

Catalysis in the 21st century

lessons from the past, challenges for the future

Catalysis is a science relying on many disciplines. The advent of industrial catalytic technologies in the last century has, most often, resulted from a sequential interaction between chemists and chemical engineers, both communities developing their own fundamental and applied sciences, i.e., a multidisciplinary process. Some of the major lessons learned in the past century, and related achievements, are illustrated and discussed. Challenges for catalysis research in the 21st century are identified, based on the current knowledge of catalysis researchers, recent fundamental and applied developments, and current or long-term objectives of the global chemical industry.

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Introduction

In ancient times, fermentation (and therefore catalytic) processes allowed Noah to produce his wine and Sumerian men their beer. In the 19th century, Davy, Faraday, and Berzelius, among others, set in the basis for modern catalysis. In the last century, catalysis became one of the most powerful tools, in the petroleum, bulk chemicals, and more recently fine chemicals and pharmaceuticals sectors.

Although it is often mentioned that the field of catalysis is mature, one should remember a quote by H. Heinemann^[1]: “It may appear that a field or even the whole of catalytic technology is relatively mature. This is, however, a misconception because history teaches us that fields which appear mature are suddenly revitalized by a major discovery.”

The field of catalysis is poised for further major progress and significant successes in the 21st century, with some innovations occurring in an evolutionary manner and many more likely to result from technological discontinuities or movement to a new learning curve. During the last 20 years, catalysis has been increasingly recognized as a multidisciplinary science, setting the stage for substantial changes.

Catalysis in the 21st century will be trans-disciplinary, with continuous synergistic interactions and collaborations between chemists, physicists, biochemists, chemical, mechanical and electronic engineers, and many others. The basis for this change will be: the rational design of catalysts underpinned by the fundamental understanding of their action and of reaction mechanisms; novel routes to catalyst discovery using

combinatorial methods and high throughput experimentation; the need for cheaper and sustainable catalytic processes in all chemical sectors, with increased selectivity and lifetime (due to environmental, societal, and economic considerations); and necessarily an increased collaboration between academic and industrial scientists having a common interest in catalysis and its applications.

Sectors that are particularly open to innovation are, in order of increasing maturity and interest, pharmaceuticals, power generation, fine chemicals, natural gas conversion, and transportation. Other sectors we shouldn't overlook include the food industry, petrochemicals, and petroleum refining. These last three sectors are often considered as technologically mature, with most of research in these fields being explanatory. However, we believe that there is still ample room for “extrapolatory” research and new developments. Nevertheless, it is the former five sectors where exploratory research and emerging technologies will likely have the greatest impact.

Pushers and pullers: the R³ rule for innovation

The future of catalysis relies, as it did in the past, on technological success. Such success, even when innovative catalysts are involved, is more likely to occur when the original idea is process “pulled” (there is an industrial/societal need) than when it is catalyst “pushed” (a marvelous potentially catalytic material with as yet no application). Hence the innovation

and development of a catalytic process should be multidisciplinary (or better, trans-disciplinary) from its start, rather than becoming multidisciplinary as it progresses. Integration is mandatory. Developing a process is not a relay race... it is a rowing competition, where all rowers in a team act in unison from start to end.

As quoted recently by J.R. Rostrup-Nielsen^[2], success relies on doing the “right thing at the right time in the right way” (the R³ rule). The “right thing” is a full and correct identification of the need and problem(s); the “right time” is determined by economic and public considerations or projections; and the “right way” is putting together and operating a focused and competent research and engineering team that is aware of the problem and economic constraints.

“Pullers” almost always relate to public or economic concerns. Examples of major “pullers” in the 20th century are:

- The Chilean embargo on nitrates (a necessary ingredient for explosives in the early 1900s) to Germany that boosted the Haber and Bosch studies on the fixation of nitrogen in air to produce ammonia (1910–1916);
- The need for a more efficient automobile fuel that incited E. Houdry to research and develop the oil cracking process (ca. 1935);
- Catalytic reforming and hydrocarbon alkylation developed by UOP in the late 30s and early 40s, not only providing higher octane index fuels but also enabling, because of their availability, the British RAF pilots to win the Battle of Britain in the Summer of 1940.
- Environmental regulations that triggered the development of various catalytic hydrotreating processes, the three-way exhaust catalyst, the MTBE and TAME synthesis processes, and various technologies to reduce NO_x emissions.

Today’s major “pullers” are:

- Market driven strategy aiming at simpler and less capital intensive processes, and the access to abundant, renewable, and cheaper feeds;
- Societal concern for preservation and remediation of the environment;
- Evolving legislations by public/governmental bodies: often fluctuating with time because of the various bodies and lobbies involved, but eventually always having strict deadlines;
- “Weak signals” from world-wide scientific progress (academic and industrial): because of industry’s awareness of developments made by competitors and fortunately, also, the identification of creative projects, advances, and discoveries in academia.

Today’s “pushers” are:

- New approaches to discovering potentially new catalytic materials, including innovative preparation methods and combinatorial catalysis;
- Increased molecular understanding of the mechanism of heterogeneous and homogeneous catalytic transforma-

tions based on *in situ* investigations and extensive quantitative kinetic models and studies;

- Scientific computing making possible quantum chemistry, molecular modeling, thermodynamic and kinetic predictions, reaction and reactor modeling, and, last but not least, all the resources needed to enable quantitative high throughput evaluation of catalyst performance;
- New approaches to catalytic processes enabling product yields to exceed those predicted by thermodynamics;
- Combinatorial catalysis and high throughput catalyst testing, speeding up the discovery of novel catalysts and catalyst optimization.

Some examples are:

Scanning tunneling microscopy (STM) is now able, in most situations, to provide atom-resolved images. Recent work imaging 4 nm MoS₂ clusters, deposited on an Au (111) surface has provided evidence that sulfur vacancies appear at their edges when they are exposed to atomic hydrogen at 673K (Figure 1). This shows that such vacancies are involved in the active sites responsible for the activity of Co-Mo hydrodesulfurization catalysts^[3], and therefore confirms the concept of hydrodesulfurization also occurring via a Mars-van Krevelen type mechanism^[4].

