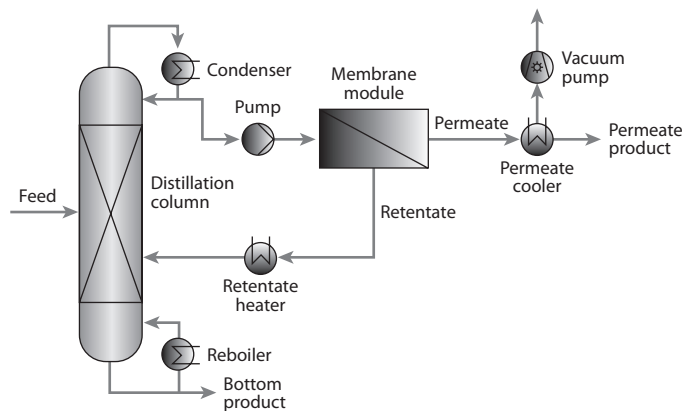
Reactive absorption (RA) is a rate-controlled process in which absorption of gaseous species is combined with a chemical reaction. In RA, the reaction contributes to better mass transfer and enhances the solubility (83). Although commonly used, RA is still not well understood owing to the complex interaction of thermodynamics, reactions, the presence of ionic species, and mass and heat transfer (84, 85). Reduction in investment and operating costs, better product purity, lower energy demands, and less corrosion are some of the main advantages of integrating reaction and absorption in one process unit. Traditionally, RA is used in the synthesis of chemicals such as nitric and sulfuric acid, waste-gas purification, refineries to remove water from natural gas, conditioning of synthesis gas, separation of organic components, and solvent regeneration (84, 86–88). Current research in RA focuses mainly on finding the appropriate absorption solvents, scale-up studies, and optimal process design (89). Extensive literature can be found on the modeling of RA. Although rate-based models are preferred for producing reliable results, models based on enhancement factors are also used (84, 90). RA has attracted a lot of attention in the past few years and will remain one of the most important separation processes in the next couple of decades, mainly as a result of air pollution issues and stricter environmental legislations. It is especially important for CO<sub>2</sub> sequestration technologies.

Reactive extraction is the combination of physical extraction and chemical reaction to enhance the capacity of the solvent. It was industrially invented during the Manhattan Project for uranium production (around 1940) (91) and had its commercial breakthrough with selective copper recovery in the 1960s (92). The technical equipment and its design methods are similar to those used for pure physical extraction (93). In reactive extraction, the dominant extractor is the mixer-settler cascade. Columns, nonagitated or agitated to amplify the mass transfer area, are increasingly applied owing to their high efficiency at high capacities. Bart et al. (94) successfully developed a method to design a column coming from measurements of a single droplet. However, insufficient scale-up rules and the use of simplified models resulted in an expensive and slow procedure. The application ranges from purification of waste streams in environmental technology to the separation of pharmaceuticals, though most of the published industrial applications and research papers exist in the fields of hydrometallurgy and nuclear reprocessing (95–97).

Reactive crystallization (RC) can be applied to increase conversion if the solubility of a product is lower than its reactants and by-products. RC is applied to influence multiple properties (e.g., morphology, polymorphology, purity, and crystal particle size) simultaneously with specific characteristics of the reaction (e.g., reaction equilibrium, selectivity, and recovery) (66, 98). Within the chemical industry, RC is a common process with frequent application within pharmaceuticals.

The implementation of a heterogeneously catalyzed reaction into a chromatographic separation is called reactive chromatography (26). An essential property of these systems is the difference in affinities of products and reactants for the catalytic packing material. Because of this feature, equilibrium-limited reactions can be driven to higher conversions. The application of reactive chromatography is of special interest when the educts and/or products have very low vapor pressure or are thermally instable. Besides the ordinary batch process, it is possible to run a reactive chromatographic process in a continuous manner by applying simulated moving-bed chromatography. Although there are no known industrial applications, several patents have been submitted; examples include the syntheses of bisphenol A and vitamin C (99, 100).

**Hybrid separations.** The combination of the membrane processes pervaporation and vapor permeation with distillation to form a hybrid separation process (**Figure 10**) is the most promising process concept (101). It offers several advantages such as reduction of energy consumption,



**Figure 10**

Hybrid process combining distillation with pervaporation for a binary system with a low-boiling azeotrope.

improvement of product quality, and avoidance of entrainers. Therefore, it is especially suitable for close-boiling or azeotropic mixtures. Unfortunately an algorithmic synthesis of hybrid separation sequences is still not possible (102).

