

Forever young – The Catalysis Frontier

(Alois Fürstner)

“At a glance”: Catalysis research is an interdisciplinary and highly enabling science at the molecular frontier, ranging from quantum mechanics to engineering; as it helps unravelling the fundamental principles of nature and, at the same time, substantially contributes to the well-being of mankind, one may safely forecast that this field will remain forever young and further grow in importance.

It was already in the 1830s that the Swedish chemist Jöns Jacob Berzelius recognized that certain chemicals exert an influence on reactions without being changed or consumed themselves. These key observations laid the basis for the now commonly accepted definition of a “catalyst” as a substance that accelerates a chemical transformation in which it serves as a reactant and a product alike.

What sounds like dull chemical terminology is no less than a fundamental principle of nature and, at the same time, a tremendously important force shaping our industrialized economies. The photocatalytic conversion of sunlight into organic material by plants is a precondition for life on earth and the ultimate energy resource of the globe. Likewise, the vast majority of reactions in a living organism are catalytic processes. In addition to these biological ramifications, catalysis has profoundly changed our way of life. Imagine what the western world would look like without catalytic cracking of hydrocarbons (oil refinery) as the basis of our energy- and raw materials supply, without catalytic fixation of nitrogen as the basis for modern agriculture, without catalytic polymerization as the basis of the “plastic age”, or without reduction of acid rain by catalytic purification of exhaust gases from cars and factories. The fact that over 80% of all chemicals produced by industry see a catalyst at least once in their life cycle is another illustration for the importance of this field that can hardly be overestimated.

Ever since its foundation, the Kaiser-Wilhelm/Max-Planck-Society was heavily engaged in catalysis research. This commitment paid extraordinary dividends for society (Ziegler polymerization, Fischer-Tropsch coal liquefaction etc.) and won several leading scientists of the KWG/MPG the Nobel Prize. In view of this legacy, however, one might assume that catalysis research must have become a mature discipline and hence be tempted to ask if a long-term strategic commitment remains justified.

Catalysis is a process-integrated way to save energy, reduce waste, and secure unrivalled levels of selectivity and productivity. Therefore it is more timely than ever and its importance is likely to grow even further. At the same time, catalysis research has entered a new phase, marking the end of an era dominated by trial and error. Analytical tools of ever increasing sophistication and the rapidly growing power of computational methods not only allow us to gain detailed insights into the basic principles but also to understand real catalysts under real (rather than model) conditions. Catalysis defines a molecular frontier of science, at which the traditional borders between “heterogeneous”, “homogeneous” and “bio” become increasingly irrelevant. However, a description of all traditional branches of catalysis within the framework of a single coherent theory still challenges contemporary quantum physics and computational chemistry and will drive the development of ever more advanced spectroscopic techniques in the foreseeable future.

Despite much progress, the exact description of real catalyst systems at the molecular level remains the exception rather than the rule. First, catalysis is all about rates which are inherently difficult to predict. Moreover, the selectivity observed in a catalytic process results from the *difference* between the rates of two (or more) competing processes, whereby only a few kilocalories per mol may lie between success and disastrous failure. To predict such small numbers in absolute terms with the necessary level of accuracy for systems as intricate as proteins, ribozymes, irregular mixed-metal oxide surfaces or open-shell metal complexes still needs to be mastered. The challenges are further increased by complex equilibria before and/or after the actual catalytic event, by the intricate dynamic properties of the catalysts themselves, as well as by still poorly understood solvent effects. Despite these many complications, computational catalysis research has been one of the fastest growing sub-disciplines, with tremendous advances both in first-principles and multi-scale methods designed to meet these challenges. The development of ever more accurate methods and effective algorithms coupled with rapidly increasing computation power forecasts a bright future for this field. Yet, experimentation will never get replaced. Advanced levels of automatization, combinatorial synthesis, high throughput experimentation and improved reactor design are about to increase the hit rate in catalyst discovery and optimization. Because this type of research requires a long time frame, needs expensive equipment and is particularly labour intense, it fits well into the agenda of the MPG.