New formulations of organometallic catalysts, enabling their recovery and re-use, promote the development of homogeneous catalysis processes. They include the design of supported liquid phase catalysts^[5] and that of ligands with either hydrophilic or hydrophobic properties permitting their use in non-conventional solvents: water, ionic liquids, supercritical CO₂, and fluorinated compounds^[6]. These catalytic systems are particularly useful for asymmetric hydrogenation, carbonylation, and hydroformylation reactions.

Process approaches to exceed equilibrium yields predicted by thermodynamics are steadily becoming more popular. They include the use of membrane reactors (for example, when they can be used to selectively remove hydrogen from the reaction environment), catalytic distillation (when the heat of reaction can be used to distill one of the products off the reaction mixture), and the coupling of the main reaction with a second one that consumes one of the reaction by-products.

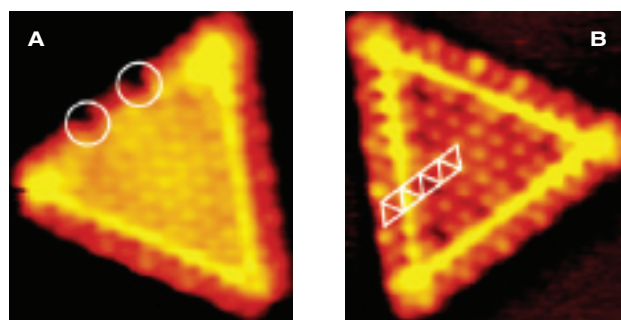


Figure 1 Atom-resolved STM images of a 4 nm MoS₂ cluster deposited on an Au (111) surface after (A) and before (B) exposure to atomic hydrogen at 673K^[3]. (Reproduced with permission from the American Physical Society.)

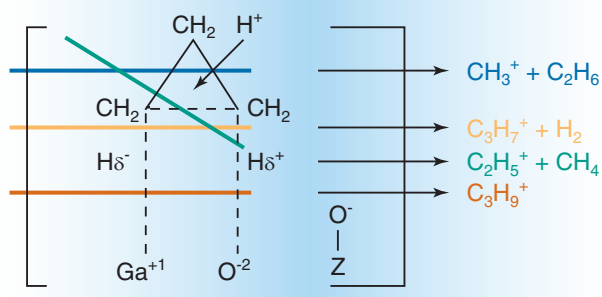


Figure 2 The protonated pseudo-cyclopropane (PPCP) transition state describing the low temperature activation of propane on Ga-modified H-ZSM-5^[15]. (Reproduced with permission from Elsevier Science Publishers.)

Specific areas that receive increasing attention today are the activation and functionalization (including selective oxidation) of light alkanes, the application of heterogeneous catalysis to fine chemicals synthesis, asymmetric catalysis, environmental catalysis, and the accelerated discovery, evaluation, and optimization of catalysts.

Activation and selective oxidation of light alkanes: adding value to abundant and cheaper feeds

The selective activation and functionalization of light (C_1 – C_3) alkanes is a challenge. Alkanes have no “pi” electrons enabling the catalytic active site to “grab” easily the molecule; therefore, single C–C bonds are more resistant to chemical attack than C=C double bonds. Activation of the first C–H bond is the most difficult and thus products are oxidized more easily than the primary reactant. Reactions usually have to be conducted at rather high temperature to achieve reasonable rates, and also for thermodynamic reasons. All of the above explain the low selectivities that are usually observed. An exception is the selective oxidation of n-butane to maleic anhydride that is favored by the high electronic and conformation stability of the product.

Current approaches to resolving the above problems are “protection” strategies preventing further oxidation of the product of interest, the high temperature, non-oxidative activation of light alkanes, and the search for new (generally bifunctional) activation routes. They are illustrated below.

The direct and selective oxidation of methane to methanol is a particularly difficult reaction, as methanol is much more reactive than methane and swiftly degenerates to total oxidation products. Catalytica’s “protection” strategy has resolved this problem. It consists of trapping the methanol product, resulting from the oxidation of methane in mild conditions by oxygen on Hg or Pt organometallic catalysts, as a methyl ester by reaction with a strong acid (typically H_2SO_4 (conc.))^[7,8]. Hydrolysis of the ester releases methanol and the acid which can, in principle, be recycled after regeneration. Unfortunately, the latter appears to be the bottleneck to the development of an economically viable process as large amounts of sulfuric acid are required (such

catalysis does not work for sulfuric acid concentrations below 95%). Nevertheless, a lesson to be learned from this exciting research is that higher yields in a desired product are not necessarily obtained only by searching for ways to directly increase selectivity but also by finding means to prevent the formation of undesired by-products.

The non-oxidative upgrading of light alkanes is receiving renewed attention since it produces higher value liquid products and hydrogen. The UOP-BP Cyclar® process for the conversion of C_3 – C_4 alkanes with Ga-modified H-ZSM-5 zeolite catalysts^[9,10] is now ready to be commercialized in Saudi Arabia.

More recently, it has been shown that Mo-modified zeolite H-ZSM-5 efficiently catalyzes the non-oxidative aromatization of methane at high temperature (973–1023K), with benzene and naphthalene being the major products and conversion to equilibrium (ca. 10%) being reached^[11,12]. Molybdenum carbide formed during catalyst activation acts as the dehydrogenation component activating methane. Solutions have been identified recently for the major problem of catalyst deactivation. In particular, good catalyst stability, with respect to time-on-stream, can be achieved by adding small amounts of CO (ca. 2%) to the methane feed^[13] or by pre-activating the catalyst in such a way that the alpha rather than the beta form of molybdenum carbide, supported on the zeolite, is obtained^[14]. A remaining major challenge for this methane upgrading process is how to reach higher yields of liquid products while also operating at a lower temperature — in particular alkylated aromatic hydrocarbons such as toluene, ethylbenzene, and xylenes, and branched aliphatic compounds that could be added to the gasoline pool. The use of membrane reactors and the addition of light alkanes to the methane feed are approaches currently being considered.

A detailed mechanistic investigation of the activation of propane on Ga-modified H-ZSM-5, using ^{13}C MAS-NMR and propane-2- ^{13}C as strategically labeled reactant, led to the proposal of a novel **low temperature** (as low as 573K) **activation route for propane**^[15]. The active site consists of highly dispersed gallium species (probably GaO^+) in intimate interaction with the zeolite acidic sites. The concentration of species can be optimized by repeated reduction (H_2)-oxidation (O_2) treatments of the catalyst. Figure 2 shows the structure of the proposed protonated pseudo-cyclopropane (PPCP) transition state formed by simultaneous interaction with the gallium (GaO^+) and zeolite Brønsted acid sites.