Most industrial applications focus on the dehydration of solvents, with 80% of examples applied to the absolute of ethanol and isopropyl alcohol (103). As Roza et al. (104) reported regarding the dehydration of different solvents, hybrid separation processes can offer significant energy savings of up to 50% compared with extractive and pressure swing distillation. This characteristic leads to lower operating and investment costs. Fontalvo et al. (105) showed that total cost reductions of up to 60% are possible using a hybrid membrane–distillation process for acetonitrile dehydration. The separation of multicomponent mixtures or purely organic mixtures using hybrid separation processes is not yet well established in industry, but several publications show the benefits and possible cost reductions of these processes for solvent recovery (106) and the separation of methanol from methyl esters (107).

The integration of membrane separation and RD combines the advantages of reactive and hybrid separation processes and represents a highly intensified process unit. An industrially applied process for the production of fatty acids was presented by von Scala et al. (108). The authors claim that the process demonstrates an energy savings of up to 50%. Buchaly et al. (81) developed a new methodology for analysis of membrane-assisted RD processes, which was applied to the synthesis of *n*-propyl propionate. In the case of esterification reactions, a decanter can be placed at the top of an RD column. Kloeker et al. (109) reported on the use of a decanter in the synthesis of ethyl acetate to purify further the product in the distillate stream. Altman et al. (110) coupled a pilot-scale RD column with a decanter to recover nonconverted 1-propanol in the synthesis of *n*-propyl propionate.

In membrane crystallization, a solvent is removed from a solution containing the solute to be crystallized via permeation through a membrane. The solvent passes over to the permeate side, which contains a stripping solution, pure water, or a vacuum. The resulting super saturation is the driving force for crystallization. Because the feed and permeate sides are independent, crystallization kinetics can be influenced without any impact on the crystallization solution by tuning the membranes and process parameters. Potential applications discussed in the literature are the crystallization of proteins or the recovery of crystalline materials from the brine in seawater desalination (111, 112). The integration of membrane crystallization into a membrane desalination process leads to an economically attractive process versus conventional desalination. Because 90% of all products require a crystallization step for production in the pharmaceutical industry,

membrane crystallization is a promising new methodology (113). Despite the possibility of producing crystals with easily controllable morphologies at mild operating conditions, commercial applications for membrane contactors have not yet been published.

Another hybrid separation is extractive crystallization, which combines crystallization and extraction. One of the major benefits of extractive crystallization is the very low energy demand versus that of evaporation crystallization. Depending on the process configurations, either the solvent or the solute can be extracted and crystallized from a solution. Three major process configurations have been studied at the laboratory and pilot scales. Solute extraction has the potential for extraction of energetic compounds, solvent extraction for bulk chemicals (e.g., salts or extremely dense soda ash), and gas absorption with crystallization for the capture of acid gases (114–116).

Hybridization of several separation processes can also be used to purify biomolecules. Such processes would avoid the typical drawbacks of column chromatography, which is key to enable technology given its high selectivity, versatility, and good implementation (99, 117). Membrane chromatography possesses the potential for faster processing of large molecules, providing the same selectivity as conventional chromatography (118). The serial connection of a large chromatographic column followed by a small-membrane chromatography module creates a hybrid operating unit, in which the strength of both individual technologies (high binding capacity of a column and rapid uptake kinetics of membrane adsorption) are unified (119).

Another alternative to increase productivity and yield is to shift from batch separation to continuous separation. The multicolumn solvent gradient purification process is a new continuous chromatographic process that combines solvent gradient batch chromatography and continuous countercurrent simulated moving-bed chromatography (120, 121).

## TEMPORAL DOMAIN: MANIPULATION OF TIME

The PI approaches in the temporal domain are basically twofold, involving either manipulation of the times, at which different process steps proceed, or the introduction of dynamic states into a process, usually in the form of periodicity.

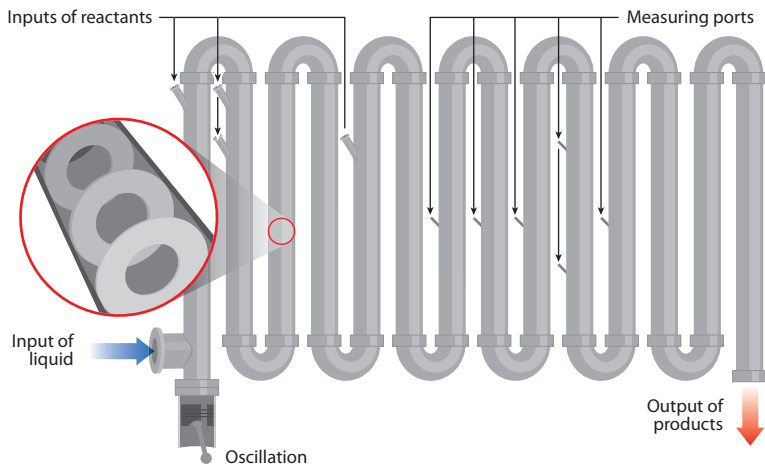
### Changing Characteristic Times of Events

Manipulation of the characteristic times of the events can be seen in the so-called millisecond reactors, where molecules are brought under extreme temperature conditions for a very short time (122) or in microfluidic systems using high-gravity fields, where mixing times are reportedly reduced by two orders of magnitude (123).

