

# FUTURE PERSPECTIVES IN CATALYSIS

NRSC-Catalysis

Dutch National Research School  
Combination  
Catalysis Controlled by  
Chemical Design



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## PREFACE

### A tipping point in catalysis research

Catalysis is the quiet force behind the modernization of our chemical industry. It ensures more efficient use of finite natural resources, it helps prevent waste and air pollution, and it makes our industry safer.

In the past century, catalysis became the basis of large-scale processes in bulk chemistry and petrochemistry. But shifting demands and new environmental challenges require new catalytic solutions. Changes in our energy economy have driven a growing demand for gas and coal, presenting new challenges for catalytic technology in areas such as liquefaction. In addition, catalysis is also increasingly applied in smaller systems and devices, such as fuel cells and batteries. There are also tremendous new developments in the application of catalysis for fine chemicals and pharmaceuticals. This brings new challenges to the field and increases the possibilities for greater efficiency and sustainability of such systems.

Catalysis research has entered a new phase, marking the end of an era characterized primarily by trial and error. The past 20 years have provided us with a solid scientific foundation, bringing directed design of catalysts within reach. Scientists have found a common molecular basis for the chemical processes for which catalysis is used. These research fields have now been unified to form a general scientific framework. That means heterogeneous, homogeneous and bio-catalysis can now be studied within a single coherent theory, using similar molecular modeling techniques. Significant progress has also been made in molecular chemical synthesis methods, enabling the production of catalysts with high molecular precision. Many new systems have been developed in laboratories and are awaiting further exploration. However, for many catalytic systems we are far removed from designing catalysts without an experimental laboratory. The systems are still too complex to predict their behavior with sufficient precision. The challenge for the coming decade is to unravel the underlying complexity and hence improve the design process.

The Netherlands has invested heavily in catalysis research, such as that conducted by the NRSC Catalysis program, which recently celebrated its tenth anniversary. This has brought about a coherent research community that is ranked among the world leaders in the field. Talented young scientists were able to develop towards key positions in research. Having

completed ten years of research within the NRSC Catalysis program, we are now on the verge of a tipping point in the Catalysis-Science-Development Curve.

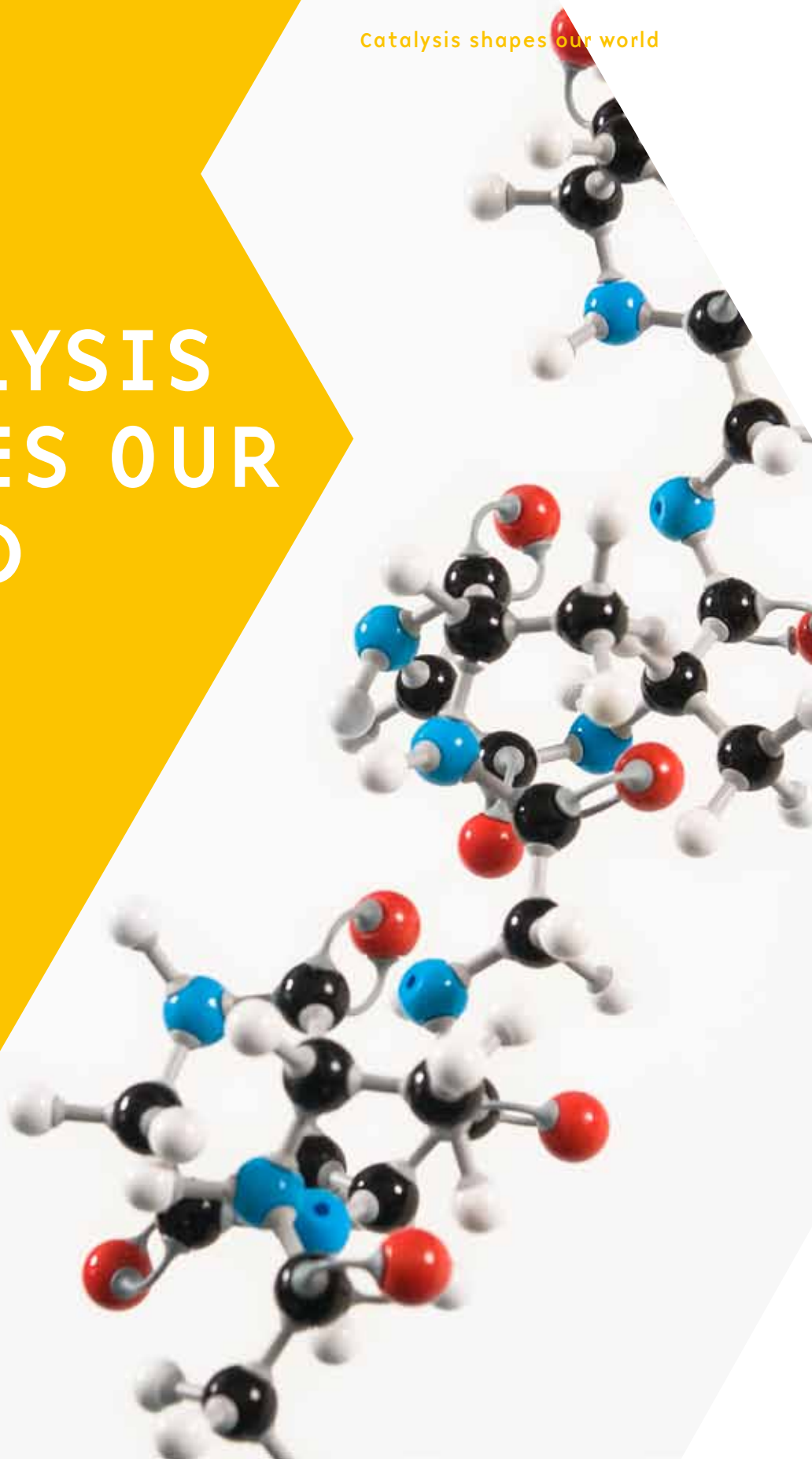
To master the complexity of catalytic systems, it is necessary to explore new fundamental approaches to current catalytic systems. This is a key strategic objective of the Dutch National Research School Combination Catalysis Controlled by Chemical Design (NRSC Catalysis) for the 2009-2013 period. To achieve this objective, it is necessary to bring together experienced scientists, who are acknowledged experts in their respective disciplines, which need not necessarily be directly related to catalysis. By working in close cooperation, we believe it is possible to generate innovative breakthroughs that may lead to novel catalytic systems.

Many fundamental and practical barriers have been surmounted thanks to the intensification of research. Now our research community should head towards the challenges of the 21st century, in which we are faced with the depletion of natural resources and the limits of environmental stamina.

This publication considers new challenges in catalysis research. Based on numerous visits and intensive discussions with key Dutch catalysis research groups, we gained insight into the most important scientific challenges for the coming ten years. This provided the foundation for this report, in which we put forward an agenda for new research.

“Towards integration of different catalytic components and the design and study of complex catalytic systems” – that is the key theme of the 2009-2013 research program.

# CATALYSIS SHAPES OUR WORLD



## CATALYSIS FACILITATES CHEMICAL REACTIONS

The catalytic converters in our cars are like small chemical plants that process noxious exhaust fumes. The “cat” splits noxious nitrogen oxides to form harmless nitrogen and oxygen molecules. At the same time, incompletely burned fuel components are processed. These chemical reactions normally occur at high temperatures, which would make it prohibitive to proceed in the car exhaust pipe. But platinum, one of the catalytic agents in the catalyst, serves as a moderator facilitating chemical reactions, so that they can take place at lower temperatures.

Just like a real chemical plant, a system of sensors in the catalytic device, together with special electronics, controls the process conditions. This system adjusts engine function, so that exhaust fumes have the best possible composition and the catalyst operates under optimum chemical conditions.

### How?

Here’s how it works. When molecules collide with the platinum particle, some of them may stick to the surface. This is because chemical bonds form between the molecule and platinum. As soon as a molecule adheres to the platinum, other bonds within the molecules become weaker. That’s what chemists are after, because this makes it easier to break the molecule up into its constituent parts. This facilitates chemical reactions. In short, a catalyst changes the structure of molecules, thus facilitating the making and breaking of chemical bonds.

But let’s not oversimplify the process. In reality, a complex sequence of different configurations and actions often occurs, which facilitates a specific chemical reaction, while the catalyst remains unchanged. In the past decade, experts devoted much of their research to unraveling the chain of events in a catalytic action. Better insight into such processes makes it possible to design better catalysts for specific chemical reactions.

Since the introduction of catalysts on car exhausts in the 1970s, noxious emissions causing acid rain have been reduced substantially. All sorts of catalysts are also used in other industries, facilitating chemical processes and reducing noxious emissions. Nowadays, catalysts are applied in the production of fuels, plastics, and pharmaceuticals. Catalysts are at the heart of nearly every chemical process.

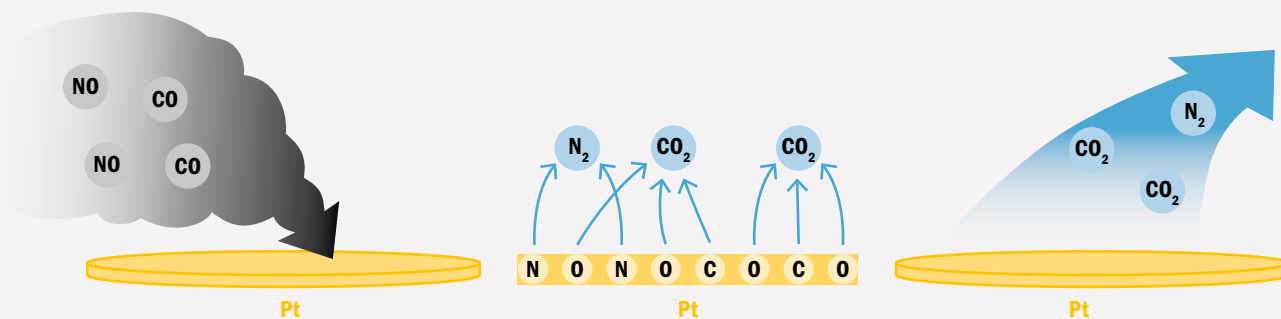
### A little does a lot

It is important to understand that catalysts aren’t altered by chemical reactions. The platinum in a car catalyst can repeat its action over and over again. That means that you only need a small amount of platinum to process huge volumes of exhaust fumes. This makes catalysts so valuable for the industry and in the protection of our environment. Small quantities can do a tremendous amount of work.

But catalysts don't perform magic. They don't create reactions that are otherwise impossible. They simply facilitate existing reactions. It's like a walk in the mountains. The path to a neighboring valley may lead over a hill. But catalysts are like the local guide, who shows you an old, unused railway tunnel, so that you can avoid a tiring climb. The guide makes it easier to reach the other valley. Chemists would say that catalysts don't change the thermodynamics (i.e. the outcome), they only change the kinetics (which comes from the Greek "motion towards").

In our hiking metaphor, the mountains stand for the energy barriers that have to be overcome in a chemical reaction. By avoiding the hilltops, catalysts can save enormous amounts of energy. But catalysts can also help us to avoid waste. In many industrial processes, different reactions occur at the same time, some are desirable, while others give undesirable byproducts. As catalysts favor one reaction over others, the amount of waste is reduced. This selectivity means that catalysts improve the yield of a process. And by decreasing the quantity of byproducts, they usually also make it easier to separate the product from unwanted waste.

In short, catalysts help us to effect chemical reactions in the most efficient, economical, and environmentally responsible manner.



#### CATALYTIC CONVERTERS IN CARS

Vehicle catalysts help to convert poisonous carbon monoxide (CO) and environmentally harmful nitrogen oxides (NO<sub>x</sub>) into carbon dioxide (CO<sub>2</sub>) and nitrogen (N<sub>2</sub>) by oxidation and reduction.

At the same time, incompletely burned fuel components are processed. The platinum and the noble metals that constitute the catalyst are not altered by these chemical reactions. That's why a catalyst in a car can repeat its action over and over again.

## Multiple forms

Catalysts come in different forms – as a gas, a liquid, or a solid. This makes no difference for the mechanism of influencing the making and breaking of chemical bonds. But there are practical differences. A solid catalyst can be contained in a pipe, so that the reactants can flow through it. This is perfect for a continuous process, that proceeds as long as new feedstock is pumped into the pipe. A liquid or a gaseous catalyst cannot be separated as



easily and hence is more difficult to apply in a continuous process. Because of this practical difference, chemists have long made a distinction between heterogeneous catalysis (where a solid catalyst is involved) and homogeneous catalysis (involving other forms). As the molecular processes involved in heterogeneous and homogeneous catalysis were better understood, experts in these two fields began to realize that they are not so different after all. One of the great achievements of the past decade is that these two fields of chemistry have merged. Experts have found common tools to study reactions and now share a common understanding of the molecular foundations of catalysis. This facilitates more rapid progress.