Evolution of the PPCP transition state leads to ethylene, propene, and a variety of C_1 – C_3 carbenium ions. The latter species can react with electron rich molecules — e.g., olefins in the aromatization of propane^[15] and benzene to produce toluene, ethylbenzene, and xylenes^[16]. Most recently, it has been shown that the same catalytic system was also effective for the **direct ammoxidation of propane** by ammonia and oxygen, the PPCP transition state also being most likely

Comparison of process characteristics and requirements in the petrochemical, fine chemicals, commodity chemicals, and pharmaceutical industries.

Fine chemicals and pharmaceuticals	Petrochemicals and commodity chemicals
• Batch, discontinuous processes	• Continuous processes
• Multipurpose units	• Dedicated units
• Complex molecules	• “Simple” molecules
• Several combined functionalities	• Small number of functionalities
• Multi-step syntheses	• Few synthesis steps
• Mostly liquid phase processes	• Mostly gas phase, fixed bed processes

Table 1

responsible for the initial activation of propane^[17,18]. Propane conversions reaching 45% with 35% selectivity to acrylonitrile were observed. Most interestingly, the major by-products are *i*-butane and *i*-butene, and the yield in undesired CO_x is less than for conventional mixed oxides catalysts. This attractive new catalytic system for the direct ammoxidation of propane is currently being optimized^[19] and detailed mechanistic studies are in progress.

Heterogeneous catalysis for fine chemicals: sustainable processes

So far, heterogeneous catalysis has found few applications to the synthesis of fine chemicals and pharmaceuticals relative to its wide use in the petroleum and commodity chemicals sectors. Reasons for this situation are summarized in Table 1.

Nevertheless, the application of heterogeneous catalysts to the synthesis of fine and specialty chemicals, and pharmaceuticals, is receiving increased attention as it is a route to the design of safer, cleaner, and more sustainable processes. Polyoxometallates (POM)^[20,40] and zeolites^[21] are two classes of catalysts whose potential has been widely studied and reported in the recent literature. The following two examples illustrate the importance of confinement effects in catalysis by zeolites and the use of **zeolites as Friedel-Crafts (acylation) and selective oxidation catalysts**.

The principles of molecular confinement in the intracrystalline volume of zeolites and the behavior of zeolites as solid solvents^[22,23] have set a new scene for their use as heterogeneous catalysts in organic synthesis. Because such reactions are usually operated at a rather low temperature and/or in the liquid phase, confinement effects are responsible for the preferential adsorption of a substrate in the intracrystalline volume of a zeolite when there is a close fit between the size and shape of the substrate and those of the zeolite channels.

Zeolite catalysis in liquid phase distinguishes itself from zeolite catalysis in gas phase by:

- high concentrations of reactants, intermediates, and products which lead to a high utilization of the intracrystalline volume of the zeolite;

- competition of the reactants for the zeolite intracrystalline volume, which is governed by molecular shape selectivity, confinement, and polarity effects;
- increasing concentration of product(s) in the liquid phase, as a function of contact time, when operating in batch conditions. This results, as the reaction proceeds, in a less favorable desorption of the products and a decrease of the catalyst productivity because of the possible accumulation of some products in the zeolite pores;
- possible adsorption of the solvent which may compete for the intracrystalline volume where most reaction occurs.

These effects, that arise from the ability of zeolites or other microporous solids to act as solid solvents^[22,23], are responsible to a large extent for the generally poor performance of zeolite catalysts when they are used for the synthesis of fine chemicals in batch conditions. Partition equilibria determine the distribution of the reactants and products between the bulk liquid phase and the zeolite phase. Thus, the optimal productivity of microporous catalysts in such conditions can indeed only be achieved when the reactants only occupy the zeolite intracrystalline volume (no competition from the solvent, if present). Inside the zeolite pores the reactants can achieve the correct stoichiometric ratio, which will be different from the ratio of reactants in the liquid phase since the adsorption equilibrium constants (partition coefficients) are most likely to be different. Also, the product is easily desorbed, i.e., when the access of the reactants to the intracrystalline volume is not inhibited. Figure 3 illustrates these considerations.

Friedel-Crafts reactions are of major importance in organic synthesis. In particular, acetylation and benzylation are useful routes for the synthesis of aromatic ketones that are intermediates in the manufacture of many fine and specialty chemicals as well as pharmaceutical compounds.

So far, only limited success has been reported when using zeolites for such catalysis, except for the use of large pore zeolites (BEA, FAU)^[24] in the synthesis of *p*-methoxyacetophenone by acetylation of anisole^[25] and that of 3,4-dimethoxyacetophenone by acetylation of veratrole^[26]. Rhône Poulenc (now Rhodia) has commercially operated the latter processes, replacing the classical AlCl₃

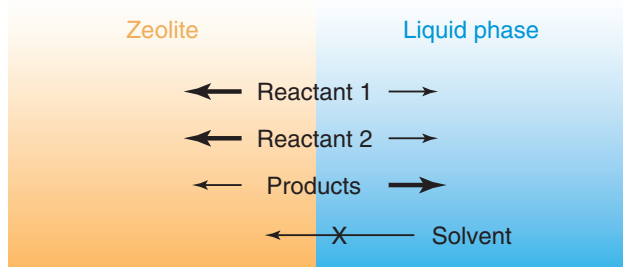


Figure 3 Partition of the reactants, products, and solvent between the liquid phase and the zeolite, acting as catalyst and solid solvent, is governed by confinement effects determining the adsorption equilibrium constants^[23]. (Reproduced with permission from Elsevier Science Publishers.)