### Introducing Dynamics (Pulsing) in Reactors

Introducing an artificial and purposeful periodicity can significantly improve reactor performance (124). The so-called periodic forcing of catalytic processes (by oscillating pressures, concentrations, or temperatures) has been widely described in the literature (125). Periodic operation can change and improve the mixing characteristics of the system. For example, the so-called oscillatory baffled flow reactor (**Figure 11**) allows for a near-plug flow operation at low overall flow velocities and long reaction times by changing a pipe into a large number of stirred tanks in series (126).

Introduction of periodicity can also increase interfacial mass transfer rates in trickle-bed reactors, and it brings significant improvement in mass transfer rates, in catalyst wetting, and in the radial uniformity of liquid flow (127). This method can also improve heat management in the reactor. Flow reversal in the reversed-flow reactors is a typical example here (128).

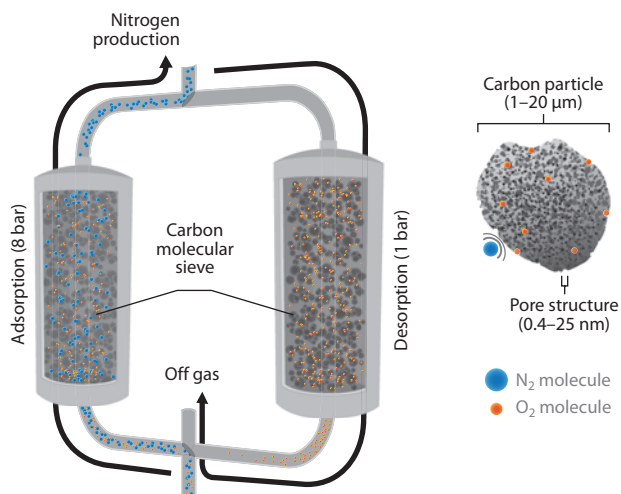


**Figure 11**

Oscillatory baffled flow reactor.

### Periodicity in Separations

The main applications of periodicity in separations are pressure-swing adsorption (PSA) (2) and pulse drying (129). PSA consists of two major steps (130): a production step, in which high-pressure vapor is introduced into the column for adsorption, and a regeneration step, in which the pressure is drastically reduced for desorption (shown for the generation of nitrogen in **Figure 12**) (131). The use of two columns with alternating production and regeneration steps enables a continuous adsorption process. Nowadays, the PSA process finds wide application in the energy-efficient dehydration of high-ethanol containing vapor by preferable adsorption of water on 3-Å zeolites following a distillation column (130).



**Figure 12**

Generation of nitrogen using pressure-swing adsorption based on a carbon molecular sieve.

## SUMMARY

Intensified reaction and separation systems can be best realized by simultaneous and multiscale application of the selected concepts of process intensification, respectively, in the spatial, thermodynamic, functional, and temporal domains. Exploration of some of these domains remains in the embryonic stage. The superimposing of different phenomena for chemical reaction, momentum, mass, and heat transfer in a certain space and at the same time can be of great advantage, but the operation window of integrated units must be determined carefully. In developing new concepts of intensified reaction and separation systems, bridges need to be built between chemical engineering and other disciplines, including chemical physics, (bio)chemistry, catalysis, materials science, electronics, etc. This will require more openness among researchers working in the field of chemical and process engineering to new ideas from neighboring areas.

### FUTURE ISSUES

#### 1. Spatial domain:

- Ultrahigh-surface structures with specific interfacial areas exceeding  $100,000 \text{ m}^2 \text{ m}^{-3}$  need to be developed.
- The surfaces in those systems for specific tasks (e.g., shape-selective catalysis or affinity separations) need to be engineered.

#### 2. Thermodynamic domain:

- A selective, gradientless, and local energy supply in spatially structured systems needs to be developed, e.g., via targeted introduction of electric, magnetic, and electromagnetic fields.
- Local thermal conditions in reaction and separation systems need to be manipulated by choice of materials or by acting on media.
- Different driving forces such as gravity, microwaves, separation, and magnetism in modular units need to be integrated.

#### 3. Functional domain:

- Alternative energy forms (e.g., electric and laser fields) or energy and materials (e.g., catalyst and energy source or energy-absorbing material) need to be combined.
- New materials (e.g., catalysts and membranes) for expanding the operational feasibility windows in integrated devices and processes need to be developed.
- The material for design approach, in which the requirements of the process determine the properties of the materials, needs to be tailored for the process needs (new adsorbents, designer solvents, etc.).
- Suitable tools of process system engineering need to be developed to automate the sequencing of integrated reaction and separation processes.