A good catalyst is stable enough to survive many process cycles. That is why noble metals – that are intrinsically very stable – are so popular in catalyst design. However, the materials required are often costly. Platinum costs €40,000 per kilogram, and the price is increasing. Cheaper metals also perform well in certain reactions. In 1927, two Dutch entrepreneurs started to use nickel to make fat out of oil in their newly formed company Margarine Unie, which later evolved into the multinational Unilever. There are also other popular materials, like *zeolites*, which are micro-porous structures that are often made of silicon, aluminum, and oxygen. *Zeolites* are widely used to increase the octane rating of gasoline. Many liquid catalysts are based on organic molecules that have a metal atom. Organic molecules bound to a metal allow endless variations of the catalyst, making it possible to fine-tune them to specific reactions.

The last decade has seen a myriad of new substances that are considered potential catalysts. For instance, so-called metallic-organic-frameworks (MOFs) have been tested in endless variations. These materials are interesting, because of the extent to which they may be varied, offering ample opportunities to find a catalyst that suits a specific reaction. Unfortunately, none of these MOFs have proved to be useful catalysts yet, but the exploration of new terrain often requires great patience.

Maybe the most promising inspiration for new catalysts comes from biology. Chemists are cooperating closely with biologists to discover how nature synthesizes materials, in many cases using enzymes as catalysts. In the past decade, they have made great progress in unraveling nature's chemistry. This has resulted in catalysts that play an integral part in the production of pharmaceuticals and food.

### ZEOLITES

Zeolites are minerals with regular microscopic pores and cavities of the same sizes as molecules. This gives the zeolites a large effective surface, concentrated in a small volume. It is ideal for solid catalysts that require a large contact area. The porous structure can accommodate a wide variety of molecules. The confine-

ment in small spaces enables control of reactions that go with structural changes, which makes them uniquely selective. Since they are solid acids, they can catalyze reactions at high temperatures. Synthetic zeolites are widely used as catalysts in the petrochemical industry, for instance in fluid catalytic cracking and hydro-cracking. In these reactions

heavy molecules are broken down into smaller molecules useful as fuel and hydrocarbons are converted into branched molecules that can replace benzene in gasoline. Application of zeolites has dramatically improved the efficiency of these processes by suppression of undesirable coke formation

Finding a good catalyst has never been easy. Some substances, like platinum alloys, are rather unspecific, and may facilitate a host of different reactions. Others have a specific structure that only works on a limited range of molecules, but they are highly selective. Finding good catalysts involves sound knowledge of chemical mechanisms, a bit of luck, and a patient fine-tuning of its properties to the desired process. The last decade has seen impressive progress towards rationalizing and accelerating catalysis discovery. Tools have been developed to automate experiments, to observe the chemical reactions involved and to understand the reaction mechanisms. The next decade will see a much more elaborate toolkit to design catalysts to the benefit of our environment and industry.

## Historical development

In the 1830s, the Swedish scientist Jöns Jakob Berzelius was the first to discover that catalysts may influence a reaction as an agent that itself remains unchanged: “Several bodies exercise on other bodies an action very different from chemical affinity. They produce decompositions of their elements and different recombinations of these same elements, to which they remain indifferent.”

Catalysts had in fact been used in laboratories before that time, for instance by the Dutch chemist Martinus van Marum, who observed the dehydrogenation of alcohol on metal catalysts. But Berzelius was the first to recognize that the metal was not simply a source of heat, but that it had a very special, unknown effect. He proposed the existence of a new force which he called the “catalytic force.”

Thirty years later, the British physicist and chemist Michael Faraday discovered that this effect takes place on the surface of the catalyst. He demonstrated the ability of platinum to recombine hydrogen and oxygen. Towards the turn of the century, the Riga-born German chemist Wilhelm Ostwald discovered that catalysts only influence the rate of a reaction, not its final outcome. By that time, the molecular view of matter had become accepted, but there was no idea how catalysts worked.

As is often the case in scientific development, war sparked rapid progress in the application of catalysts. Around 1900, German chemistry shifted gear when it risked being cut off from the supply of natural saltpeter, a key ingredient of dynamite. It was primarily imported from Chile, where the substance was extracted from the thick layers of bird droppings or guano that accumulate on the country's cliff faces. The stakes were high, as a shortage of saltpeter could threaten munitions supply. This prompted a major research effort. A catalytic process to synthesize ammonia was quickly developed. The process was then scaled up and, just before the outbreak of the First World War, Germany opened the world's first nitrate plant.

The overall project was crowned with three Nobel Prizes – one each for Fritz Haber, Wilhelm Ostwald and Carl Bosch, who are among the founding fathers of modern chemistry. Later, the non-military application of nitrogen made it to one of the most important chemical processes in industry, because nitrates also form the basis for fertilizer production. This fundamentally changed agriculture and proved to be a blessing for humanity.

It was also launched a quest to research and understand the underlying process. In 2007, the German scientist Gerhard Ertl was awarded the Nobel Prize for Chemistry for unraveling the mechanisms of the *Haber-Bosch process*. In the 1960s, he began using the equipment used in the burgeoning semiconductor industry to analyze what happens on the surface of a catalyst. With advanced high-vacuum experimental equipment, he observed the behavior of individual layers of atoms and molecules on extremely pure surfaces. Ertl created a methodology with various complementary experiments, that can provide a complete picture of a catalyst reaction. This was an important turning point in the understanding of catalyst action. It also shows that progress in our understanding is often slow and requires the work of successive generations of scientists.

New scientific discoveries have also been rewarded by recent Nobel prizes. New catalysts that are found are metal-organic complex molecules, that are highly selective, in a way that compares to the properties of enzymes. Yves Chauvin, Robert Grubbs, and Richard Schrock got their Nobel price for the development of the metathesis method in organic synthesis. In 2001 William Knowles, Ryoji Noyori, and Barry Sharpless received the same honour for their chirally catalyzed hydrogenation and oxidation reactions. This shows the enormous progress that has been achieved in molecular homogeneous catalysis.

The development of catalytic processes marks an important transition in the chemical industry. In the first decades of industrial development, many industries displayed behavior that is also found in newly formed ecosystems, such as land reclaimed from the sea, newly formed dunes or an island thrown up by a volcanic eruption. Such ecosystems initially develop in an aggressive way. The first species to establish themselves are ones that produce lots of seeds. These pioneering species survive in a difficult environment by multiplying rapidly and spreading to new locations. Just as locusts care little about the fields they strip bare, factories sucked up raw materials and spat out the residues without any thought to the depletion of the earth or the burden they were imposing on the environment. This behavior, so characteristic of the first phase of the industrial revolution, fortunately has now disappeared nearly everywhere in the Western world.

#### **HABER-BOSCH PROCESS**

Catalysis makes it possible to extract nitrogen from the air to produce ammonia. The so-called Haber-Bosch process uses an iron based catalyst to produce ammonia in industrial quantities. Ammonia may be converted to nitrates, that can be used to make explosives. The same process is also an important step

to produce fertilizers. This is currently the main application. Both applications had far reaching historical consequences. Humans have been fixing nitrogen faster than nature since 1980. Billions of people now depend on this process for their daily food.

During the course of the past century, industry set down roots, grew branches, and began to deploy more sustainable techniques. Scarce natural resources were replaced by manufactured chemical components. Catalysis made chemical processes more selective and hence more economical in their use of materials. It's like an ecosystem that has grown towards a complex biotope, such as those we find in an oak-beech wood or a tropical rainforest, where more species are interdependent on one another, and the waste products of one provide nutrients for another.

And so too the industrial ecosystem has developed from pure colonization to a close-knit relationship with its surroundings. Like nature, industry can use waste output as the raw material for other products, which means it is beginning to interact more economically with its environment.

Compared to natural processes our large chemical plants are significantly more efficient. Driven by the need for increased efficiency of energy and materials, factories have grown bigger and, because of the investment required, less flexible. New technologies were developed that enable efficient production in smaller plants, with substantial gains in flexibility.

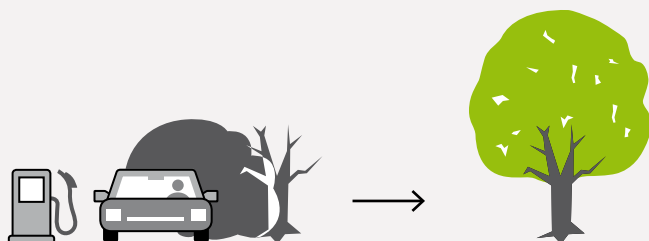
Bringing back flexibility is one of the great challenges our chemical industry now faces. And again, catalysis technology may bring this change. There is a shift in attention from process development for large plants towards the design of small integrated devices, where catalysts are used at precisely controlled conditions and ultimately may perform a variety of tasks. The smaller scale and controllability of these devices may bring about the improved flexibility required for the stable industrial ecosystems of the future.

## Catalysis for our environment and health

Catalysts have improved our environment and our quality of life. Chemical reactions controlled by catalysts have reduced emissions in modern cars, as well as waste from the chemical industry, and they have facilitated much more efficient energy conversions. On top of that, new Nobel price winning catalytic techniques have considerably improved the synthesis of pharmaceuticals.

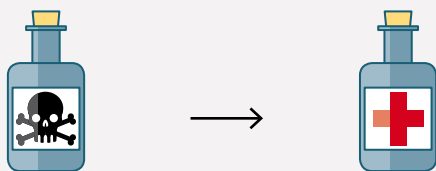
Up to now, many fine-chemical processes produce drugs that are a mixture of active and inactive agents. Many molecules exist in two varieties that are a mirror image of each other. Reactions for the production of drugs are often classical reactions, which produce both varieties in equal amounts. Our body usually accepts one variety, the other being inactive or even noxious. Often these two varieties have to be separated from each other, a costly process step, which produces a lot of waste. Developments in homogeneous catalysis make it possible to selectively produce one mirror image. This enables much more effective drugs and more efficient processes.

Our environment has also benefited from new catalytic technology. Catalytic converters in cars have had an impressive effect on the reduction of air pollution. They have cut the emission of smog-building NO<sub>x</sub> gases into the atmosphere by 90% (in kg/km). Emission of hydrocarbons was reduced by no less than 97%, while CO emissions were reduced by 96%,



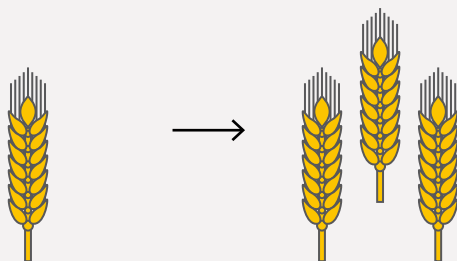
#### CLEANING THE AIR

Catalytic converters in cars have cut the emission of smog-building NO<sub>x</sub>-gases into the atmosphere by 90% (in kg/ km). Emission of hydrocarbons was even cut by 97%, while CO emissions were reduced by 96%. Cars also take advantage from catalysts in refineries, that make it possible to produce sulfur free liquid fuels, that cannot be produced directly form oil, coals or gas.



#### PURIFYING PHARMACEUTICALS

Reactions for the production of drugs often deliver a range of molecules that closely resemble each other (enantiomers). Our body usually accepts one variety, the other being inactive or even noxious. Developments in homogeneous catalysis make it possible to selectively produce one variety.



#### PROVIDING FOOD

The application of nitrogen is one of the most important chemical processes in industry, because nitrates also form the basis of fertilizer production. This fundamentally changed agriculture and made ammonia the world's most important chemical in terms of mass.

and engine performance was improved at the same time. But still there is plenty of room for improvement. New low-emission vehicles may cut residual hydrocarbon emission by 75% and will halve remaining NO<sub>x</sub> emissions.

Here's another example: silver is used as a catalyst to convert ethylene into ethylene oxide. Ethylenoxide is the chemical that produces the anti-freeze needed for driving in winter conditions. The silver promotes the desired oxidation of ethylene and thereby reduces the useless combustion of ethylene to form carbon dioxide and water. With the original catalyst, discovered around 1935, more than 50% of all ethylene was burned and tons of the greenhouse gas carbon dioxide were released into the atmosphere. With the proper catalyst and greater insight, this amount was reduced to less than 10%. Similarly, the synthesis of polyethylene has evolved around the development of several catalysts that promote ethylene polymerization at lower temperatures and pressures. Successive improvements have helped to make the production of plastic more environmentally benign. Catalysts also aid the removal of sulfur from oil. The specification of modern diesel fuel is much better than 20 years ago, thanks to improvements in catalytic processes.