It may not come as a surprise that biology has become a major source of inspiration for catalysis research. In a living cell, nature exercises many catalytic processes in a highly orchestrated manner, resulting in complex feedback loops and cybernetic networks. Nature

implements the necessary compartmentalization of chemically opposing catalysts in a masterful way and has devised exceedingly clever solutions for switching its catalysts on and off. Despite the much larger arsenal of solvents and conditions at the chemist's disposal, we are not anywhere close at achieving such "systemic" goals. Likewise, the emulation of nature's inexorable force of evolution for the optimization of biocatalysts in the test tube has just started to emerge and will almost certainly gain tremendous importance in the future. Furthermore, the power of genomics increasingly allows the metabolism of a living cell to be "re-programmed" towards the production of predefined but non-natural chemical entities. Such exercises at the chemistry/biology interface can power the quest for novel drug candidates as well as the benign production of fine chemicals.

However, chemists do not only learn from nature but also start to challenge it. One may ask, for example, if an entire protein is really necessary to secure high levels of activity and selectivity. The vibrant field of "organocatalysis" provides intriguingly simple answers to such tantalizing questions by using small, cheap and readily available organic molecules as effective alternatives to biopolymers. Can these entities also be endowed with other desirable attributes of biocatalysts such as allosteric control or molecular switching? In any case, the now rapidly growing field of organocatalysis was recognized as a new frontier only during the last decade. Its sudden emergence showcases that even the traditional portfolio of catalysis research still needs to be revisited.

A good catalyst must survive many process cycles, which may explain why the intrinsically stable noble metals play such important roles in heterogeneous and homogeneous catalysis alike. In striking contrast, nature in its bioinorganic branch is noble-metal free, yet has evolved catalysts of undisputed and often unrivalled selectivity. Will the increased understanding of the basic principles allow us to find alternatives to the dominant noble metals, which are cheap, benign, robust, practical and ultimately even industrially viable?

The recognition of the catalytic properties of metal- or metal oxide surfaces marked one of the beginnings of this field. It remains a prime objective of surface science to unravel the secrets surrounding the elementary processes of adsorption, activation and desorption of the reactants and products by a solid matrix; to this end, the analytical and spectroscopic toolbox needs constant expansion and refinement. Especially methods which are able to look into the catalytic process under reaction conditions are urgently needed, since the catalyst prior or after reaction may differ substantially from the real active species. Defect sites play a decisive role as active centers in redox- and acid/base-catalysis alike. How do we properly characterize imperfections? Even more challenging, how can defects be tailor-made to optimize the

properties of a solid catalyst? In addition to the surface aspects, other questions such as the correlations between activity and size need further scrutiny. Why do clusters perform differently than bulk materials in certain cases? What are the catalytic properties of, for example, nano-structured surfaces or inorganic/organic hybrid materials that can now be tailor-made with molecular precision? Such materials offer great opportunities to control the different “scales” relevant for a solid catalyst beyond the active center, such as the surrounding shells, the porous network of the solid and its bulk properties.

As the world that surrounds us is “chiral”, chemists had to learn how to distinguish between molecules that are nothing but the mirror images of each other (“enantiomers”). Although the concept of ligand design in homogeneous catalysis was tremendously successful in this regard, many reactions still lack useful asymmetric versions. New paradigms for ligand design are urgently needed that provide more opportunities for fine tuning and combinatorial synthesis. Moreover, one may ask if the inherently more process-friendly heterogeneous catalysis will also be able to come up with similarly successful asymmetric transformations. Encouraging examples do exist but are still rare; it remains to be explored if there is a continent in front of us which is wide open for basic research and discovery.

Catalysts are indispensable for material science. Catalytic polymerization is just one prominent example, which is driven by society’s never-ending demand for high performance materials. New catalyst design, however, will be necessary to allow the use of highly functionalized monomers. The use and catalytic transformation of renewable raw materials, which are often over-functionalized by nature, is a formidable challenge yet to be solved in the context of a likely changing feedstock base.