#### 4. Temporal domain:

- Instrumentation to observe, measure, and control time and space scales of molecular events needs to be developed.
- Reliable models for integrated multiscale (from nano to macro) control of complex systems need to be developed.



## DISCLOSURE STATEMENT

A.G. is an inventor on the German patent *Strukturierte Mehrzweckpackung DE 19701045 A1* (1998), the world patent *Device and method for separating and isolating substances WO 083859 A1* (2010), and two other patents pending. A.S. is a consultant to Royal DSM N.V. (The Netherlands).

## LITERATURE CITED

1. Ramshaw C. 1983. Hige distillation—an example of process intensification. *Chem. Eng. (London)* 389:13–14
2. van Gerven T, Stankiewicz A. 2009. Structure, energy, synergy, time—the fundamentals of process intensification. *Ind. Eng. Chem. Res.* 48:2465–74
3. Easton CJ. 2005. Cyclodextrin-based catalysts and molecular reactors. *Pure Appl. Chem.* 77:1865–71
4. Dodziuk H. 2006. Molecules with holes—cyclodextrins. In *Cyclodextrins and Their Complexes: Chemistry, Analytical Methods, and Applications*, ed. H. Dodziuk, pp. 1–30. Weinheim: Wiley-VCH
5. Davis RJ. 2003. New perspectives on basic zeolites as catalysts and catalyst supports. *J. Catal.* 216:396–405
6. Stöcker M. 2005. Gas phase catalysis by zeolites. *Microporous Mesoporous Mater.* 82:257–92
7. Davis ME, Katz A, Ahmad WR. 1996. Rational catalyst design via imprinted nanostructured materials. *Chem. Mater.* 8:1820–39
8. Mosbach K. 2006. The promise of molecular imprinting. *Sci. Am.* 295:86–91
9. Weiss RG. 1988. Thermotropic liquid crystals as reaction media for mechanistic investigations. *Tetrahedron* 44:3413–75
10. Cybulski A, Moulijn JA. 2006. **Structured catalysts and reactors.** New York: Taylor & Francis
11. Poechlauer P, Kotthaus M, Vorbach M, Deak M, Zich T, Marr R. 2006. *WO Patent No. 2006125502 A1*
12. Spiegel L, Meier W. 2003. Distillation columns with structured packings in the next decade. *Chem. Eng. Res. Des.* 81:39–47
13. Billingham JF, Lockett MJ. 1997. *U.S. Patent No. 5,632,934*
14. Parten WD. 2001. *U.S. Patent No. 6,206,349*
15. Zich E, Jansen H, Leben J, Rietfort T, Zellmer J, Kaibel B. 2004. *U.S. Patent No. 6,783,119*
16. Olujić Ž, Jödecke M, Shilkin A, Schuch G, Kaibel B. 2009. **Equipment improvement trends in distillation.** *Chem. Eng. Process.* 48:1089–1104
17. Bender P, Moll A. 2003. Modifications to structured packings to increase their capacity. *Chem. Eng. Res. Des.* 81:58–67
18. Pangarkar K, Schildhauer TJ, van Ommen JR, Nijenhuis J, Kapteijn F, Moulijn JA. 2008. Structured packings for multiphase catalytic reactors. *Ind. Eng. Chem. Res.* 47:3720–51
19. Schultes M, Chambers S. 2007. How to surpass conventional and high capacity structured packings with Raschig Super-Pak. *Chem. Eng. Res. Des.* 85:118–29
20. Gelbein AP, Buchholz M. 1991. *U.S. Patent No. 5,073,236*
21. Götze L, Bailer O, Moritz P, von Scala C. 2001. Reactive distillation with Katapak. *Catal. Today* 69:201–8
22. Górak A, Kreul L. 1998. *DE Patent No. 19701045*
23. Górak A, Hoffmann A. 2001. Catalytic distillation in structured packings: methyl acetate synthesis. *AIChE J.* 47:1067–76
24. Leveque J, Rouzineau D, Prevost M, Meyer M. 2009. Hydrodynamic and mass transfer efficiency of ceramic foam packing applied to distillation. *Chem. Eng. Sci.* 64:2607–16
25. Coppens MO. 2005. Scaling-up and -down in a nature-inspired way. *Ind. Eng. Chem. Res.* 44:5011–19
26. Amalgamated Research Inc. 1997. *Fractal technology.* <http://www.arifractal.com>
27. Bulthuis J, van Leuken JJ, Stolte S. 1995. Hexapole state selection and focusing versus brute force orientation of beam molecules. *J. Chem. Soc. Faraday Trans.* 91:205–14
28. Hain TD, Moision RM, Curtiss TJ. 1999. Hexapole state-selection and orientation of asymmetric top molecules: CH<sub>2</sub>F<sub>2</sub>. *J. Chem. Phys.* 111:6797–806
29. Loesch HL, Remscheid A. 1990. Brute Force in molecular reaction dynamics: a novel technique for measuring steric effects. *J. Chem. Phys.* 93:4779–90