Improvements of this kind are often a matter of gradually tuning process conditions and catalyst design. Another good example is the synthesis of ammonia, the world's most important chemical in terms of mass, mainly because of its role in the production of fertilizer. The foundation of the catalytic route was laid in 1913, with the Haber-Bosch process, and has basically remained unchanged. Since that time, however, the energy required for

production was reduced by 75%, mainly through the introduction of new plant design. But there is still room for improvement, because the actual energy requirements are 50% higher than the theoretical minimum.

Catalysis ensures much more efficient use of raw materials and energy, and helps us reduce waste. Catalysis also makes safer processes possible. It reduces the need to store large volumes of noxious auxiliary substances, substantially improving the safety of chemical plants. After all, it makes a big difference if only 10 liters of an agent such as chlorine is stored, rather than 10,000 liters.

Furthermore, catalytic processes allow for much greater precision, using each atom of the feedstock to make a useful product. This makes it possible to operate chemical processes on a smaller scale. This reduces the need for transportation and storage, as well as associated safety measures.

## Industrial relevance

The petroleum, chemical and pharmaceutical industries rely on catalysts to produce everything from fuel and paint to drugs and cosmetics. Catalysts are the key enabler in 90% of chemical manufacturing processes. That means catalysts are essential for a healthy economy. Catalysts enable the production of alternative fuels, they reduce harmful byproducts in manufacturing, they help keep the environment clean, prevent future pollution, and help to create safe pharmaceuticals. Catalysts constitute only a tiny fraction of the total costs incurred by the chemical industry, but their added value is substantial, because they can be used during many process cycles. They remain fundamentally unchanged, adding their value over and over again. In doing so, they are used in the production of about €1,000 billion worth of products worldwide, whereas the actual investment in catalysts is only about 1% of this amount. This multiplier effect makes it interesting to invest in the development of new catalysts. A process improvement through a better catalyst may be repeated over and over again. That helps to keep the chemical industry competitive.

Catalysis also makes many processes more environmentally benign, as mentioned previously. Cleaning up our environment has intrinsic economic value, which is usually not accounted for in current economical models. The manufacture of cleaning systems is also a growing economic activity, ranging from catalytic converters for car exhausts, via fuel cells to future photochemical systems. In more general terms, industrial activities that promote responsible and sustainable production have good growth potential. Catalysis helps increase the selectivity of chemical processes for the precise production of intermediate and fine chemical substances.

Moreover, new materials are possible thanks to catalytic chemical routes. The more precise production of polymers makes it possible to better tailor material properties to their desired use. Catalysts help produce drugs more precisely, tuning a variety of possibilities to the needs of a specific treatment. And another class of new processes is applied in the synthesis of electronic materials. These conducting polymers and chemically produced varieties of semiconductors open the door to a new generation of mass-produced electronics.



Overall catalyst market:  
10 billion EURO

Revenue generated by processes  
using catalysts: 1,000 Billion EURO

In the next decade, the chemical industry will be faced with new challenges as fossil oil reserves are depleted and climate change leads to strict regulations on the use of hydrocarbons and their release into the atmosphere. Photocatalytic processes may make sustainable forms of energy available, with catalytic devices serving as batteries for energy storage, for the production of hydrogen, or for the conversion of biomass into useable fuels. Catalysis will help us to move our economy beyond the limitations of fossil feedstock.

## Learning from nature

The increasing molecular precision of the catalysts that chemists make, start to compete with the intricate regulation of processes that one finds in living organisms. Our body manages to regulate its chemistry at moderate temperatures and under very benign conditions. This involves an enormous variety of catalysts, mostly enzymes, which are precisely tuned to a single chemical reaction. The metabolism of food, for example, involves a series of consecutive reaction steps, each with its own specific enzyme, but all in the same vessel at the same temperature.

Chemists can only dream of combining such complex processes in a single vessel. But this is how nature does it, and we are starting to learn from it. Chemists are still amazed by the precision with which enzymes in our body perform their tasks. They are still more selective and active than many industrial catalysts.

Here's an example: we still make fertilizer by way of a process involving pressure between 150 and 250 atmospheres and temperature between 300 and 550°C, requiring lots of energy (the so-called Haber-Bosch process). At present, about 2% of all energy expended goes into the production of fertilizers. World food production is probably limited by the amount of energy that we can afford to allocate to this process. In contrast, an enzyme called nitrogenase does the same at ambient temperatures, but with less overall energy efficiency as we humans. There are a few bacteria that use this enzyme and fixate nitrogen in the soil, with energy that is ultimately derived from the sun. Given the abundance of sunlight, nature has never worried about an efficient use of it.

In the subsequent step to transform nitrogen into ammonia, the industry has to operate under conditions that are unfavorable for the efficiency of this process. Nature does a much better job.

This example shows that it doesn't pay to make a carbon copy of natural processes. Instead, we should try to master the concepts that nature uses and apply this knowledge in the very different conditions that our industry uses in processes often unknown to nature. Whereas overall energy efficiency of many natural processes is not very high, the biological machinery has optimized molecular information transfer. Nature controls chemical processes on molecular scale with a degree of precision that is very difficult to emulate, but would have immense benefit.

Nature not only inspires us to make processes more eco-friendly, but also teaches us how to be very precise. There are many processes that demand greater precision. For example, we are not very precise in stringing together molecules into a long polymer to make





a certain plastic. It is extremely difficult to give all polymer strings the same structure and length. Connecting the molecules in slightly different ways changes its properties. There is only a subtle difference between the materials used to make biodegradable sandwich bags, bullet-proof cockpit doors and biocompatible artificial hips. Nature knows how to fine-tune processes of this kind. A lot of inspiration for improvement is there to be discovered.

Enzymes can often also distinguish between molecules that closely resemble each other. Many complex molecules are asymmetrical and can exist in two varieties, which are exactly the same, except that one is the mirror image of the other.

## Enzyme research

The last decade has seen a lot of research into nature's catalysts. Over 150 biocatalytic processes are now routinely applied in industry. One of the greatest challenges is to adapt natural enzymes to the needs of industry. Many natural enzymes are not very stable, they degrade quickly after a few hundred reaction steps. In our body, this is not so important. Enzymes are biodegradable and a new supply is quickly produced by other enzymes in an intricate web of interrelated chemical reactions. For industry, the stability of enzymes is a major issue, partly because they are very costly. The solution is often to use bacteria to produce the desired enzyme in abundance. This is nothing new. Since the Middle Ages, biological organisms have been used as a biocatalyst for the reduction of ketones. A more recent example is the oxidation of ketones to an ester by an enzyme that is produced by an engineered E-coli strain.

But chemists have started to adapt enzymes to the needs of industry, making them more robust in abiotic industrial environments. In a sense, chemists have more freedom than nature in designing their enzymes. Evolution has selected an extremely limited number of building blocks – primarily carbon and hydrogen – for all essential functions. Many other substances would disturb the environment in living organisms. But that doesn't stop a chemist from using different building blocks. This greater design freedom means that new properties can be added to natural catalysts. There is still plenty of scope for improvement of the fantastic designs that nature has come up with.

Chemists have different strategies for adapting enzymes to our needs. For example, they can change the structure bit by bit, to see how the properties change. In a sense, this mimics the process of natural selection in nature. By picking the outcomes that best fit the desired properties, chemists gradually evolve the enzyme into an industrial catalyst in an evolutionary process.

If we succeed in mimicking aspects of natural processes, we will take the precision and selectivity of our chemistry to an entirely new level. This will not only result in better industrial processes, but, by mimicking biological processes, we can also better understand them. And a more precise knowledge of how our bodies function at the molecular level will ultimately enable us to detect and combat illness more effectively.

# TEN YEARS OF COOPERATION IN CATALYSIS RESEARCH



## Program 1999-2008

The Dutch National Research School Combination Catalysis Controlled by Chemical Design (NRSC Catalysis) was founded in 1999 as a highly innovative research program. It brought together scientists from various key disciplines at eight Dutch universities.

The program aims to achieve fundamental progress in the field of catalysis. It is a long-term effort to extend the boundaries of our knowledge.

Looking back, the progress made during the course of this program has been remarkable. Knowledge about homogeneous and heterogeneous catalysis has been brought together in a common framework, enabling scientists in both fields to better understand and design catalytic reactions. There was once a divide between the fields of homogeneous and heterogeneous catalysis. Scientists in both fields developed their own understanding, tools, and applications. This gap has been closed. Scientists now share a common scientific language, theoretical description, and tools. This has greatly accelerated the pace of progress.

Great progress has also been made in the field of biocatalysis in the past ten years. The subtle processes found in nature inspired a whole new generation of chemists. Bit by bit they unraveled the intricate web of reactions that keep us alive. This produced clues on how to design completely new supramolecular systems and catalytic routes. Supramolecular systems, hybrid organo-inorganic materials, and chemically modified biocatalysts with completely new properties have been developed. In heterogeneous catalysis, advanced spectroscopic techniques and new insights in the synthesis of nano-size controlled particles have generated new systems for Fischer-Tropsch type processes that are essential for converting fossil and non-fossil raw materials to liquid fuel, as well as for hydrogen storage. Sophisticated spectroscopic tools have been developed that allow the gathering of molecular information under practical conditions of the catalytic reaction, generating new options for process intensification.

Another exciting development involves molecular systems that induce motion or self healing of technically important materials. Many of them will be reviewed in latter section of this publication.

The great advance in the science of heterogenous inorganic material based catalysis is the understanding of the great variety in reactivity of such materials. Whereas on average the composition of such materials will be the same, their chemical reactivity will closely depend on sometimes rather unique structures that can form on the surface of such materials. In order to develop useful correlations between different catalysts, one has to be able to identify such sites. They can only be explored on a molecular level. This has only recently become possible. It implies a step change in catalysis science, which also dramatically improves the efficiency of practical research.

These accomplishments were made possible by the growing scale of fundamental research, a process initiated ten years ago. At that time, there was a growing awareness that new developments in molecular chemistry would demand more intensive and cooperative research. Only a true multidisciplinary approach would make it possible to advance our understanding of the dynamics of complex chemical transformations and the design of

complex new catalytic systems. An extra effort was thought necessary to meet the challenge of a sustainable society in the next century.

One of the guiding principles of the research program is that we need to work towards a society that uses its resources in a sustainable manner. New chemical transformations under eco-friendly conditions will contribute to achieving this goal. And indeed, the NRSC Catalysis program has generated a wide array of improved reactions, with higher yields, under more benign conditions, as well as products that are better reusable or degradable.

The NRSC Catalysis program is committed to fundamental research for the long term, with a horizon that extends beyond the scope of industry. That is why there was no direct participation of industry in the program. There were and are other research programs in the Netherlands that are more suitable for industrial cooperation, such as the IOP Catalysis program, that was then initiated and funded by the Dutch Ministry of Economic Affairs.

Only the best chemists in the country were invited to participate in the NRSC Catalysis program, those with the highest rating in the latest review of Dutch research. In so doing, the program brought together scientists from different fields of chemistry, with expertise in homogeneous and heterogeneous catalysis, as well as spectroscopy. At a later stage, bio-inspired catalysis was integrated in the program, and electrocatalysis has now also been incorporated. The approaches are both experimental and computational. Much emphasis is placed on the detailed understanding of the mechanism of chemical transformations and catalyst synthesis by way of theoretical analysis and computer modeling.

The incorporation of spectroscopy expertise into the program made it possible to view catalytic reactions as they happen.

New chemistry has been developed at the interphase of supramolecular, bio, and inorganic chemistry. This has resulted in the design of complex biomimicking catalytic systems, with motion-controlled drug release and information transfer.

NRSC Catalysis program is part of a longer research tradition in the Netherlands. The Dutch School of Catalysis, which focuses on the molecular basis of heterogeneous catalysis, has for decades been internationally recognized for its outstanding research. The 1990s saw the formation of the Netherlands Catalysis Foundation in Eindhoven. In 1992, the Netherlands Institute for Catalysis Research (NIOK) was established, which studies the integration of heterogeneous and homogenous catalysis, biocatalysis, and reactor engineering. The NRSC Catalysis program is an initiative involving the following research schools:

- Netherlands Institute of Catalysis Research (NIOK, [www.niok.nl](http://www.niok.nl))
- Holland Research School of Molecular Sciences (HRSMC, [www.hrsmc.nl](http://www.hrsmc.nl)).
- Dutch Polymer Institute (DPI, [www.polymers.nl](http://www.polymers.nl))

NRSC Catalysis is one of the top six research schools selected by the Netherlands Organization for Scientific Research (NWO) in 1998. The program is co-funded by the Netherlands Ministry of Education, Culture & Sciences as part of its “In-depth” Strategy Research Program. This fund supports a limited number of research schools that meet high inter-

national standards. In 2006, the Minister decided to extend financial support to cover the 2009-2013 period.