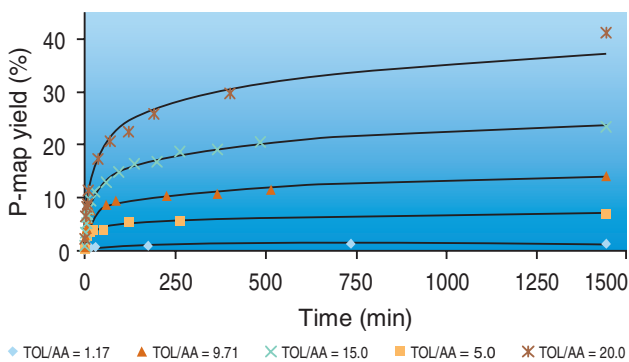


Figure 4 Acetylation of toluene by acetic anhydride with zeolite H-Beta (Si/Al = 12) as catalyst ($T = 388\text{K}$)^[28]. (Reproduced with permission from Academic Press Inc.)

catalytic system, for more than five years. They benefit from major economic, safety and environmental advantages, i.e., increased selectivity to the desired product, the absence of corrosion problems and chlorinated solvents, a recyclable catalyst, six times fewer physical and chemical process steps, ten times less solid waste, and a hundred times less aqueous discharge.

The role of confinement effects in this type of catalysis has been recently analyzed in detail^[27,28] for the acetylation of anisole and toluene by acetic anhydride. As shown in Figure 4, the acetylation of toluene (a poorly activated aromatic substrate) can be successfully performed using zeolite H-Beta. This is provided the toluene/acetic anhydride ratio in the liquid phase is sufficiently high — thereby compensating for the higher adsorption constant of acetic anhydride relative to

toluene (a factor of 5–10), providing the proper stoichiometry of the reactants in the zeolite channels, and with toluene in excess acting as a solvent for the p-methyl-acetophenone product. It was also demonstrated that continuous operation using a fixed bed reactor led to stable and better yields than those achieved with conventional batch reactors^[29]. This is obviously an area that could greatly benefit from a more synergistic interaction between organic and zeolite chemists, as well as reaction and reactor chemical engineers.

Another exciting recent development in the application of zeolites to fine chemicals synthesis has been the use of TS-1, a titanium-containing zeolite of the MFI (ZSM-5) structure type, as a most versatile oxidation catalyst using hydrogen peroxide as oxidant^[30,31], thus avoiding the production of solid waste. Figure 5 summarizes some of its most important applications, which include the epoxidation of olefins, the hydroxylation of phenol to hydroquinone and catechol, the hydroxylation of aromatic compounds, the oxidation of alcohols to ketones and even of alkanes to alcohols, and the ammoxidation of cyclohexanone (with NH_3 and H_2O_2).

Asymmetric catalysis: mimicking nature

Asymmetry pervades nature from governing the behavior of fundamental particles such as fermions which, in chemistry, famously manifests itself as the Pauli Principle, to the evolution of life on earth where a single optical handedness has been rigorously selected. An amazing example of this is the transfer of genetic information from one generation to the next: only DNA with a right-handed helix performs this most fundamental life process. This property of asymmetry leads many other organisms and molecules to exhibit profoundly different physiological effects to opposite enantiomers, the thalidomide tragedy being the most potent example (see Table 2), with new legislation forcing increasing control on the manufacture and sale of single enantiomer products.

Consequently, a major impetus exists for the chemicals and pharmaceuticals industries to establish enantioselective catalytic methods whereby pure enantiomeric forms can be produced. At present, of the various chiral technologies available, homogeneous enantioselective methods remain very much at the vanguard of industrial processes^[32]. In contrast, heterogeneous enantioselective catalysis is a more fledgling technology, but offers the significant advantage of non-

Many bioactive substances are asymmetric, with the two enantiomers having very distinct properties.

• <i>D</i> -thalidomide: cure for morning sickness during pregnancy.	• <i>L</i> -thalidomide: mutagenic agent, teratogen.
• <i>S</i> -limonene: odor of lemon.	• <i>R</i> -limonene: odor of orange.
• <i>S</i> -penicillamine: antiarthritic drug.	• <i>R</i> -penicillamine: highly toxic.
• <i>S</i> -propranolol: beta-blocker (heart disease).	• <i>R</i> -propranolol: contraceptive.

Table 2

stoichiometric production of chiral molecules from non-chiral substances, combined with ease of handling and separation.

Creating successful heterogeneous enantioselective catalysts is thus an important goal for the chemicals and pharmaceuticals industries, with considerable attention being focused on chirally modified metals as promising candidates^[33]. Recent surface science investigations throw a new and intriguing light on these modified metal surfaces, highlighting new phenomena such as complex adsorption phases, two-dimensional organization, and the surprising creation of extended chiral surfaces^[34].

Figure 6 shows that switching enantiomers of tartaric acid adsorbed on a Cu (110) surface plane reverses the chirality of the extended modified surface, and that chiral “landing strips” for the asymmetric reaction of substrate molecules appear between the rows of tartaric acid molecules resulting from molecular self-organization^[34]. This molecular level information provides important and fresh input into future design strategies for the design of chiral surfaces.

Combinatorial catalysis: accelerating catalyst discovery and evaluation

In about five years, combinatorial methods have gone from being a curiosity generating a lot of skepticism, to occupying center stage in catalysis research^[35]. Major players in this arena are Symyx Technologies (USA), HTE (Germany), and Avantium (The Netherlands). Several R&D companies also elected to develop their own in-house capabilities, e.g., General Electric, DuPont, UOP, ICI, Johnson Matthey, to cite but a few^[36].

The term “combinatorial catalysis,” which harks back to its original use in the rapid screening of drug candidates, is now broadly applied to any miniaturized, high-throughput R&D system, in particular those used for the accelerated discovery and development of new catalysts and materials.

Figure 7 illustrates the various stages involved in the discovery and development of catalytic processes, including their attrition over the ca. 12 year period usually necessary to reach commercialization. Combinatorial catalysis, via high-throughput screening and testing of potential catalytic materials, aims to collapse the time necessary to discover or optimize, and define new catalytic formulations, i.e., compressing it from 4–5 years to 6–12 months.