---

2. First to present a fundamental approach to process intensification.

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---

10. The most comprehensive book on structuring catalysts and reactors.

---

---

16. Shows the newest development in structured internals for physical and reactive separations.

---

30. Friedrich B, Herschbach DR. 1991. Spatial orientation of molecules in strong electric fields and evidence for pendular states. *Nature* 353:412–14
31. Loison JC, Durand A, Bazalgette G, White R, Audouard E, Vigué J. 1995. Molecular axis orientation by the “brute force” method. *J. Phys. Chem.* 99:13591–96
32. Kong W. 2001. Studies of electronic properties of medium and large molecules oriented in a strong uniform electric field. *Int. J. Mod. Phys. B* 15:3471–502
33. Slenczka A, Friedrich B, Herschbach D. 1994. Pendular alignment of paramagnetic molecules in uniform magnetic fields. *Phys. Rev. Lett.* 72:1806–9
34. Friedrich B, Herschbach D. 1995. Alignment and trapping of molecules in intense laser fields. *Phys. Rev. Lett.* 74:4623–26
35. Stapelfeldt H. 2003. Aligning molecules with strong laser pulses. *Eur. Phys. J. D* 26:15–19
36. Kandel SA, Zare RN. 1998. Reaction dynamics of atomic chlorine with methane: importance of methane bending and torsional excitation in controlling reactivity. *J. Chem. Phys.* 109:9719–27
37. Hoffmann R. 2000. Exquisite control. *Am. Sci.* 88:14–17
38. Rakitzis TP, van den Brom AL, Janssen MH. 2004. Directional dynamics in the photodissociation of oriented molecules. *Science* 303:1852–54
39. Kappe CO. 2004. Controlled microwave heating in modern organic synthesis. *Angew. Chem. Int. Ed.* 43:6250–84
40. Durka T, van Gerven T, Stankiewicz A. 2009. Microwaves in heterogeneous gas-phase catalysis: experimental and numerical approaches. *Chem. Eng. Technol.* 32:1–13
41. van Gerven T, Mul G, Moulijn JA, Stankiewicz A. 2007. A review of intensification of photocatalytic processes. *Chem. Eng. Process.* 46:781–89
42. Thompson LH, Doraiswamy LK. 1999. Sonochemistry: science and engineering. *Ind. Eng. Chem. Res.* 38:1215–49
43. Kumar A, Gogate PR, Pandit AB, Delmas H, Wilhelm AM. 2004. Gas-liquid mass transfer studies in sonochemical reactors. *Ind. Eng. Chem. Res.* 43:1812–19
44. Neis U. 2002. Intensification of biological and chemical processes by ultrasound. *Rep. Sanit. Eng.* 35:79–90
45. Aoune A, Ramshaw C. 1999. Process intensification: heat and mass transfer characteristics of liquid films on rotating discs. *Int. J. Heat Mass Transfer* 42:2543–56
46. Oxley P, Brechtelsbauer C, Ricard F, Lewis N, Ramshaw C. 2000. Evaluation of spinning disc reactor technology for the manufacture of pharmaceuticals. *Ind. Eng. Chem. Res.* 39:2175–82
47. Zhao H, Shao L, Chen JF. 2010. High-gravity process intensification technology and application. *Chem. Eng. J.* 156:588–93
48. Rao DP, Bhowal A, Goswami PS. 2004. Process intensification in rotating packed beds (HIGEE): an appraisal. *Ind. Eng. Chem. Res.* 43:1150–62
49. Mah RSH, Nicholas JJ Jr, Wodnik RB. 1977. Distillation with secondary reflux and vaporization: a comparative evaluation. *AIChE J.* 23:651–58
50. Jana AK. 2010. Heat integrated distillation operation. *Appl. Energy* 87:1477–94
51. Gadalla MA. 2009. Internal heat integrated distillation columns (iHIDiCs)—new systematic design methodology. *Chem. Eng. Res. Des.* 87:1658–66
52. Iwakabe K, Nakaiwa M, Huang K, Matsuda K, Nakanishi T, et al. 2006. An internally heat integrated distillation column (HIDiC) in Japan. *Proc. Distillation Absorp. Conf., 2006, London, UK*, pp. 900–11. Rugby: Inst. Chem. Eng.
53. Dejanović I, Matijašević L, Olujić Ž. 2010. Dividing wall column—a breakthrough towards sustainable distilling. *Chem. Eng. Process.* 49:559–80
54. Kaibel G. 1987. Distillation columns with vertical partitions. *Chem. Eng. Technol.* 10:92–98
55. Müller I, Kenig EY. 2007. Reactive distillation in a dividing wall column: rate-based modeling and simulations. *Ind. Eng. Chem. Res.* 46:3709–19
56. Ptasinski KJ, Kerkhof PJAM. 1992. Electric field driven separations: phenomena and applications. *Sep. Sci. Technol.* 27:995–1021