A total of about 250 scientific staff members are involved in the groups participating in NRSC Catalysis. The long-term commitment of the NRSC Catalysis makes it possible for them to start projects that may only bear fruit in the long run. The budget for the 1999-2008 period is € 33.6 million, on top of the existing university budgets of the participating groups. This is largely spent for PhD projects and post-doc positions. During 2007, a total of 50 staff members were on the program payroll. Ten percent of the budget was reserved to reward new, unforeseen insight gained during the course of the program.

The NRSC Catalysis has an expert international supervisory board, that is mainly responsible for the quality control of the program.

Now that the program has been extended for the coming five years, it is time to assess the challenges that we face in the coming decade.

# NEW CHALLENGES



## CATALYST DESIGN

“Give me a reaction and I’ll tell you which catalyst you should use” – many chemists would love to say these words. It would be ideal to have a good catalyst for every chemical process we wished to employ. But catalytic materials and processes cannot be designed from the scientist’s desk at present. Finding the right catalyst has many elements of trial and error. We still have no way of knowing beforehand which materials will be good catalysts for a reaction.

The process of trial and error has even been rationalized in robotized labs. It resulted in sophisticated devices that test tens or hundreds of process conditions in parallel, with integrated precision analysis of reaction products, and computer logic that decides how to best make the next guesses. These so-called screening devices are now a common tool for chemical engineers. They are constantly being perfected, for instance with selection rules based on Darwinian logic. New control technology gives these automated labs an unprecedented throughput. But it remains trial and error.

Computational technology is now on the brink of predicting catalytic behavior, thus enabling more directed experimentation, with a view to ultimately producing computational tools that may completely replace trial and error. This will be combined with validation using spectroscopy, enabling us to study complex chemistry as it happens.

Computer modeling of catalytic processes is difficult because of the different processes taking place at many levels of scale. Atomic interactions lasting picoseconds on a scale of nanometers have the same relevance as flows that take seconds on a centimeter scale, and everything in between. Computational catalysis has emerged from the confluence of many different computational methods and the advent of high-performance computers. But this is only the beginning. The ultimate goal of gaining fundamental insight into the mechanisms of catalysis can only be achieved by breakthroughs in theoretical insight and computational methods.

Further insight into catalysis is also expected from the incredible control that has been gained in the synthesis of catalytic materials. For many materials, atomic precision is within reach. For flat (two-dimensional) structures, chemists have learned a lot from processes in nano-electronics. For extended (three-dimensional) materials, new principles of self-organization have to be used to achieve this precision.

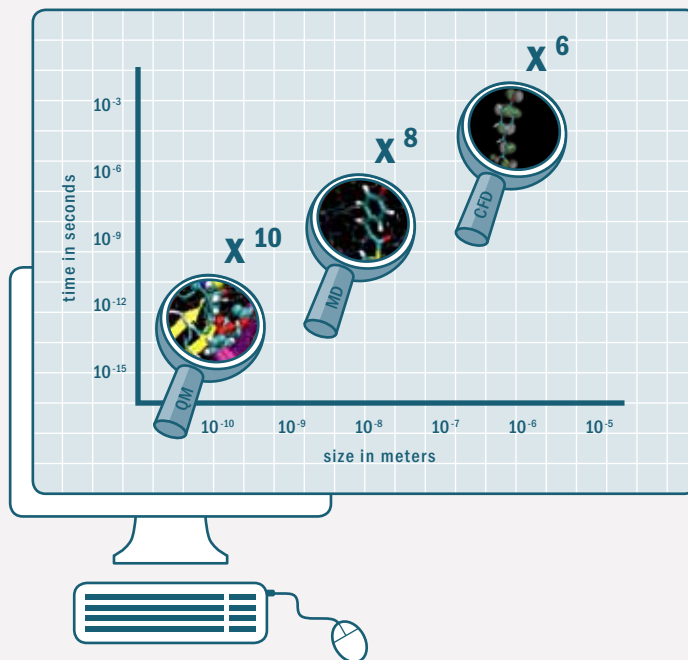
This greater precision makes it possible to study catalytic processes in a systematic way. Because catalysis takes place at an atomic scale, the catalytic materials must be controlled at an atomic scale in order to study their catalytic action. This high accuracy makes it possible to better test computational models.

The development of computational technology will also benefit from the availability of large bodies of experimental data that are being generated in ever-increasing detail. New spectroscopic instrumentation allows precise observation of ultra-fast catalytic processes as they happen.

Knowing the precise details of catalytic mechanisms from preparation, observation and calculation will enable us to control the making and breaking of chemical bonds, to

### MULTISCALE MODELING

Catalytic reactions have important features at different scales. At the smallest level, we see the exchange of atoms between different molecules and reactions with atoms at the catalyst surface. Also larger scale processes contribute to the reactions, such as the transport of the molecules in and out of the micropores of the catalyst and exchange of heat in the catalyst. Modeling a catalytic system involves the connection of such processes that have different length and time scales. Different computational methods have to be fused to bridge the gaps in spatial and temporal scales.



make any desired molecule at practical, meaningful rates. The greater precision and better understanding also makes it possible to design catalysts that are compatible with device requirement; engineering demands that make it necessary to take different time and length scales into account. This will bring us closer to the ultimate goal of predicting the performance of real catalysts under real reaction conditions. This, in turn, will give us important tools for designing catalysts and controlling catalytic processes.

One ultimate goal is to simulate the functionality of the complex biochemical systems with their incredible control. Developments in the fields of supramolecular and metallo-organic catalysts show great promise in this regard. They can be tuned with high precision.

### From the molecular to the complex

For centuries, scientists have been trying to understand the material world by breaking it up into ever simpler parts. Chemists have been decomposing matter down into molecules and atoms. The separate elements that constitute materials can then be studied independently of one another. Recently developed techniques enable us to study those molecules individually.

This reductionist approach proved to be very powerful. We have gained in-depth understanding by analyzing phenomena at a molecular scale. All this analysis has produced a tidal wave of information. We have reached a high level of sophistication in arranging and



rearranging atoms in myriad different molecules. This simplification has enabled chemists to identify elementary transformational laws of nature and identify a host of useful chemical processes. We know how to build molecules out of atoms, or larger molecules out of smaller ones. New molecules and processes are added to our vast catalog of knowledge on a daily basis, but no truly innovative concepts are to be expected in the coming years. Organic chemists can produce every variety of molecule at will, but are often unaware how this can best be achieved. The challenge now is to produce molecules more efficiently, with less waste, under more benign conditions.

Catalysts help us produce materials in a different, more effective way. This often involves various processes working in concert, any of which can cancel or reinforce each other. As a result, there is no longer a simple relationship between the constituent elements and the behavior of the system as a whole. And we are rather clueless when it comes to interaction in larger systems. Often there are simply too many factors involved, all inter-related and all influencing each other.

Nature is often too complex for simple reductionist study. That is why we have so little understanding of the complicated chemical processes in our body. Complex interactions may also occur when using impure base materials, or when various catalytic steps are combined in a single device. Designing catalysts that adapt themselves to varying conditions also involves complex interactions.

All these systems display new properties that are only present in the system as a whole, not in the constituent components. When studying these properties, it would be useless to simply put everything together and see what happens. New approaches are required to find a balance among several mutually dependent processes in order to develop new catalysts.

Knowledge of previously ignored cofactors and feedback loops in many chemical conversions leads to considerable improvement of processes. This leads to increasingly complex catalytic systems, even for the synthesis of rather simple molecules.

The production of such systems demands immense materials skills. This was demonstrated in recent years in the production of microporous materials, with atomically defined micropores between 0.5 and 1 nm (i.e. a few atoms wide) and ordered mesoporous materials (2-10 nm). Other examples include the precise production of liquid crystal devices and the synthesis of cell-like structures, where molecules bind the walls together using a smart combination of attractive and repulsive forces.

The challenge now is to bring together many distinct scientific fields, ranging from materials science to mathematics. This should make it possible to integrate all different aspects in the study. In this so-called systems approach, components or parameters are combined rather than isolated, and functions and interactions are studied in full. The aim being to combine homogeneous, heterogeneous and biocatalysis in a truly profound manner.

The new insights will make it possible to integrate processes in practical devices, with the aid of nano-engineering and microfluids, for instance. In this approach, chemistry is no longer considered a linear sequence of feedstock, conversion, and product. The chemistry of the 21st century involves devices for energy conversion, storage, control, analysis, parallel experimentation, and interpretation, all of which are highly interrelated systems.

We are now facing the challenge of harnessing the complexity of interrelated causes. That is why the paradigm in chemistry is shifting from reduction to synthesis, with greater emphasis on interactions and systems. This approach will lead to more in-depth insight into catalytic processes, the design of novel processes and devices, and possibly, one day, to replication as life itself.

## From process to device

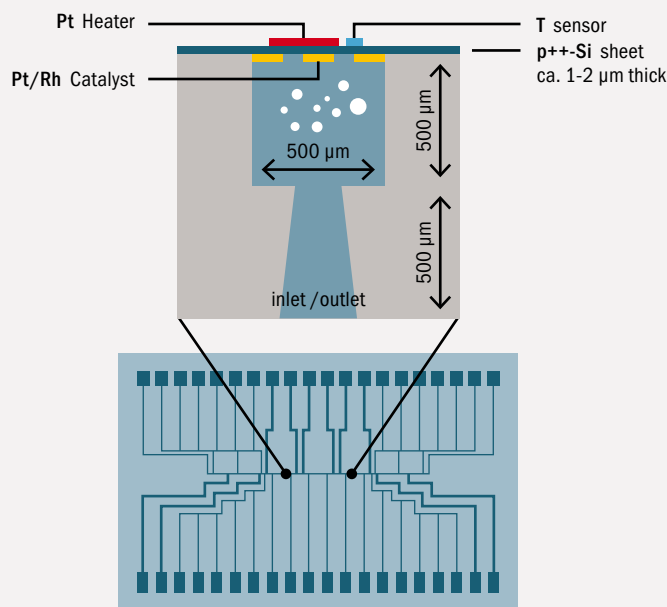
Efficient exploitation of chemical processes has always required large installations. Even the precision production of pharmaceuticals involves a large hall full of machines. That is about to change, thanks to advances in electronics, nanoprocessing, and automation.

Increased scale has long been the chemical industry's watchword, and there are compelling technical and financial reasons for this. A large vessel, for instance, is easier to insulate than a small one. The costs of investment, personnel, maintenance, administration and land use have all traditionally been lower per unit of product for a big plant.

Progress in catalysis technology has gradually eroded the underlying reasons for upscaling. Smaller scale processes are possible, where conditions are more benign, with moderate temperatures, readily available feedstock, and less need to get rid of excess heat and to process waste. Improvements in microelectronics and sensor technology make it possible to control smaller plants and devices. It is now possible to construct devices to a precision of a few micrometers. This opens up all sorts of new opportunities to downscale chemical processes and to produce materials with a nanometer precision. It is possible to miniaturize all the vessels, pipes, and distillation columns that make up a chemical plant. A lab on a chip like this is produced using the same microscopic etching techniques we find in microelectronics. It is even possible to etch small, moving structures onto a chip, such as a microscopic pump that pushes fluid through a tiny channel. So far, this approach has only been applied in laboratory equipment. The next breakthrough will be to use it in chemical production – to create a factory on the scale of a chip.

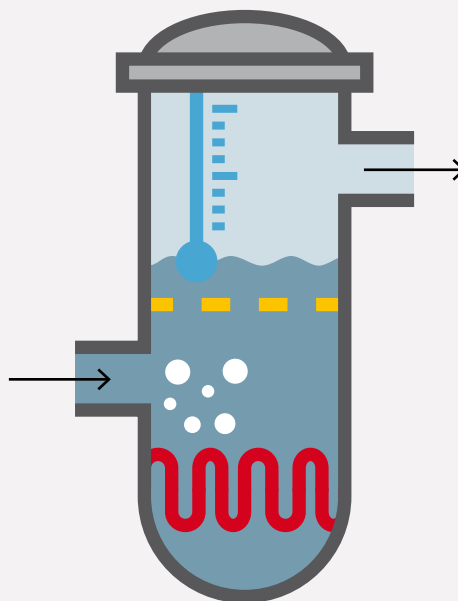
It is a great challenge to use such tiny factories on a scale suitable for production. The tiny scale of devices like this will also substantially improve regulation and control. It will be possible to introduce exactly the right amount of raw material. You can then remove the product molecules immediately, preventing further reaction and the formation of by-products. In other words, it will be possible to separately regulate the reaction rate and the transport rate in a micro-reactor of this kind. That's very different from a large reaction vessel, where the reagents frequently remain in the reaction until the end. It is not possible to control heat and mass transfer with enough accuracy for precise production. The micro-scale will make it easier to apply the necessary heat in a precise way. This too will help prevent the formation of byproducts and avoid incomplete reactions. Endothermic and exothermic reactions can also be combined, with the energy released in one reaction being fed into another.