The approach is still maturing and involves a number of steps, as shown in Figure 8. The design and construction of catalyst libraries, which may comprise thousands of candidate materials, involves theory, modeling, careful screening of the journal and patent literature, chemical intuition and continuous feedback — this through various algorithms, of information generated by the primary screenings and secondary screenings (tests) that are progressing. Primary screening is usually highly sophisticated, involving highly miniaturized reactor systems and specific, sometimes home-designed, analytical techniques. Secondary screening is performed with parallel multichannel microreactor systems

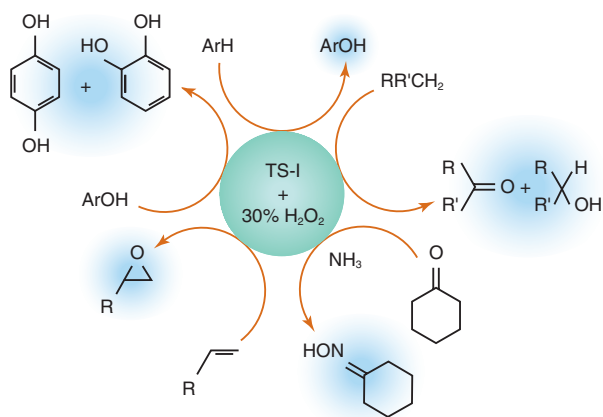


Figure 5 Zeolite TS-1 as a versatile oxidation catalyst. (Reproduced with permission from Kluwer Academic/Plenum Publishers.)

equipped with more conventional analytical tools. A third screening stage at the conventional microreactor scale is still likely to be needed in order to generate data necessary to reach the pilot stage.

Many challenges are met by this novel approach to accelerated catalyst discovery and optimization. Considering the large number of potential catalytic materials which will have to be generated, the tremendous amount of data (operating conditions and catalytic system performance) that will have to be stored and mined, and the need for state-of-the-art automation at all levels, scientific computing will play a decisive role. This will be even more so when the potential contributions of theoretical methods, such as quantum chemistry and molecular modeling/simulations, are taken into account. Another major challenge is the preparation of

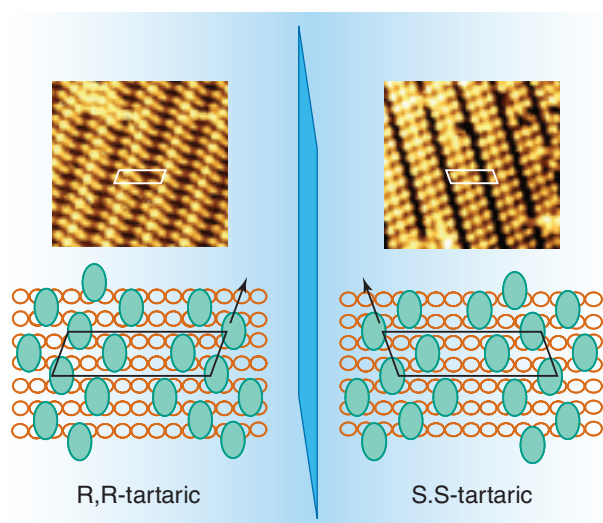


Figure 6 Switching Extended Surface Chirality: R,R-Tartaric acid versus S,S-Tartaric acid. Switching enantiomers reverses the chirality of the extended modified surface. This chiral switching is illustrated by (a) 108 Å x 108 Å STM images and (b) schematic models of mirror adlayers created when R,R-tartaric acid and S,S-Tartaric acid are adsorbed on Cu(110)^[34,41]. (Reproduced with permission from Kluwer Academic/Plenum Publishers.)

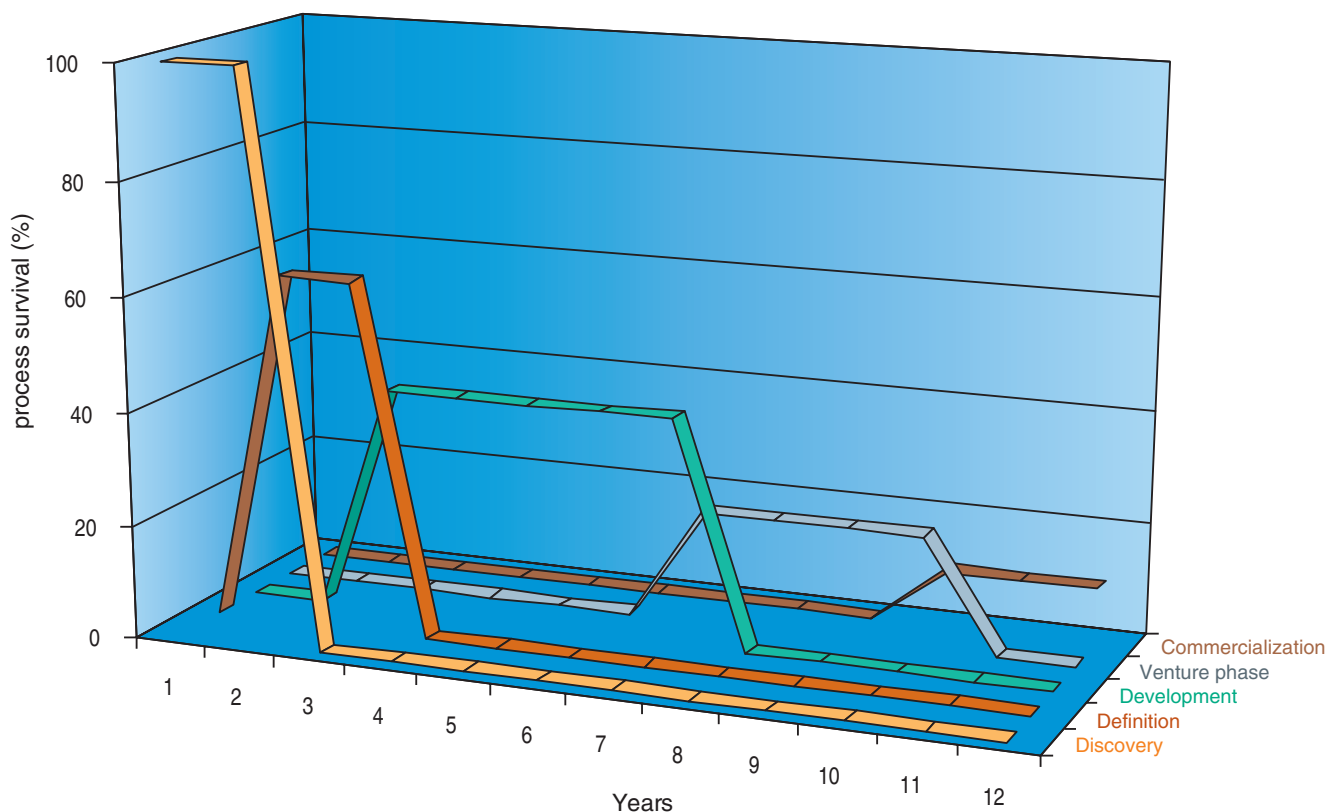


Figure 7 From discovery to commercial application: projects stages and attrition.