---

42. An excellent paper on the fundamental and practical issues in sonochemistry.

---



---

48. An excellent overview of separation technologies in rotating beds.

---

57. Dodds J, Espitalier F, Louisnard O, Grossier R, David R, et al. 2007. The effect of ultrasound on crystallization-precipitation processes: some examples and a new segregation model. *Part. Part. Syst. Charact.* 24:18–28
58. Jones DA, Lelyveld TP, Mavrofidis SD, Kingman SW, Miles NJ. 2002. Microwave heating applications in environmental engineering—a review. *Resour. Conserv. Recycl.* 34:75–90
59. Reay D, Ramshaw C, Harvey A. 2008. *Process Intensification*. Oxford: Elsevier
60. Coss PM, Cha CY. 2000. Microwave regeneration of activated carbon used for the removal of solvents from vented air. *J. Air Waste Manag. Assoc.* 50:529–35
61. Gunn DJ. 1967. The optimization of bifunctional catalyst systems. *Chem. Eng. Sci.* 22:963–77
62. Dietrich W, Lawrence PS, Grünewald M, Agar DW. 2005. Theoretical studies on multifunctional catalysts with integrated adsorption sites. *Chem. Eng. J.* 107:103–11
63. Nishiyama N, Ichioka K, Park DH, Egashira Y, Ueyama K, et al. 2004. Reactant-selective hydrogenation over composite silicalite-1-coated Pt/TiO<sub>2</sub> particles. *Ind. Eng. Chem. Res.* 43:1211–9
64. Moulijn JA, Stankiewicz A, Grievink J, Górak A. 2008. Process intensification and process systems engineering: a friendly symbiosis. *Comput. Chem. Eng.* 32:3–11
65. **Schmidt-Traub H, Górak A. 2006. *Integrated Reaction and Separation Operations*. Heidelberg: Springer**
66. Stankiewicz A, Moulijn JA. 2004. *Re-Engineering the Chemical Process Plant*. New York: Marcel Dekker
67. **Sundmacher K, Kienle A, Seider-Morgenstern A. 2005. *Integrated Chemical Processes*. Weinheim: Wiley-VCH**
68. Kulprathipanja S. 2001. *Reactive Separation Processes*. New York: Taylor & Francis
69. Schembecker G, Tlatlik S. 2003. Process synthesis for reactive separations. *Chem. Eng. Process.* 42:179–89
70. Harmsen GJ. 2007. Reactive distillation: the front-runner of industrial process intensification. A full review of commercial applications, research, scale-up, design and operation. *Chem. Eng. Process.* 46:774–80
71. Hiwale RS, Bhate NV, Mahajan YS, Mahajani SM. 2004. Industrial applications of reactive distillation: recent trends. *Int. J. Chem. Reactor Eng.* 2:R1
72. Sundmacher K, Kienle A. 2002. *Reactive Distillation: Status and Future Directions*. Weinheim: Wiley-VCH
73. Kreul LU, Górak A, Barton PI. 1999. Modelling of homogeneous reactive separation processes in packed columns. *Chem. Eng. Sci.* 54:19–34
74. Nisoli A, Malone MF, Doherty MF. 1997. Attainable regions for reaction with separation. *AIChE J.* 43:457–64
75. Taylor R, Krishna R. 2000. Modelling reactive distillation. *Chem. Eng. Sci.* 55:5183–229
76. Noeres C, Kenig EY, Górak A. 2003. Modelling of reactive separation processes: reactive absorption and reactive distillation. *Chem. Eng. Process.* 42:157–78
77. Tuchlenski A, Beckmann A, Reusch D, Düssel R, Weidlic U, Janowsky R. 2001. Reactive distillation—industrial applications, process design & scale-up. *Chem. Eng. Sci.* 56:387–94
78. Subawalla H, Fair JR. 1999. Design guidelines for solid-catalyzed reactive distillation systems. *Ind. Eng. Chem. Res.* 38:3696–709
79. Stankiewicz A. 2003. Reactive separations for process intensification: an industrial perspective. *Chem. Eng. Process.* 42:137–44
80. Kiss AA. 2010. Separative reactors for integrated production of bioethanol and biodiesel. *Comput. Chem. Eng.* 34:812–20
81. Buchaly C, Kreis P, Górak A. 2007. Hybrid separation processes—combination of reactive distillation with membrane separation. *Chem. Eng. Process.* 46:790–99
82. Gomez-Castro FI, Rico-Ramirez V, Segovia-Hernandez JG, Hernandez S. 2010. Feasibility study of a thermally coupled reactive distillation process for biodiesel production. *Chem. Eng. Process.* 49:262–69
83. Zarzycki R, Chauck A. 1993. *Absorption: Fundamentals and Applications*. Oxford: Pergamon
84. Kenig EY, Górak A. 2005. Reactive absorption. In *Integrated Chemical Processes*, ed. K Sundmacher, A Kienle, A Seidel-Mongestern, 9:265–311. Weinheim: Wiley
85. Taylor R, Krishna R. 1993. *Multicomponent Mass Transfer*. New York: Wiley
86. Aaron D, Tsouris C. 2005. Separation of CO<sub>2</sub> from flue gas: a review. *Sep. Sci. Technol.* 40:321–48