The higher precision of these devices makes it possible to use catalysts in a very controlled way. This not only presents new ways to produce materials, but also makes it



#### FACTORY ON A CHIP

The smaller a plant, the more precise its chemistry. The entire panoply of chemical installations (right) can be miniaturized



down to the size of microelectronics (left). A 'factory on a chip' would make an ideal chemical plant.

possible to better study catalysis. The devices may also be used to produce catalysts in a very controlled way. These techniques are now used in different laboratories. It is a truly multidisciplinary task. Sensors and electronics will have to be closely integrated in the device. Moreover, it will no longer be possible to first design the reaction and then the reactor. The chemical process and its environment are closely interrelated on this micro-scale, with design demanding close cooperation between chemists and reactor engineers. The technology is very promising for the fine chemicals and pharmaceutical industry, which are both sectors where precision is crucial and output is often measured in small quantities.

These devices - once we are able to use them for large scale production - will also allow a different strategy for upscaling. Rather than making larger and larger installations, it will be a question of more of the same. That will make it easier to respond rapidly and flexibly to new developments in the market or to consumer demands. It will no longer be necessary to concentrate all production in one place, enabling manufacturers to install micro-plants wherever their products are needed.

The combination of different components on a single chip may also make these devices highly versatile. This would allow different products to be made using a single device. One day, we may be able to thread atoms at will to form a molecule, much like a printer that produces all kind of texts. Catalysis technology makes it possible to produce chemicals where they are needed, when they are needed.

## Adaptive systems

Nature knows how to design its catalysts. Whenever new bacteria or viruses enter our body, a completely new system of chemical reactions is designed to prevent the new disease from spreading. Our immune system triggers a catalytic reaction that is reinforced and adapted through the presence of the intruder.

What happens is that the catalyst forms itself out of building blocks that are already present in our body and can adopt a wide range of structures. Our body tries different varieties of catalysts in an attempt to combat the intruders. Molecules that prove to be successful are replicated to increase the level of activity. This molecular recognition triggers a faster replication of the catalyst. The immune system thus “evolves” in an almost Darwinian way in seeking the most effective molecular weapons against illnesses.

Such self-organizing processes are omnipresent in nature. They are also the foundation of cellular replication. In our body, molecular systems constantly create copies of themselves. DNA is the ultimate example of replication. During cell division, a strand of DNA is duplicated with the aid of proteins.

It is still one of the world’s great unsolved mysteries how such complex chemical systems as our bodies could evolve from a formless, unorganized soup of primordial molecules. Louis Pasteur showed in a famous experiment in 1860 that no life could spontaneously generate from lifeless materials.

But how then did life evolve from the inanimate material that once covered the uninhabited earth? There are several known processes that may give rise to stable patterns, thus bringing structure in simple, unstructured chemical mixtures. It may well be that a sequence of such processes organized matter in increasingly complex structures. Chemists now think that some form of molecular evolution preceded the formation of life. The process of self-organization made ever more complex molecules, through successive adaptations, reinforcing the replication of certain molecules. Important landmarks in the creation of life were the formation of RNA, that replicates genetic information, and the so called Krebs process cycle, that stores and releases energy and lies at the heart of metabolism. This whole evolution took a long time and was a matter of specific conditions. Chemists have very different views of the details of this evolution, but common concepts include self-organization, evolution and replication of molecules. These concepts have all been replicated in laboratories. The quest for more insight in the molecular evolution of our planet may offer new perspectives on life itself, which may be of great cultural value.

But this quest also has practical relevance. By reconstructing and understanding the processes that have formed the complex molecules on our planet, we find inspiration for new chemistry. What might have happened in nature without any auxiliary systems or process installations, may also give rise to simple industrial processes. In this sense, it is not necessarily relevant whether life evolved in this manner, because the quest for possible evolutionary routes has an intrinsic value, as it may reveal processes that are easily mimicked.

Some chemists have made this mimicry into an art in itself. Their great challenge now is to integrate different processes in one life-like system. They try to make artificial

cellular structures, that include some kind of molecular memory, a replication mechanism, and a means of absorbing and utilizing energy. Several experiments indicate that this may be possible. If they succeed, it would show that lifeless material can be designed to have a life-like character.

This is not only of philosophical importance. When we master some of the processes that underlie life, it may enable us to make materials much more efficiently and sustainably. Many chemists are inspired by the complexity of nature and the evolution of life. It offers them the possibilities to extend the reach of their efforts to adapt chemistry to the needs of mankind.

## Alternatives for fossil feedstock

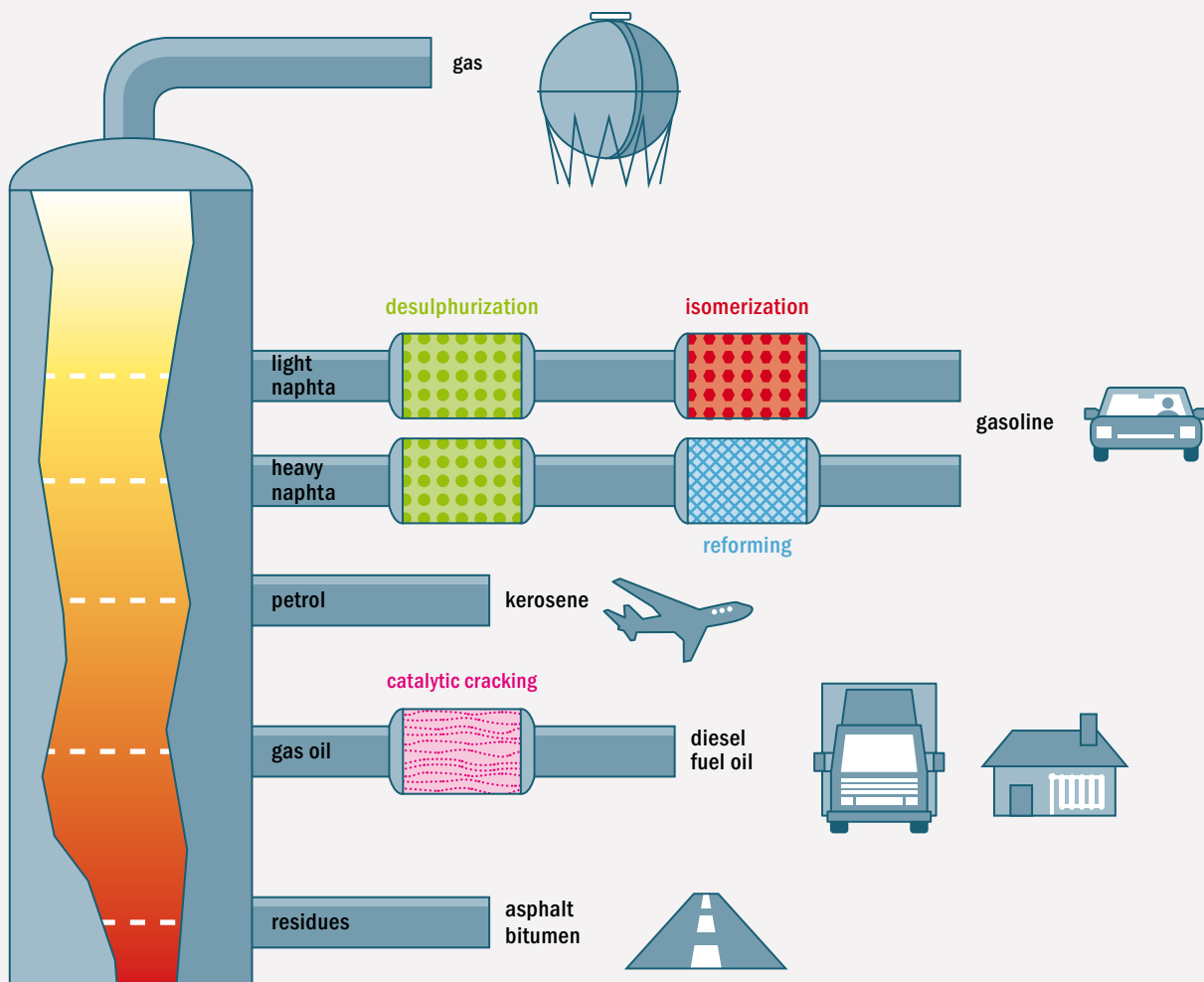
As concern grows regarding the greenhouse effect and the depletion of fossil fuels, we rediscover that fuels can also be cultivated. Mankind learned millennia ago that almost everything nature produces is flammable. Wood is still the earth's number one energy source and is still used worldwide for cooking and heating, especially in poorer parts of the world. Crops are increasingly being grown for the specific purpose of generating energy. This includes sugar cane, rapeseed, and palm trees. The sugar and oil they produce is chemically processed to convert it into fuel.

Using biofuels could help to reduce the greenhouse effect, as they can – in principle – close the carbon cycle. The plants take carbon dioxide from the atmosphere and then return it when they are burned, which means biofuels provide energy without releasing additional carbon.

Biofuels are suitable to serve virtually every purpose that fossil fuels currently serve. You can process them to make all kind of plastics, alcohols, or simply as fuel. It is generally not a good idea to grow crops for fuel purposes only. That diverts food away from the human food chain, leading to food shortages and price increases. It uses scarce sources of water, that could otherwise be used for the production of food. It consumes a lot of energy for the necessary fertilizers.

Second-generation biofuels are more promising. No impact on food production is expected from using biomass generated from household waste, or from residual non-food parts of existing crops, such as stems and leaves, or from crops that are unsuitable as nutrients. It often comprises parts of plants that are too solid to be digested, with a lot of woody or fibrous biomass, where the useful sugars are locked in by lignin and cellulose. The harshness of these materials is a key to the survival of plants, offering natural resistance to pests.

There are different ways to process this reluctant type of biomass to make it suitable as feedstock for the chemical industry. Wood for instance is often gasified, breaking up complex molecules into carbon monoxide and hydrogen, which is subsequently processed to give liquid hydrocarbons. This process doesn't involve catalysts. The subsequent conversion of syngas to hydrocarbons is a catalyzed chemical reaction in which the gas is converted into a liquid hydrocarbon.



### REFINERY

Catalytic processes determine each stage of bulk processes of our chemical and petrochemical industry. The picture

shows a refinery, where crude oil is converted into gasoline, diesel oil, liquefied petroleum gases, heating fuel oils, lubricating oils, asphalt and petroleum

coke. Catalysts make these steps more efficient and the plant as a whole more flexible for changes in the input and output streams.

This so-called *Fischer-Tropsch process* (coal-to-liquid) was invented in Germany in the 1920s to produce an ersatz fuel, based on gasification of coal, which meant Germany no longer had to import petroleum. Nowadays, production of liquid fuels from natural gas or gasified biomass is seen as a promising substitute for the classic refinery. The processes, however, involve high capital costs, as well as high operation and maintenance costs. The challenge is to reach the same level of selectivity, efficiency, and flexibility that we have accomplished in a century of development of fossil-based petrochemistry. The *Fischer-*

*Tropsch process* may be improved now that we are able to produce catalysts with nanoprecision. But we lack insight as to how catalyst nanostructure influence the efficiency of the process. It is also unclear which surface properties of the catalysts are responsible for extracting reactive carbon out of carbon monoxide in syngas. This requires intensive research.

Many other alternative energy sources require some form of catalysis. The catalytic capture of energy from light in chlorophyll is an future alternative to the present photocells bases on semiconductor technology. Similarly, the improvement of fuel cells that convert hydrogen into electricity involves catalysis. Until now, the electrocatalysis involved in these processes has been undervalued. Study of this so-called photocatalysis promises to generate novel devices that produce hydrogen out of water or fixate carbon dioxide.

We almost certainly will not be able to become fully independent from fossil feedstock in the coming decades. Particularly for the synthesis of large organic molecules, oil is by far the most efficient feedstock. The future will probably see a diversification, where energy is increasingly derived from other sources, while precious fossil feedstock is reserved for chemical processes for which it is especially suitable.

There will also be an increasing demand for processes that capture carbon dioxide from fossil feedstock, possibly in combination with the production of hydrogen for transportation.

Catalysis lies at the heart of many of these processes. It is more important than ever to gain insight into how we can get the most out of our energy sources. And we need to make haste, because we don't have another century to match the present level of sophistication of fossil-based processes.