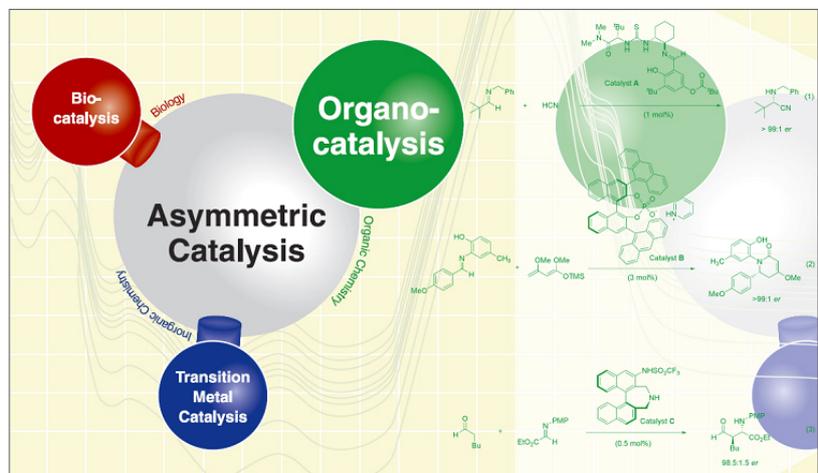
The production of pharmaceuticals also provides unique opportunities for further growth. As it stands today, the traditional production of active drug ingredients produces many more kilograms of waste per kilogram of product than, for example, the petrochemical industry. The chemistry needed in the life sciences is extremely diverse and the synthetic routes usually consist of many steps. Therefore, this area can provide a particularly strong stimulus for innovation, as catalysis research will not come to an end before each and every transformation can be performed in a catalytic rather than stoichiometric fashion. A look into the textbooks suffices to show that there is room for innovation for generations of chemists to come. Improved reaction design must then help to translate such new solutions into economically viable processes.

On the other extreme, catalysis remains confronted with the activation of the least reactive molecules one can think of. Nitrogen fixation beyond the Haber-Bosch process, the catalytic

fixation of carbon dioxide, the catalytic splitting of water, or the selective activation of C-H bonds without over-oxidizing of the hydrocarbon source represent grand challenges for basic research with potentially enormous ramifications for society. A detailed understanding at the molecular level for the catalysts which nature has evolved to perform such demanding transformation may provide valuable guidance.

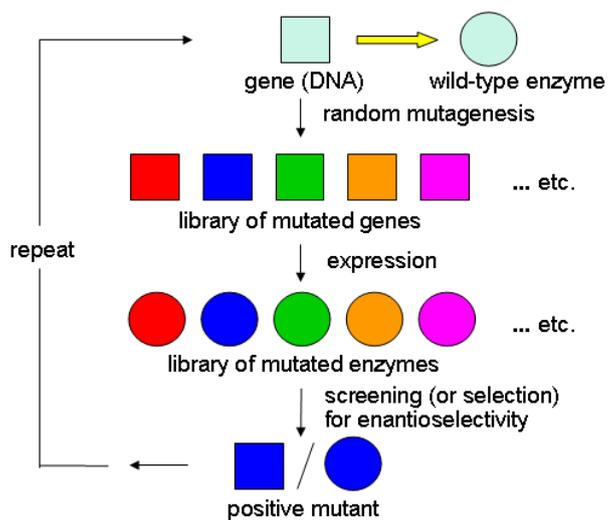
Most of the successful implementations of catalysis into industrial practice during the 20th century have been “large scale” operations for the production of commodities and fine chemicals. In order to meet the increasing environmental challenges, “down-sizing” exercises will be necessary that allow the inherent advantages of catalysis to be exploited in much smaller and non-traditional “reactors”, as e. g. in chromatographic and membrane reactors. Catalysis for fuel cells and batteries, or light harvesting devices might spearhead this development.

Future directions: Catalysis research continues to unravel the secrets surrounding the elementary processes, and at the same time, tries to understand real catalysts under real (rather than model) conditions, independent of whether these catalysts are organic or inorganic compounds, solid materials or biological entities. These lines of research provide the driving force for the development of novel analytical tools of ever increasing sophistication and inspire advances in theory and computational methods. In parallel, combinatorial synthesis, high throughput experimentation and improved reactor design will gain tremendous importance for the experimentalists. Attempts to reach more “systemic” goals will gain importance, which may either be accomplished by emulating nature’s concepts in the test tube, by reprogramming the metabolism of living cells towards the production of non-natural chemical entities, or by the “de novo” design of artificial catalysts, catalyst ensembles or multifunctional materials. A changing feedstock base will increasingly force catalysis to address renewable, yet over-functionalized raw materials. In parallel, catalysis will almost certainly conquer the “high end” chemistry that enables innovations in the life sciences and medicine. Yet another grand challenge is the catalytic activation of highly unreactive bonds, if possible, without recourse to noble metals, which still dominate significant parts of (applied) catalysis today. Whereas the last century was dominated by large scale operations, innovative reactor design should allow for more decentralized applications of catalysis in small devices; this development will not only impact on chemistry proper but also profoundly change energy production and –conversion (fuel cells, batteries, light harvesting devices etc.).