---

65. Comprehensively presents the fundamentals of different reactive separations.

---



---

67. Contains the contributions of many well-known researchers in the field of reactive separations.

---

87. Safarik DJ, Eldridge RB. 1998. Olefin/parafin separations by reactive absorption: a review. *Ind. Eng. Chem. Res.* 37:2571–81
88. Srivastava RK, Jozewicz W. 2001. Flue gas desulfurization: the state of the art. *Int. J. Air Water Pollut.* 51:1676–88
89. Notz R, Asprien N, Clausen I, Hasse H. 2007. Selection and pilot plant tests of new absorbents for post combustion carbon dioxide capture. *Chem. Eng. Res. Des.* 85:510–15
90. Keil FJ. 2007. *Modeling of Process Intensification*. New York: Wiley-VCH
91. Coleman CF, Leuze RE. 1978. Some milestone solvent extraction processes at the Oak Ridge National Laboratory. *J. Tennessee Acad. Sci.* 54:102–7
92. Power KL. 1971. Operation of the first commercial liquid ion-exchange and electrowinning plant. *Proc. Int. Solvent Extract. Conf., 1971, The Hague, Netherlands*, pp. 1409–15. London: Soc. Chem. Ind.
93. Bart HJ. 2001. *Reactive Extraction (Heat and Mass Transfer)*. Heidelberg: Springer
94. Bart H, Garthe D, Grömping T, Pfennig A, Schmidt S, Stichlmair J. 2006. Vom Einzeltröpfchen zur Extraktionskolonne. *Chem. Ing. Tech.* 78:543–47
95. Thornton JD. 1992. *Science and Practice of Liquid-liquid Extraction*. Oxford: Clarendon
96. Bart H. 2005. Extraction columns in hydrometallurgy. *Hydrometallurgy* 78:21–29
97. Lo TC, Baird MHK, Hanson C. 1983. *Handbook of Solvent Extraction*. New York: Wiley & Sons
98. Ulrich J, Heinrich J. 2005. Reaktivkristallisation. *Chem. Ing. Tech.* 77:1759–72
99. Schmidt-Traub H. 2005. *Preparative Chromatography*. Weinheim: Wiley-VCH
100. Ströhlein G, Assunção Y, Proplesch R, Mazzotti M, Morbidelli M. 2005. Reaktive chromatographie. *Chem. Ing. Tech.* 77:1819–28
101. Lipnizki F, Field R, Ten P. 1999. Pervaporation-based hybrid process: a review of process design, application and economics. *J. Membr. Sci.* 153:183–210
102. Marquardt W, Kossack S, Krämer K. 2008. A framework for the systematic design of hybrid separation processes. *Chin. J. Chem. Eng.* 16:333–42
103. Wynn N. 2001. Pervaporation comes of age. *Chem. Eng. Process.* 97:66–72
104. Roza M, Maus E. 2006. Industrial experience with hybrid distillation—pervaporation or vapor permeation applications. *Proc. Distillation Absorp., London, UK*, pp. 619–27. Rugby: Inst. Chem. Eng.
105. Fontalvo J, Cuellar P, Timmer JMK, Vorstman MAG, Wijers JG, Keurentjes JTF. 2005. Comparing pervaporation and vapor permeation hybrid distillation processes. *Ind. Eng. Chem. Res.* 44:5259–66
106. Ohlgschläger A. 2006. Development of a hybrid solvent recovery process (combination of distillation and vapour permeation). *Proc. Distillation Absorp., London, UK*, pp 854–58. Rugby: Inst. Chem. Eng.
107. Maus E, Brüschke HEA. 2002. Separation of methanol from methylesters by vapour permeation: experiences of industrial applications. *Desalination* 148:315–19
108. von Scala C, Fässler P, Gerla J, Maus E. 2005. Kontinuierliche Herstellung von kosmetischen Fettsäureestern mittels Reaktivdestillation und Pervaporation. *Chem. Ing. Tech.* 77:1809–13
109. Kloeker M, Kenig EY, Schmitt M, Althaus K, Schoenmakers H, et al. 2003. Influence of operating conditions and column configuration on the performance of reactive distillation columns with liquid-liquid separators. *Can. J. Chem. Eng.* 81:725–32
110. Altman E, Kreis P, van Gerven T, Stefanidis GD, Stankiewicz A, Górak A. 2010. Pilot plant synthesis of n-propyl propionate via reactive distillation with decanter separator for reactant recovery. Experimental model validation and simulation studies. *Chem. Eng. Process.* 49:965–72
111. Profio DG, Perrone G, Curcio E, Cassetta A, Lamba D, Drioli E. 2005. Preparation of enzyme crystals with tunable morphology in membrane crystallizers. *Ind. Eng. Chem. Res.* 44:10005–12
112. Drioli E, Curcio E, Profio DG, Macedonio F, Criscuoli A. 2006. Integrating membrane contactors technology and pressure driven membrane operations for seawater desalination. *Chem. Eng. Res. Des.* 84:209–20
113. Profio DG, Curcio E, Drioli E. 2009. A review on membrane crystallization. *Chim. Oggi* 27:27–31
114. Meijer J, Geertman R, Oosterhofe H, Witkamp GJ. 1998. *WO Patent No. 99/33750*
115. Veltmans W, Wierckx F. 1999. *Patent No. 99200592.6*
116. Versteeg G, Kumar P, Hogendoorn J, Feron P. 2003. *Patent No. PCT/NL03/00337*
117. Schlinge D, Scherpien P, Schembecker G. 2010. Comparison of process concepts for preparative chromatography. *Chem. Eng. Sci.* 65:5373–81