#### **FISCHER-TROPSCH PROCESS**

Coal, natural gas and biomass may be used to make liquid fuels. Gasification creates hydrogen and carbon monoxide, that may be combined in a catalytic process to make hydrocarbons. The process is already applied on a large scale, but

it is still expensive. New catalytic routes may make the process more attractive. It is a promising way to create transportation fuel from coal or biomass without crude oil.

# RESEARCH TOPICS FOR THE NEXT TEN YEARS





## AREA 1: NANOSTRUCTURED HETEROGENEOUS CATALYSTS

### Control of heterogeneous catalysts on an atomic scale

Many traditional heterogeneous catalysts, that are now widely applied in industry, have been developed in an empirical way. They often consist of a mixture of ill-defined inorganic phases distributed over high surface area supports, whose porous nature also is not well controlled.

Important improvements of these catalysts, with resulting benefits to process efficiency, have derived from growing insight into the composition of these catalysts and more refined control of the composition and structure of these catalysts.

The scientific approach that is at the base of these developments is the development of a molecular science of heterogeneous catalysis. This approach has proven to be very powerful. It has taken the science and industry of catalysis very far, actually to the level of understanding and sophistication that we have now in catalysis. One may expect that a multitude of new catalysts and new catalytic protocols will be developed in the next decades using these proven reductionist research strategies.

A unique, different and rapidly developing field is that of the inorganic materials made at the nanoscale level. Molecular control of catalytic systems requires that catalyst structures are made with atomic precision. Present materials used for heterogeneous catalysts are not uniform and contain a distribution of particles and pores of different sizes. It is an important goal of the nanoscience approach to better control these structures.

The discovery of special agents that influence shape and structure of materials brought a real breakthrough in the design of catalytic systems. These structure directing agents are lipophilic molecules (i.e. detergents), that organize themselves in a manner comparable to the molecular organization in liquid crystals. This ordering acts as a mould that shapes the inorganic catalytic materials.

Liquid crystal preorganization of lipophilic structure directing molecules is exploited in the synthesis of nanoporous materials such as MCM and SBA. Such inorganic materials can be made with uniform nanoporous channels connected in many different two- or three-dimensional ways.

Molecular recognition properties are used in the synthesis of zeolites. The shape and dimensions of the smaller zeolitic channels is determined by the type of organic base used in zeolite synthesis. Different organic bases create different sized channels and cavities.

In order to apply this knowledge, we have to control the surface structure of catalytic particles on a nanoscale.

Other improved synthetic routes to make catalytically reactive particles are required, for instance on the basis of advanced preparation methods using complexing agents or

precipitation procedures, including the modification of the heat treatment conditions (temperature ramping, gas atmosphere, emerging developments are based on electro-, or photo deposition procedures. In all fields of catalysis, whether it be heterogeneous, homogeneous or biocatalysis, the rational design and synthesis of new nanostructured materials is a key to future success.

To unambiguously describe the functioning of the active site of a heterogeneous catalyst and its response to its environment such uniquely defined materials are needed. For heterogeneous catalysts, three fundamental aspects have to be considered simultaneously to arrive at both breakthrough developments and improved catalysts.

- The chemical nature of the active center (0.1 nm length scale) that controls the bond-breaking and bond-making actions of the catalyst. Synergy between different catalytically active components;
- The local environment, with its hydrophilic or hydrophobic nature, and stereochemistry, that is influenced by processes on nanometer length scales;
- The accessibility of the active centers (nm– $\mu\text{m}$  length scale) that affects local concentrations and rate of transport of molecules.

In the past decades, science has made significant progress in understanding the behavior of active sites by studying model systems, i.e. 2D catalysts. With such systems the reactivity of the catalytically active material can be studied without interference of the complexity of support properties. The obtained information was crucial to arrive at the point where we are now, but further steps have to be taken to properly understand and tune the 3D catalyst systems further.

One of the phenomena that seems crucial for catalysis, but is currently poorly understood, is the effect of the environment in the vicinity of the catalytically active site (e.g. pore wall, solvent, ligands, interaction with adsorbates) on the performance of that site.

Zeolites are ideal subnanometer materials to study such effects. They have micropores defined with crystallographic precision, and can therefore be studied with atomistic detail. Zeolites are also the workhorses of the petrochemical industry, where they are widely applied as solid acid catalysts.

Sophisticated molecular synthesis techniques can also be used to activate these zeolites for other reactions such as selective oxidation or dehydrogenation.

The small oxidic clusters responsible for these reactions vary greatly in reactivity as their redox state and size is varied. By combination of experimental characterization and computational modeling, structure-activity relationships have been established through research in Eindhoven for small  $\text{GaxOy}$  clusters incorporated in the micropores of the zeolite Mordenite. It has even been possible to establish by such techniques that the behavior of such clusters can show complexity features such as self-repair. Reaction with water reforms the particles in their reactive state by reoxidation clusters reduced in dehydrogenation reactions. Super-active, new, single-site zeolite catalysts have been created in the preparation of supported Fe catalysts for the oxidation of benzene control of the inorganic chemistry

using metal-organic aluminum complexes.

To understand this so-called second-shell effect, such precise synthesis of well-defined 3D catalysts is essential. Only then unambiguous structure-activity relations can be established.

Second-shell effects are not limited to the catalyst itself (pore structure, ligands) but are, in principle, also brought about by interaction with neighboring molecules in the reaction medium. In gas-phase conditions, such effects may not be really significant, while in liquid-phase operation they most likely are very important. Also, interaction of the active site itself with solvent molecules is relevant, influencing both adsorption of reactants as well as desorption of products via competition effects.

Substantial progress has been made in synthesizing nanoporous materials with hydrophobic and hydrophilic parts. Selective oxidation catalysts have been designed by incorporation of single site silsesquioxane clusters connected through a hydrophobic polymeric matrix embedded in the channels of nanoporous inorganic support. Silsesquioxane clusters are small molecular complexes of Silica or alumina, that contain reactive single-site atoms with similar reactivity as on the inorganic support of a heterogeneous catalyst. In the silsesquioxane cluster, these are uniquely defined.

## Precise synthesis of catalysts

Carriers can now be used for ordering on a nanometer scale. High surface area carriers are needed in heterogeneous catalysis to disperse and stabilize the catalytically active material as small particles and expose as many as possible reactive centers to the reaction medium.

The ordering of the pore structure differs from the synthetic carriers based on classic sol-gel-chemistry. A conventional silica carrier consists of unordered material, with a random network of pores that varied in size. For precision catalysis, these sizes have to be controlled more stringently, as is possible with e.g. carbon nanotubes. The challenge is to control various length scales in catalyst systems. This concerns the nanometer scale on which the chemistry takes place, but also the millimeter scale which determines the currents in liquids during a catalyst reaction, thus determining the conveyance of materials.

Supramolecular organization constitutes the basis for generating nanostructured materials. Nanopores can be structured over several length scales. Colloidal techniques are often used to make well-defined nanoparts (2-10 nm).

Research in Utrecht, for example, makes use of structured nanoporous materials, that were made by coating micelles. This results in structured pore systems of SiO<sub>2</sub> with uniform 3 nm pores that have a total surface area of 1,000 nm<sup>2</sup> per gram of catalytic material. Using electron tomography (3D-TEM), single-pore analysis of occupancy with nanoparticles is carried out.

A promising technique to make well-defined nanostructured materials is chemical vapor deposition on metal surfaces and particles. Using this technique, carbon nanofibres are made, that may be used as a carrier upon which active substances such as magnesium and nickel can be deposited. In this way, the carbon nanofibres can be coated with a nickel hydroxide-plate structure.

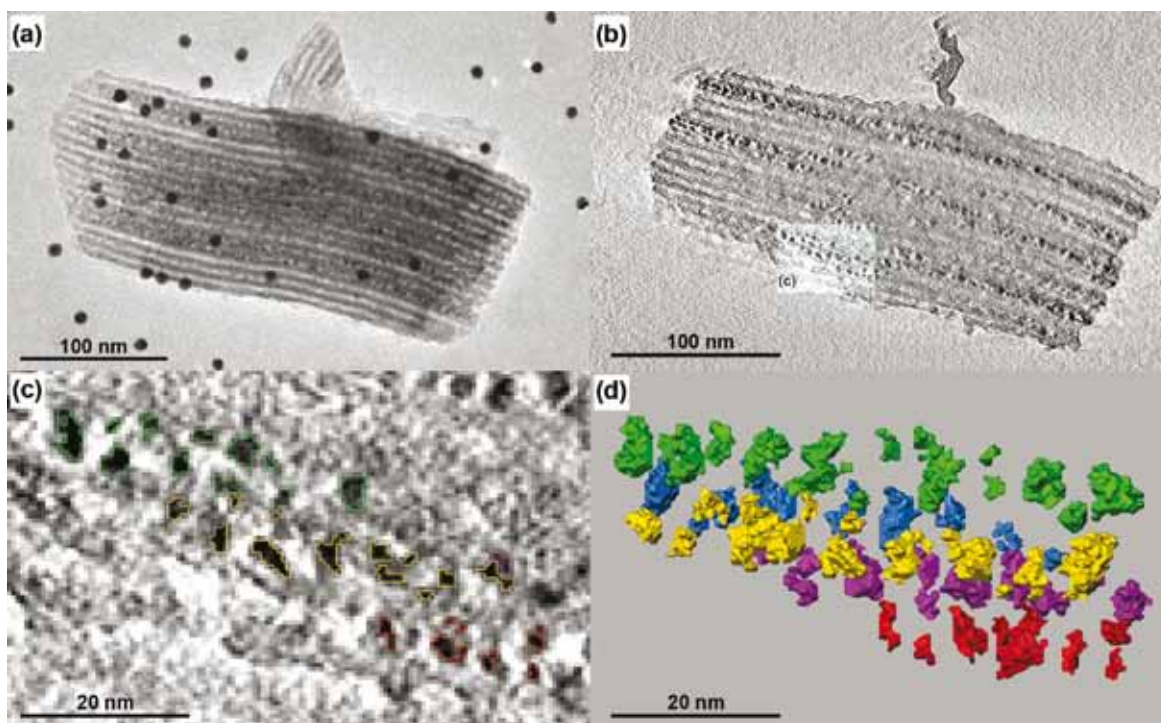


Fig.1

Image (2D projection) of small NiO crystallites in the pores of an ordered mesoporous silica support (SBA-15). The dark spots are 10 nm colloidal gold used for 3D imaging (a), numerical slice through the 3D image of the same NiO/SBA-15 structure at half height (b), magnified part of numerical slice with NiO crystallites outlined in different colors (c), surface view of NiO crystallites in five pores of SBA-15 support (d). The crystallites belonging to the five pores are drawn in different colors. (Groep: Krijn de Jong, Universiteit Utrecht)

It is interesting to structure nickel and cobalt catalysts using similar techniques. Possibly better catalyst materials can be made using these new carriers. In order to achieve this goal, high-level spectroscopy and electron tomography are necessary. One has to know exactly what materials look like.

Further research will clarify the mechanisms determining the structure of materials. Why is it that with new techniques a clearer particle-size classification is achieved, than when using classical methods? Why is it that particles take certain sizes?

For this, a deeper theoretic understanding is necessary, for instance in particle size effects and diffusion in nanoporous systems. In Eindhoven, promising advances have recently been made in computer modeling of the reactivity of metal hydrides.

Liquids may also be controlled on a nanoscale. Confined liquids are an emerging topic in nanotechnology, according to recent publications such as those involving aqueous rubidium bromide solutions in the slit-shaped pores of carbon materials: the average coordination number of the hydrated  $Rb^+$  ions dropped from 6 for the bulk solution to values as low as 4.7 to 2.5 for confined solutions. Confinement has also been shown to have a tremendous

impact on, for example, the properties of nanocrystals inside carbon nanotubes. Liquid phase catalysis involving confined liquids and confined active phases may therefore be a promising new research direction. In Utrecht, special properties of confined fluids are used to unravel and to steer nanoparticle synthesis.

One way of doing this is through the use of microreactors, as earlier mentioned. Catalyst particle synthesis can be precisely controlled using silicon-based microfluidic networks. In so doing, it is necessary to integrate the various reaction steps in a chip. This includes sending impulses, calorimetrics, as well as temperature and solvent cycling. In this way, for example, cadmium oxide and a selenide precursor can be combined in a controlled manner. The production in microreactors leads to a uniform synthesis of nanoparticles. This is done at the Delft University of Technology and elsewhere.