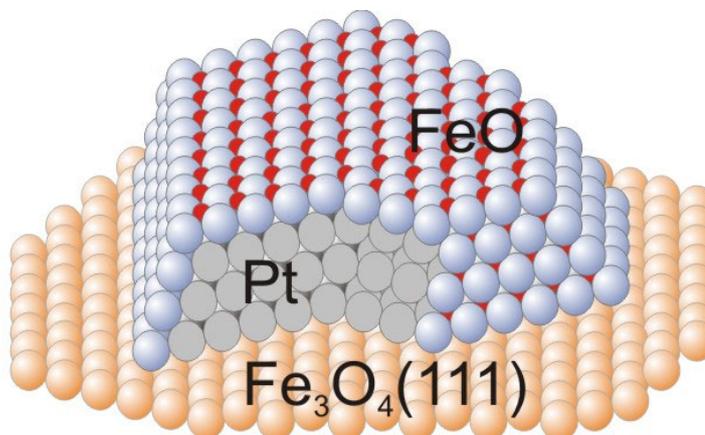
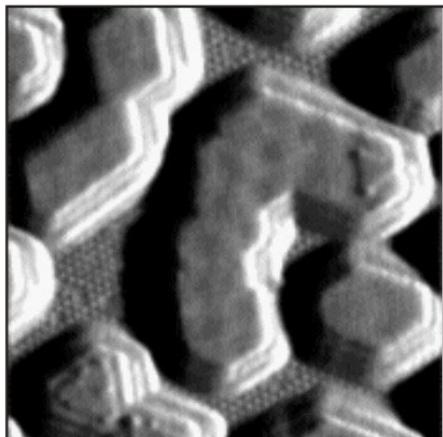


It was only during the last decade that organocatalysis was recognized as a general principle and hence as an additional branch of asymmetric catalysis, rivalling and complementing the more established fields of biocatalysis and transition metal catalysis.

Creation of Catalysts by Laboratory Evolution



Basic concept of the directed evolution of biocatalysts in the test tube



Scanning tunnelling microscopy (STM) image of Pt particles supported on a thin, crystalline Fe₃O₄(111) film. The scheme illustrates the atomic structure of the well faceted Pt particles encapsulated by an ultra-thin FeO film as a result of strong metal-support interaction. The Moiré superstructure between the FeO(111) and the Pt(111) lattices is most clearly seen on the top facets of the largest particles. The encapsulated particles showed much higher activity in the low temperature CO oxidation reaction as compared to the clean Pt particles. These unexpected results may have strong impact on a rational design of metal catalysts through promotional effects of ultra-thin oxide layers on reactivity of metal nanoparticles supported on reducible oxides.

Selected References:

W. Lubitz, E. J. Reijerse, J. Messinger: Solar water-splitting into H₂ and O₂: design principles of photosystem II and hydrogenases. *Energy Environ. Sci.* 2008, 1, 15-31.

H. M. Senn, W. Thiel: QM/MM Methods for Biomolecular Systems. *Angew. Chem. Int. Ed.* 2009, 48, 1198-1229.

M. T. Reetz: Directed Evolution of Enantioselective Enzymes: An Unconventional Approach to Asymmetric Catalysis in Organic Chemistry. *J. Org. Chem.* 2009, 74, 5767-5778.

J. Kirby, J. D. Keasling: Biosynthesis of Plant Isoprenoids: Perspectives for Microbial Engineering. *Annu. Rev. Plant Biol.* 2009, 60, 335-355.

B. List, J. W. Yang: The Organic Approach to Asymmetric Catalysis. *Science* 2006, 313 (5793), 1584-1586.

B. D. Sherry, A. Fürstner: The Promise and Challenge of Iron Catalyzed Cross Coupling. *Acc. Chem. Res.* 2008, 41, 1500-1511.

H.-J. Freund, G. Pacchioni: Oxide Ultra-thin Films on Metals: New Materials for the Design of Supported Metal Catalysts, *Chem. Soc. Rev.* 2008, 37, 2224-2242.

H.-J. Freund: Clusters and Islands on Oxides: From Catalysis via Electronics and Magnetism to Optics, *Surf. Sci* 2002, 500, 271-299.

A. Seidel-Morgenstern, Analysis and experimental investigation of catalytic membrane reactors, in "Integrated Chemical Processes Synthesis, Operation, Analysis, and Control" (K. Sundmacher, A. Kienle, A. Seidel-Morgenstern, Eds.), Wiley-VCH, 2005, p. 359-389.