118. Vicente T, Sousa M, Peixoto C, Alves P, Carrondo M. 2008. Anion-exchange membrane chromatography for purification of rotavirus-like particles. *J. Membr. Sci.* 311:270–83
119. Górak A, Kreis P, van Beijeren P, Faber R, Demmer W, Constantin F. 2010. *WO Patent No. 2010/083859 A1*
120. Aumann L, Morbidelli M. 2007. A continuous multicolumn countercurrent solvent gradient purification (MCSGP) process. *Biotechnol. Bioeng.* 98:1043–55
121. Aumann L, Morbidelli M. 2006. *WO Patent No. 2006116886*
122. Stefanidis GD, Vlacos DG. 2008. Millisecond methane steam reforming via process and catalyst intensification. *Chem. Eng. Technol.* 31:1201–9
123. Ducreé J, Haeberle S, Brenner T, Glatzel T, Zengerle R. 2005. Patterning of flow and mixing in rotating radial microchannels. *Microfluid. Nanofluid.* 2:97–105
124. Zwijnenburg A, Stankiewicz A, Moulijn JA. 1998. Dynamic operation of chemical reactors: friend or foe? *Chem. Eng. Prog.* 94:39–47
- 125. Silveston P, Hudgins RR, Renken A. 1995. Periodic operation of catalytic reactors—introduction and overview. *Catal. Today* 25:91–112**
126. Ni XW. 2006. Continuous oscillatory baffled reactor technology. *Innov. Pharm. Technol.* 20:90–96
127. Boelhouwer JG, Piepers HW, Drinkenburg AAH. 2001. The induction of pulses in trickle-bed reactors by cycling the liquid feed. *Chem. Eng. Sci.* 56:2605–14
128. Matros YS, Bunimovich GA. 1996. Reverse-flow operation in fixed bed catalytic reactors. *Catal. Rev. Sci. Eng.* 38:1–68
129. Zbicinski I, Benali M, Kudra T. 2002. Pulse combustion: an advanced technology for efficient drying. *Chem. Eng. Technol.* 25:687–91
130. Simo M, Brown CJ, Hlavacek V. 2008. Simulation of pressure swing adsorption in fuel ethanol production process. *Comput. Chem. Eng.* 32:1635–49
131. Schulte-Schulze-Berndt A, Krabiell K. 1993. Nitrogen generation by pressure swing adsorption based on carbon molecular sieves. *Gas. Sep. Purif.* 7:253–57

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**125. Provides broad insight into the periodic operation in catalytic reactors.**

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## Errata

An online log of corrections to *Annual Review of Chemical and Biomolecular Engineering* articles may be found at <http://chembioeng.annualreviews.org/errata.shtml>