An important challenge lies in the design of more precise reactors. In a reactor, for instance, a plug flow can be generated using a piezoelectrically controlled reactor. The plug flow has a direct impact on the particle size. It is interesting to synthesize zeolites under high pressure using these kinds of devices. A next challenge lies with scaling up this production method. Delft has been able to make devices with thousands of identical channels that all behave in the same manner.

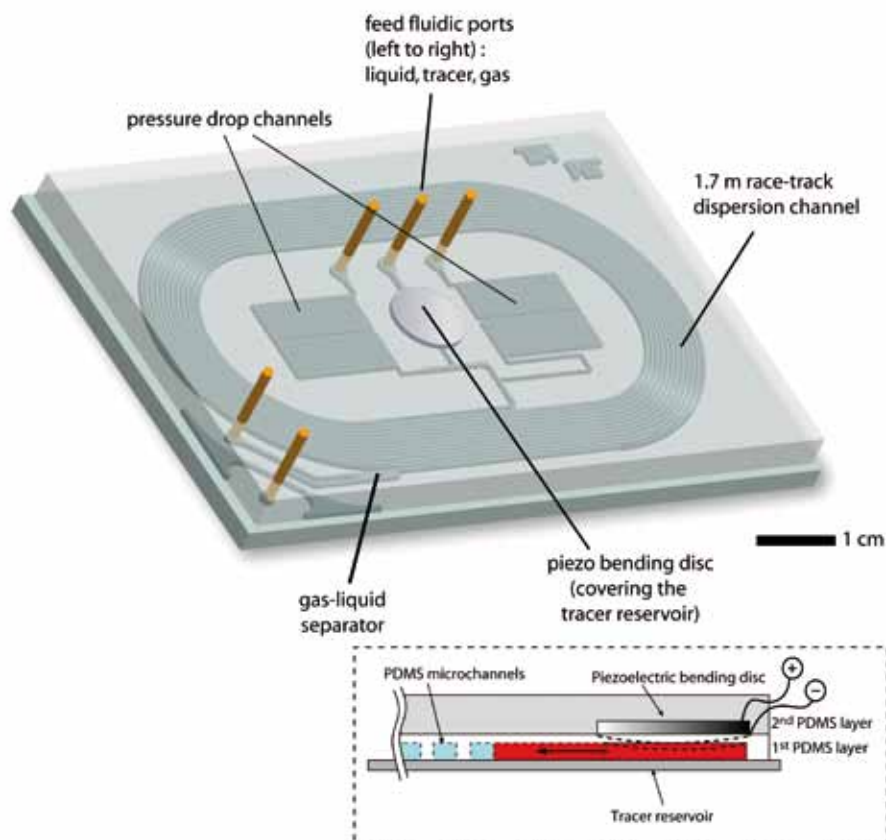


Fig. 2

Confined flows in tiny conduits (microfluidics) is fundamentally different from flows in large tubes. Chemists use these flow features in miniaturized chips to make materials that are hard to make in larger devices, such as a test tube. This particular device was used for analyzing flows to create particles of very uniform size (Groep: Michiel Kreutzer, Technische Universiteit Delft)

Metal Organic Frameworks (MOFs) are novel microporous solids that are built-up from organic linkers and inorganic building blocks. Nowadays, several hundred different MOFs are known, which are often surprisingly thermo-stable. The MOFs are new alternatives for inorganic structured materials – and the advantages of MOFs include their easy preparation and structural uniformity. Another potential advantage of MOFs is the easy modification of the overall structure by changing the building blocks (mostly the organic fragments). This provides a new tool for fine-tuning the structure. Also the implementation of functional groups should be relatively easy, by just attaching them directly or via anchors enabling post-modification.

MOFs provide a new tool to vary the second shell of MOF immobilized catalysts. MOFs have been applied in various absorption processes, including the storage of hydrogen, but few catalytic applications have been described in available literature, in view of their limited thermal stability. Examples include olefin hydrogenation below room temperature or trans-esterification.

Microfabrication techniques that are commonly used for electronic devices, e.g. e-beam lithography, are now commonly used to create 2-D model catalysts with controlled dimensions in a range that is interesting for this field. Increasingly, techniques allow control over layering in the third dimension, e.g. subsurface alloys, and these 3D materials create new properties through implementation for catalysis. Also, non-lithographic techniques, e.g. block copolymer self assembly allow precise synthesis of catalysts to investigate size effects. It is foreseen that this fast-moving technical field will open new avenues for 3D model catalysts. On a related note, microfabrication techniques also allow the creation of precise chips that facilitate on-chip operando analysis, and we foresee the successful application of integrated devices for catalysis research, in which model catalyst synthesis and probing technique are combined.

## Understanding how structure and environment affects catalytic behavior

In heterogeneous catalysis, many examples exist in which two functions are combined in a single catalyst. For example, for the hydroisomerization of alkanes to branched alkanes, a (de)hydrogenation function and an acidic function are needed. In enzymatic catalysts or catalytic antibody catalysis, both acidic and basic functions often need to be combined in one material. The challenge is to arrive at a material in which these functions are at the desired distance from and orientation to each other, with a tuned polarity in order to selectively bind reactants. This can be done with a weakly acidic solid support (SiO<sub>2</sub>) on which organic bases are immobilized. In this way, they succeeded in preparing a material in which a nearly continuous range of acid-base distances was available, thus making this material versatile for different acid-base reactions. The polarity of the support could be tuned by modifying the available OH groups on the support.

Catalyst accessibility should be part of the design on both the nano- and microscale. On the microscale, if one discusses accessibility, one discusses mass transfer effects, most

particularly diffusion in pores. For many chemical reactions, mass transfer to and from the catalytic site will be of vital importance for the performance of the catalyst. This mass transfer is determined by the microporous structure of the catalyst support. Therefore, in the design of a catalyst, this should also be taken into account, as a very active catalyst site, influenced by mass transfer effects, can easily be non-selective by catalyzing a consecutive reaction or it can be deactivated. Although mass transfer processes on a larger scale (external mass transfer to the catalyst bodies) are of great importance to many processes, they are considered beyond the scope of this theme. On the nano-scale, the accessibility of a catalytic site can determine the reactivity of a molecule. For example, in cinnemaldehyde hydrogenation, the approach of the reacting molecules via the support to the metal catalyst particles, or the direct adsorption on the catalyst nanoparticles, results in different reaction selectivities. This challenge demands meso-pore engineering, e.g. by introducing mesopores to a microporous catalyst, or by using emerging catalyst support materials, such as thin layers of carbon-nanofibers.

There are many examples in scientific literature in which the catalyst performance (in terms of activity and selectivity) changes dramatically by changing the solvent. Some of these effects are well understood and are clearly due to bulk solvent characteristics, such as solubility, but there are also many examples in which these effects are not understood at all. It is tempting to suggest that in these cases the catalyst performance is influenced (if not dominated) by second-shell effects. The relevant effects include the influence of solvation of active sites and adsorbed species, solvation of activated complexes, as well as solvent induced desorption. The effects can be as large as switching the enantioselectivity from preferably the formation of one enantiomer to the other. To study these types of effects, new technology and new systems need to be developed that would, firstly, allow these effects to be understood, and second, would enable control and variation of the second shell of the catalysts. Molecular capsules could be a tool, but there are other conceivable tools to study this.

## Scientific conflicts

Not many catalytic mechanisms are fully understood. Unraveling the intricate details that determine the outcome of a reaction, often involves intensive calculations that are often beyond the scope of even the best hardware and computer models.

It is therefore hardly surprising that intense debates and differences in insight exist on fundamental questions of even basic catalytic reactions. The frontiers of theoretical insight are often characterized by different schools that disagree with one another. In the absence of serious modeling, these conflicts cannot be decided.

But the boundaries are rapidly shifting. We can decide important conflicts that diversify theoretical insight by gaining greater insight into computer modeling, by achieving progress in combining multiple scales in calculations, and by developing even more powerful hardware.

Especially by studying reactivity in heterogeneous catalysis on a molecular level, we can gain detailed insight into the precise constitution and arrangements of atoms, as well as the optimum surroundings for a specific reaction.

Key unresolved issues include the epoxidation of ethene with silver as a catalyst. Different conflicting models exist on how the precise composition of the silver surface influences this reaction. This factor determines the selectivity of the catalyst and therefore also the optimization of the process.

Another example is the hydrogenation of ethene on a metal surface. Again: what is the exact structure of the surface during the reaction? Is it the naked metal surface, or is the surface filled with organic intermediates?

We also lack basic insight into the synthesis of zeolites for catalysts. What role does molecular recognition play in building intermediates at a molecular level, when producing a zeolite? Or is the building of the structure a collective process, in which molecules are reorganized in a gel, without molecular recognition on a piecemeal basis.

In Fischer Tropsch catalysis, several groups have reported on particle size effects for cobalt. Other groups have denied these effects, stating “cobalt is cobalt is cobalt.” We are seeing the emergence of theory to understand the (non-)existence of this particle size effect.

## Catalytic devices

On a nanoscale, the design of catalysts, carriers and reactors is intertwined. The design of a catalyst on this scale often implies the development of the device in which the reaction takes place. Reaction and reactor influence each other. Therefore, it is important that the design of the catalyst, coating and reactor takes place within one group. During an integrated design, it is important to calculate all aspects of a catalytic system.

Completely new devices are being developed for gas-liquid systems. The classic method of enlarging the interface between liquid is stirring and making use of small particles.

But the use of small devices also presents new opportunities. One technique concerns the use of foams with open structures, a line of research in Eindhoven. Foams ensure low pressure drops in the system, low dispersion of energy, and little friction. The foam can be adapted to the type of the liquid reactant. Thin liquid films may also be used.

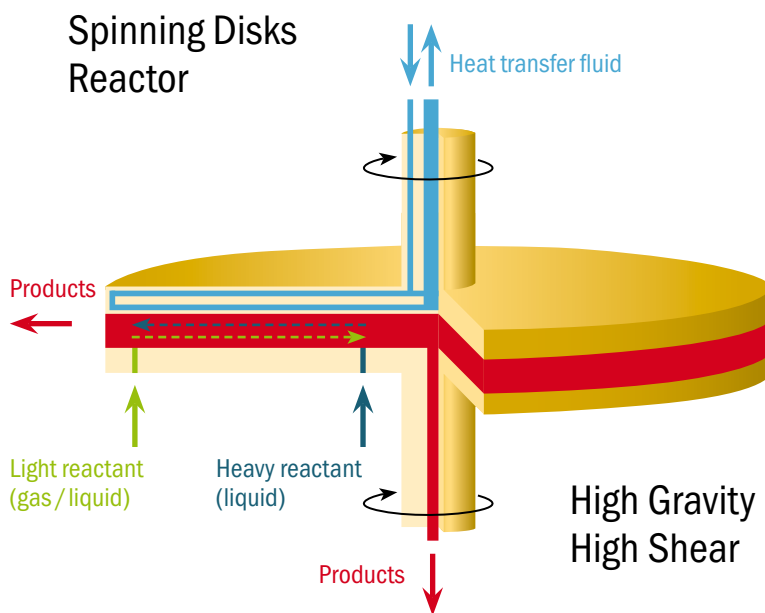
On a fast-rotating disk, various phases can be effectively brought into contact with each other. In a spinning disk reactor, multiple-step synthesis can be achieved by stacking discs. In this way, a plug flow can be generated. In doing so, the reaction times can be controlled in a very precise manner. The advantage of these kinds of microreactors is that the holdup is very small. Only a few liters of reactants are needed to keep a reaction going. Microreactors ensure safe and continuous production. This ensures more precise production and a high-quality product.

A setup using various discs makes it possible to use the system for various reactions. This provides an interesting perspective. In this way, a jukebox reactor can be constructed, which can be used as a transportable and programmable system for organic synthesis in, for instance, the pharmaceutical industry. Such a system can be placed close to the customer



Fig. 3

The spinning disks reactor is a very compact, multifunctional device that can be used for efficient contacting of gases and liquids for chemical reactions and separations. The two disks are co- or counter-rotating with each a different rotational speed. The joint rotation mimics high-gravity conditions where the difference in rotational speed and the small gap (e.g. 1 mm) between the disks generates high shear rates. The reactants are optimally mixed and high reaction rates are achieved. The disks can be efficiently cooled or heated by a heat transfer fluid. Also the disks can be made catalytically active where the structure and composition of a washcoat on the disks can be tailored to the local fluid dynamic conditions. (Groep: Jaap Schouten, Technische Universiteit Eindhoven)



and be programmed in such a way that hardly any operator is needed.

These reactors also are promising for use in electrolysis or as fuelcells. They enable unique control over the complex behavior of multiphase systems. In small devices, they can be used to fuel mobile telephones or laptops.