catalysts for the first and second screening levels by methods that can be realistically and reproducibly scaled up for their conventional microreactor testing if they become lead compositions. A related problem is the scale-down of conventional catalyst preparation methods and catalytic microreactors. In the latter case, theoretical models as well as innovative methods will be needed to engineer structured microreactors providing quantitative information when using only 1–200 mg of catalyst. Last but not least, reliable evaluation of catalytic performance, qualitative at the first screening level and nearly quantitative at the second one, require the careful identification and definition of the performance evaluation parameters and function which, in turn, necessitates the use of the appropriate, sometimes very specific, analytical methods and tools. In all cases, analytical tools will have to provide the fastest response. Ultrafast GC-analysis, as developed for example by the Borskov Institute of Catalysis in Novosibirsk and the Leverhulme Centre for Innovative Catalysis in Liverpool^[37], and on-line infrared or mass spectroscopies are certainly methods of choice... but other specific ones may have to be designed or used.

Combinatorial catalysis requires high technology and, therefore, in many ways is an opportunity and a renaissance for catalysis which has too often been considered as an art^[38]. It is certainly a field that will promote and develop close and sustained industry-university collaborations. Such examples already exist and appear to develop extremely well.

The catalyst sector has clearly become the next leading proponent of combinatorial chemistry after the pharmaceutical and agrochemical sectors. Combinatorial catalysis enables us to look with a new eye at what, unfortunately, has been many times characterized as a mature and old science or industry.

In July 2001, a NATO Advanced Study Institute was held in Vilamoura, Portugal, involving academic and industrial participants. It was agreed that the combinatorial approach, as defined earlier, is indeed a new tool that is becoming available, not only to industry but also academia. Technical developments will certainly help to promote and underpin such research. It appears that the real challenges are the down- and up-scaling of catalyst preparations, in a realistic manner, as well as the development and validation of analytical methods enabling rapid qualitative and quantitative analysis of the reaction products and the catalytic system.

There is no longer any doubt that the development of combinatorial, high throughput technology for catalyst design, evaluation, and testing is a new and proven tool for catalyst discovery. It is certainly very target-oriented. Industry and academia have complimentary objectives and novel ways must be found to enhance the synergies between these two communities.

High throughput catalyst design and evaluation is definitely not a roulette game. The combinatorial approach relies on scientific knowledge and statistical methods, and benefits

from the input of many other disciplines, including among others solid state and organometallic chemistry, automation, scientific computing, etc.

Catalysis in the 21st century

Nostradamus's predictions were only interpreted centuries after his death when events occurred that appeared to fit his apparent foresight. The following considerations should not be considered as predictions but only as views based on the current state of catalytic science, its general objectives, and the current economic and public "pullers."

First, and most important, recognizing that catalysis is an applied science involving synergies between many disciplines, it is obvious that its future lies in more intensive and open interactions between industry and academia (the former generating new processes and wealth, the latter providing additional state-of-the-art knowledge) together with a long term vision based on new concepts, methods, and techniques. Progress in the 21st century will only be possible if innovative approaches are found to promote such synergies, acknowledging a common interest in a given objective and resolving the problems associated with intellectual property rights. Fortunately, such schemes already operate today and they should be used as models.

Second, a major change should occur in catalysis research and development. Catalysis in the 20th century was recognized as being a multidisciplinary field of science, involving chemists, biologists, physicists, chemical engineers, and others. The resolution of problems and the reaching of targets were usually achieved via the sequential input and contributions of these disciplines. The 21st century should and will recognize catalysis as an inter- and trans-disciplinary science benefiting from the parallel input of many disciplines.

What is its future?

The following views are largely inspired by those of Dr. J.A. Cusumano, formerly President and Chief Strategic Officer of Catalytica Inc.

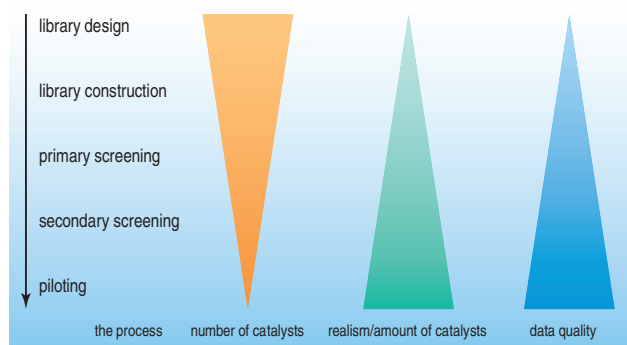


Figure 8 The combinatorial catalysis strategy. When progressing from the library design to the application level, the number of potential catalysts decreases rapidly, whereas the realism and amount of catalysts used in the tests increase, as well as the quality and quantitative value of the data, as indicated by the orientation of the triangles.

2001–2005 AD

- Zeolites as catalysts for fine chemicals and pharmaceuticals synthesis;
- Use of solid acids to replace liquid acids in fine chemicals synthesis;
- Biocatalytic removal of S, N, and metals from petroleum feedstocks;
- Extensive use of metallocenes and other single-site catalysts for polymer synthesis;
- Alkene to alkane feedstock transition;
- Catalytic combustion to decrease VOCs and NO_x emissions;

2005–2010 AD

- Nanotechnology in catalyst manufacturing;
- Chemical-biochemical bifunctional (cascade) catalysts;
- Engineered enzymes in chemicals/fuels production;
- Chiral polymeric materials;
- Heterogeneous catalysts for asymmetric synthesis of fine chemicals.

2010–2020 AD

- Fuel cell powered vehicles;
- High-temperature inorganic-organic polymers;
- Membrane and other multifunctional catalytic reactors;
- Broader use of electro- and photocatalysis;
- Advent of biopolymers, e.g., biodegradable materials and biosilk.

2020–2040 AD

- Photolytic water splitting and hydrogen economy;
- Catalytic antibodies, biomimetics, and synthetic enzymes in fine chemicals/pharmaceuticals synthesis;
- Engineering of microbes/bacteria for fine chemicals synthesis;
- Production of chemicals in living plants.

Conclusions

Alwin Mittasch remarked early in the 20th century that *“chemistry without catalysis would be like a sword without hilt, like a bell without ringing...”* Today, catalysts play a vital role in providing society with fuels, commodity and fine chemicals, pharmaceuticals, polymers, and means for protecting the environment.

Because of the complexity of catalysts and catalytic phenomena, information must be drawn from a large number of supporting disciplines:

- Organometallic chemistry;
- Solid state chemistry and materials science;
- Surface science;
- Theoretical chemistry and physics;
- Biochemistry and biomimetic chemistry;
- Chemical reaction and chemical reactor engineering;
- Chemical kinetics and dynamics.

Although research in catalysis is still dominated largely by experimental studies, the roles of scientific computing and theory are becoming increasingly important.

Catalysis research, in the 20th century, was multi-disciplinary and often progressed in a sequential manner. In

the 21st century, inter- and transdisciplinarity will predominate. Progress toward a substantially improved vision of catalytic chemistry and its applications will depend on parallel advances in several fields and continuous cross-fertilization between the various disciplines mentioned above.

Opportunities exist for developing meaningful collaborative programs relying on increased partnership

between industry, academic laboratories, and public organizations. I hope I have demonstrated that it is in this way that new innovations will arise, some by an evolutionary process, and many others from technological discontinuities or a jump to a new learning curve.

questions and answers

Is catalysis a mature science?

Many recent innovations in industrial catalysis consist of incremental advances, in particular in fields such as petroleum and petrochemical chemistry, and the synthesis of bulk chemicals. It is probably the reason for which catalysis is often viewed as a mature science. However, this is a myopic view that is unfortunately enhanced by the current short-term research focus of many chemical companies that respond to immediate economic and business constraints.

Many opportunities exist for step changes, for jumping onto new R&D S-curves that could lead to novel technologies. Examples abound of new discoveries and concepts in industry and in academia (complemented by the advent of high throughput experimentation methods), the applications of which could be triggered by any number of economic and public factors. The motivations for such a trigger could be: (i) the desire for lower cost feeds (e.g., light alkanes replacing light olefins), (ii) the desire for less capital- and energy- intensive processes, by the integration of consecutive reaction steps and the use of novel catalytic reactor technologies, (iii) the desire for more environmentally benign processes, generating less by-products and using safer feeds (and solvents), namely for the synthesis of fine chemicals, (iv) the need for a timely response to governmental (public) regulations, such as those commanding the drastic reduction of the sulfur content in fuels, and (v) the desire for catalytic reaction capabilities not previously commercially feasible.

Making modest improvements is pretty much what industry has done over the last 30 years and still does today. Breakthrough technologies, however, will emerge from increased interaction between catalysis in academia and industry, and other areas such as materials science, catalytic reaction and reactor engineering, separation technology, and scientific computing.

Is it really possible to use nanotechnology to commercially produce tons of catalysts usually prepared as extrudates? Wouldn't microscopic features at the nanolevel be lost in most catalyst scaleups?

Nanotechnology has proven itself as a tool that can produce catalytic materials on a small scale as illustrated for example by the work currently being performed at the Max Planck Fritz Haber Institute in Berlin (Prof. H. Freund), at the Technology University in Eindhoven (Prof. J.W. Niemantsverdriet), and at the University of Liverpool (Prof. R. Raval).

Scaling up catalyst synthesis has always been a problem. It is governed by chemistry and the rules of Mother Nature. Obviously, scaling up nanomaterials to macroscopic ones will mean many difficult challenges. Such a scaling up differs from the scaling up of a catalytic process because the former lacks the latter's well-defined physical and mathematical rules. What is needed for the scaling up of nanoscale catalysts is a detailed understanding of their chemical nature and properties.

Once these are identified, catalytic chemists should be able to reproduce them using more conventional and economically viable procedures. One should not overlook the creativity and innovative power of scientists when there is a strong pull towards application. For example, neither mass spectrometry nor Knudsen's law for the diffusion of gases were originally intended to be the basis of ²³⁵U enrichment processes producing nuclear fuels.

Combinatorial catalysis is, in reality, high throughput catalyst design, preparation, characterization, and evaluation. How does it differ from the classical approach used by industry and academia in the last century? Can one really extend combinatorial approaches to catalytic processes beyond the initial discovery, secondary screening, and optimization stages?

keywords

- catalysis
- alkane activation
- asymmetric synthesis
- environment
- combinatorial
- trends/challenges

acknowledgement

I am very much indebted to many friends at Haldor Topsøe A/S, Catalytica Inc., and Rhône Poulenc (now Rhodia) for enlightening discussions over our many years of intense collaboration, the conclusions of which underpin this modest contribution.

Fritz Haber's discovery of the ammonia synthesis reaction (in 1907) was stimulated by a scientific rivalry with Hermann Nernst, based on thermodynamic considerations. Support for his subsequent research was provided by BASF, whose dye production (including amiline, requiring nitric acid for nitration reactions) was its core business, and was later further boosted by the German government, who had a need for nitrates to manufacture explosives during World War I. Alwin Mittasch and his colleagues Hans Wolf and Georg Stern at BASF, for whom Haber was a consultant, with the full support and conviction of Carl Bosch, and with a large team of researchers, by 1912 had performed about 6,500 tests with 2,500 different materials. An effective catalyst had already been identified in 1910. By the time tests ended in 1922, 20,000 runs had been performed with over 4,000 different substances. New laboratory catalytic reactors enabling the easy insertion and removal of cartridges, containing ca. 2 g of catalyst, were also designed to speed up the catalyst testing process^[39].

Parallel (accelerated) catalyst evaluation is not new. It has been practised for many years in industry but may have been overseen by academic groups whose main objectives were the preparation of new materials (not necessarily catalysts), the fundamental understanding of those materials' properties, and the derivation of detailed kinetic data.

Combinatorial catalysis in the general sense (see main body), resembles in many ways the conventional approach. Automation, replacing manpower, is used to accelerate the testing process. Scientific input (prior art, quantum chemistry, data mining, and intuition) is required to design the original systems and guide the discovery process. It benefits, however, from a broad and unprecedented arsenal provided by high technology devices and scientific computing in all of its aspects, whose implementation in the field of catalysis is tremendously enhanced by sustained trans-disciplinary interactions between chemists, physicists, chemical and mechanical engineers, mathematicians and statisticians, and computer scientists.

Data mining, the first step being data storage, the last being data retrieval, and the derivation of useful correlations from a multi-dimensional parameter system, is one of the major keys to success. It feeds back into the discovery and optimization process. It should enable the discovery of the unexpected and will certainly be one of the most important contributors to the success of combinatorial catalysis.

Another issue requires urgent attention. Chemical engineers have classically focused on scaling up chemical reaction and processes. The development of combinatorial catalysis tools for primary and secondary screening now also requires an understanding of scaling down. How small can a catalytic reactor be to remain realistic? A search for structured reactors that can be miniaturized and a description of their detailed characteristics and operation are necessary. This is already recognized by several groups, including Prof. J.A. Moulijn, Delft; Prof. G.A. Marin, Ghent, and certainly several others.

Combinatorial catalysis is a new approach, an additional tool that complements (but not replaces) classical approaches. Its impact on the development of commercial homogeneous (polymerization) and heterogeneous (e.g., dehydrogenation, zeolite-based) catalysis is likely to become more visible and appreciated when tangible results are widely disseminated in the open literature by the several companies that already practice it.

What impact will the current level of consolidation in the chemical industry have on the discovery process? Will fewer companies be less aggressive about spending large sums of money on long term R&D? Will that impact on the timetable for the advent of new technologies?

The future of catalysis lies in trans-disciplinarity and increased partnership between the University, Industry, and Government sectors.

see next page

Clearly, consolidation in the chemical industry is governed by economic reasons. This necessarily impacts R&D in many companies. Many corporate laboratories, which were responsible for long term R&D, have disappeared, and the research responsibility transferred to business units that have a restricted vision due to market and corporate pressure. Many companies will therefore be less aggressive about spending, in-house, large sums of money for long-term internal research programs. This may be an opportunity for academic laboratories that offer research facilities at lower costs, provided they have a critical mass and deliver in terms of quality and time. It may also encourage industry to mine academia in order to make new discoveries and developments. The current consolidation of the chemical industry will certainly increase the pressure on academic laboratories, who will have greater difficulty in raising industrial funding and be under more pressure to deliver. Industrial support will become increasingly more selective but “Centers of Excellence” will continue to be supported and new technologies will continue to emerge, maybe even faster as a result of the increased focus.

A coherent strategy is needed and means should be developed and established to enable it. A partnership is necessary between Industry, Universities, and the Government (Public) sectors. Industry must take the lead in identifying and communication the major unsolved problems (short and long terms). Universities should conduct research aiming at creating discontinuities rather than explaining today’s catalytic chemistry and providing the intellectual underpinning of solutions rather than solutions per se. The Government sector should contribute to funding the research because of the long nature of the work and of its strategic impact on both national product and employment. Many consortia involving these three partners are likely to be created within the next few years. Several already exist in Europe.

What are the R&D needs for combinatorial catalysis that universities can constructively support — in balance with the broad efforts of major companies already developing the methodology and relevant instrumentation of this approach?

Companies active in this field are either recent ventures launched specifically for this purpose or well-established organizations interested in applying the combinatorial approach to their research. Because combinatorial catalysis is extremely multidisciplinary by nature, as well as

“classical,” a great variety of expertise and know-how are needed. Two options exist to access such skills. One is for industry to attract the best academic people, who can provide in-house the required expertise. The other is for industry to link with university teams, who have the know-how, may have developed specific and sophisticated tools, and are willing to interact closely with industry — ideally as partners. The first approach seems to be the preferred strategy of US companies whereas the latter appears to be the preference in Europe. This dichotomy will probably disappear in the future as it is more dependent on culture and existing industry-university collaboration schemes than on targets and economic pulls that will certainly eventually dominate. The role of academia will be, most probably, to provide fundamental expertise, know-how, and even maybe prototype instrumentation in specific niches, operating in synergy with industry. This is already happening in Europe (Avantium, Netherlands; HTE, Germany; and the Combicat consortium, European Union).

What can be done by the major companies to lower the million US dollar costs of combinatorial catalysis projects?

This is a question that should be addressed to the companies concerned rather than to an academic person. The prevailing view depends on the type of company and the urgency of the problem. Both time and economic factors will be determining. My view is that outsourcing part of the work to well-equipped, reputed, and reliable academic teams may be a partial solution as it will reduce research (but not development) costs. The teaming of industry and academia is also a way to attract substantial public funding. Demonstrating, through publishable and tangible examples (the role of academia) that combinatorial catalysis indeed delivers success will help sell the approach to a market that is still skeptical or at least hesitant because there are not enough resources to risk an investment into this novel tool that has yet to prove itself to be commercially efficient. There should be no doubt however that broad and accelerated catalyst testing can lead to success. Mittasch proved it in 1910 when conducting his research on the synthesis of ammonia. It took Mittasch about 12 years to perform 20,000 runs with more than 4,000 catalysts and to discover an ammonia synthesis catalyst that is still similar to the one used today. Combinatorial catalysis, in its broad definition would enable these large number of runs to be performed today in only a few months.

curriculum vitae



Eric G. Derouane received his MSc in Chemistry from Princeton University and his Dr.Sc. from the University of Liège. Since 1995, he has been the Director of the Leverhulme Centre for Innovative Catalysis at the University of Liverpool. His research interests

comprise molecular sieve synthesis, confinement catalysis in zeolites, alkane activation, the development of *in situ* techniques for catalytic studies, and combinatorial catalysis. His work has been recognized by the Ciapetta Lectureship of the North American Catalysis Society (1981), the Catalysis Lectureship of the Société Chimique de France (1993), and by the 1994 Francqui Prize (Belgium). He is a member of the Royal Academy of Belgium, Editor-in-Chief of the *Journal of Molecular Catalysis*, and an Editor of *CATTECH*. He is also an advisor and consultant to several companies worldwide.

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