A lot of questions still need answering before this technique can be used for industrial applications. How can a catalyst be regenerated in the continuous processes used in industrial companies? And how can a catalyst be removed once deactivated?

Another new development is the use of microchannels for gas-liquid and liquid-liquid systems. Such structures can be placed on chips. Various flow regimes are possible in micro channels. Only in the last few years have chips become precise enough for this technology. The channels allow the regulation of reactions down to  $10^{-4}$  seconds.

The small scale of the reaction makes it difficult to calculate the mixing behavior. It is no longer only gravity that determines the outcome, but also interface tension, surface tension, and viscosity. To this end, new calculation programs are needed.

Novel approaches that exploit miniaturization of systems, gleaned from the semiconductor industry, have led to the design of miniaturized microfluidics reactor that offers the perspective to realize a sequence of reactions without having to separate reaction intermediates after conversion steps. An interesting example is the microfluidics study in Nijmegen, that applies these systems in complex organic synthesis processes.

The NRSC Catalysis program will seek new designs for these microfluidics reactor systems. The microfluidics approach is also useful for the production of well-defined nanoparticles, that may be used in heterogeneous catalysis.

Reaction times can be better controlled in a microreactor. By removing intermediary products in time, cascade reactions can be designed in a completely new manner. Recent tests in Nijmegen using oxidation in a microreactor show that this is possible.

In Nijmegen nano-sized reactor architectures have been built, that naturally occur in cells. The idea was to construct cell-like assemblies from amphiphilic block-copolymers. A procedure has been developed to encapsulate enzymes at specific locations in these capsules. These systems have been used to perform cascade reactions. A combination of Glucose oxidase in the inner aqueous compartment of the polymersomes, horseradish peroxidase in their bilayers, and Cal-B-lipase in the outer aqueous compartment was found to efficiently catalyze a three-step reaction. This was found 100 times as active as the mixture of the three enzymes in solution. Indeed, structure does matter.

Due to the small size of the device, various parameters can be optimized independently of each other. The small size also makes microdevices highly suitable for experiments with enzymes, for example, in cases where it might be difficult to obtain large volumes of reactants and enzymes. The small devices also are an excellent vehicle for selective drug delivery, enabling more directed administering of pharmaceuticals.

Another kind of microdevices are the microplasmareactors, such as those that are made in Enschede. In these devices, electrodes are separated from the reaction channel. The small scale enables microplasmas under atmospheric pressure. This cannot be done with plasmas on a larger scale. These kinds of systems can be used in order to visualize the mechanisms of oxidative cracking of propane.

To study these systems, it is necessary to visualize what is happening in those systems on a microscale. Micro-NMR is promising technology in this regard, in that it can identify liquid quantities down to 600 nl.

Catalytic devices can also be used for photocatalysis in a kind of solar cell. Also in these systems, particle size does matter. The size has an effect on the photocatalytic activity. It is therefore important to operate with a well-defined particle size. This research is also done in Delft. Photocatalysis proved to be interesting in systems on the basis of  $\text{TiO}_2$ , but it also looks promising to develop combined systems using chromium, oxygen, titanium. The transmission of electrons can be facilitated in this way. The device itself must be conceived in such a way that a maximum amount of sunlight is concentrated in it. Experiments are now being conducted with light insertion into honeycomb-like monolithic structures using optical fibers.

Desorption can probably be stimulated using such photo devices. It is conceivable that  $\text{CO}_2$ , for example, can be directly transformed into alcohols or alkanes.

## AREA 2: MOLECULAR CATALYTIC SYSTEMS

### Post-reductionist chemistry

New strategies for the synthesis, development and testing of catalysts holds the promise of new improvements. One such new strategy is the so-called systems approach. This is now possible thanks to improved molecular understanding of catalytic systems, derived from research in the past decade.

The systems approach aims to understand and design catalytic systems in their full complexity. Components or parameters are combined rather than isolated, and the function and interaction of various components is studied within the system. The focus is on the interaction of components, giving rise to new properties that are only present in the system, not in its parts.

The knowledge and synthesis capabilities of supramolecular chemists is indispensable for such an enterprise. Systems catalysis studies functional catalytic systems in which multiple molecular processes are combined and regulated in order to perform a catalytic operation. The catalytic operation of a system may be the multi-step synthesis of a complex organic molecule by a multiple number of molecular catalysts acting in concert, it may be a responsive or adaptive action that is regulated or operated by means of catalysis, or it may be the self-selection or amplification of a multi-component system by means of catalysis or in which a catalyst is selected.

The systems approach in catalysis therefore intends to find a balance among several or even multiple catalytically active molecular components in order to develop new catalysts and catalytic protocols, as well as new catalytic reactions. Because a systems approach is about combining components, systems catalysis brings together many scientific fields, which include chemical synthesis, kinetics, mathematics, engineering and catalysis. The primary aim of systems catalysis is to study and combine homogeneous, heterogeneous and biocatalysis in perhaps the most intimate manner.

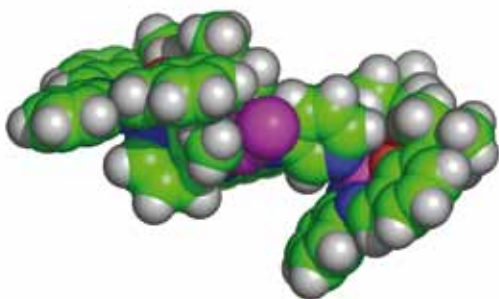


Fig. 4

The figure displays a typical example of a transition metal catalysts formed by self-assembly. The Palladium transition metal complex is encapsulated by two zinc(II)salphen building blocks, via axial coordination of the pyridyl to the zinc(II). As a consequence, the palladium complex becomes one the most active and selective catalyst for the co-polymerization of CO and Styrene, leading to high molecular weight syndiotactic polymers. (Groep: Joost Reek, Universiteit van Amsterdam)

This new topic, currently being studied at NRSC Catalysis, aims to establish the rules of systems catalysis and to explore the possibilities of a systems approach in catalysis. Research includes the study of systems of different catalysts, catalyst development by means of evolutionary selection, and responsive catalysts that operate via self-regulation or that are sensitive to external or internal stimuli. This includes the topics combination, communication, and control in catalysis. Equally important is research into the enabling tools that will be required to analyze and understand the catalytic systems. This demands collaboration among the different disciplines at NRSC Catalysis and, more specifically, those involved in theory and spectroscopy.

### Integrating multiple processes

Up to now, most catalytic processes have been designed in a sequential way. To make a final product, a feedstock undergoes a series of well-defined transformations. This implies that for every feedstock and every product the sequence of reactions needs to be identified and the catalytic components have to be carefully tuned beforehand. One example is the multi-step synthetic pathway to make a complex organic molecule, as is done in the production of pharmaceuticals. After each step, the reaction product is purified up to 95% or greater before it is taken to the next reaction step in a different vessel. In terms of operations, ending one reaction step and progressing to the next one mostly involves a number of steps that include or may include solvent and temperature swaps, liquid-liquid extractions, product crystallization, chromatographic purifications, distillation, protective group removal and/or addition, and finally reagent and catalyst additions.

The obvious way to circumvent these time- and energy-consuming operations is indeed to do without them and perform sequential reaction steps in a single pot. Domino and cascade type reactions in a certain way deal with this in an appropriate manner, but seem very much restricted to highly pre-designed substrates. Tandem type catalytic reactions seem more promising in this respect, but have not really gained popularity. Reports have, however, been published on catalytic tandem sequences that either make use of a single catalytic entity to perform a reaction sequence (an auto-tandem reaction) or use different catalytic entities in this sequence (an orthogonal tandem reaction).

The tandem reaction process is difficult to apply directly when the different reaction steps of the process require a different reaction environment or different reaction conditions to be executed. Therefore, new reaction engineering approaches are necessary.

Most examples of multifunctional catalysis are found within olefin polymerization, metathesis, and hydrogenation chemistries and few examples have been reported outside this type of chemistry. Many discoveries of tandem reactions have relied heavily on serendipity. Here, a systems approach will be very beneficial to come to a more directed way of developing catalytic reaction sequences. One major advantage of a systems approach in this respect is the awareness of and interest in interactions between the components of a system that may lead to new properties that are properties of the system only.

Some other developments:

- ‘One pot,’ multi-component catalyst systems for multi-step synthesis;
- Multi-component catalytic systems that use a variety of feed stocks and yield a variety of products. This includes systems that use one feed stock and produce multiple products, and systems that use multiple feedstock and produce a single product
- Multi-component catalytic systems that include triggered on/off switching of components

## Evolutionary design of catalytic systems

The complexity of living things is attributed to evolution, an intricate algorithm of mutation and natural selection. This process can be mimicked in order to obtain certain properties of a chemical process. In this method of directed evolution, material aspects are varied stepwise, with dozens of experiments that are performed in parallel. In this way, molecular evolution can be directed in the test tube in order to produce useful catalysts. This bottom-up design approach contrasts with the more conventional, top-down approach in which catalysts are tamed rationally using computers and rational design. We thus have the ability to tailor individual molecules, by creating genetic diversity and to screen and select for improved functions in large libraries of enzyme variants.

These are combined in a robust approach to solve challenging molecular design problems. This method is used, for instance, in protein engineering to evolve proteins with desirable properties not found in nature. The advantage of the directed evolutionary approach is that the researcher need not understand the mechanism of the desired activity in order to improve it. The likelihood of success in a directed evolution experiment is directly related to the total library size, as evaluating more mutants increases the chance of finding one with the desired properties. Combinatorial screening methods preferably make use of rapid spectroscopic methods, but chromatographic screening is another option. In addition, in molecular biology one has the possibility to develop screens based on selection; i.e. the growth of the expression host can be made dependent on the target product.

This technique is used in Delft for stabilizing and immobilizing catalytic enzymes. Natural enzymes are frequently used as a starting point. They can be improved through a process of directed evolution. Various families of enzymes can be crosslinked with each other and expressed in yeast using a plasmide. The throughput screening necessary to measure the results can be carried out in Delft.

An example of this is the use of crosslinked enzyme aggregates (CLEA's). Immobilizing techniques have also been developed for metal catalysts. In this way a chiral rhodium catalyst can be ionically anchored onto a surface without having to modify the catalyst.

Another recent example of evolutionary design is the fabrication of functionalized nanocapsules in Amsterdam. A hydrogen-bonded motif can be added to the outside of these capsules. Fully robotized, dozens of varieties can be tested in a short time. First a metal complex with substrate is made. Ligands are then added and the variety that works best is selected. In a similar way, bidenates are generated programs using dynamic pyridine-

zinc-interaction. By gradually adapting the catalyst to the substrate type, rapid improvement can be achieved.

Directed evolution nowadays has become a tool used by academic as well as industrial scientists to develop suitable biocatalysts. Despite its success, the demand for a combination of rational and directed design is highly desired, to reduce the volume of the libraries to be screened and to decrease the number of required cycles. Ultimately, a de novo design of proteins could be foreseen. In contrast, an evolutionary approach is rarely used in the area of metal-ligand and organocatalyst libraries. Chemical catalyst design could, however, benefit from the screening methodologies that have been pursued in directed evolution.

When considering a directed evolution experiment, major advancements are foreseen in all three steps of the repetition cycle, which will ultimately contribute to improved and faster evolution of tailor-made catalysts.

Rationalization in generating rounds, enabling us to improve the design of the repetition cycle. In enzyme chemistry we are hampered by near complete ignorance of how the amino acid sequence affects every aspect of enzyme performance, including its catalytic activity in a non-natural environment. Systematic knowledge on how nature performs convergent evolution (a specific activity can be evolved from different classes of enzymes, accompanied by the creation of completely new active sites); can teach us how existing scaffolds can be adapted to reach the desired reactivity.

## Complex and responsive, adaptive catalysts

Control and regulation of activity are essential in all catalytic systems. The most sophisticated mechanisms may be seen in the living cell. In the cell, metabolic pathways are tightly regulated to control the concentration of metabolites. Additionally, molecular catalytic mechanisms are available that respond to external signals and changes in conditions. Control and regulation in biological systems is achieved either by direct modification of catalyst activity (using very different approaches ranging from intra- and allosteric control) or by covalent modification.

To achieve control and regulation in systems catalysis, a crucial goal will be the development of responsive and adaptive catalysts. Responsive catalysts may be defined as catalysts whose activity can be modulated by external signals, whereas adaptive catalysts may change their chemical reactivity in response to an external signal and generate a new or different product.

To be able to change the chemistry of a catalytically active center by external stimuli, it is necessary to employ catalytic systems that have the architecture that can influence the course of the catalytic reaction with high precision. They also need to have a degree of flexibility.

Such systems are typically the metal-organic complexes developed for application in many catalytic reactions, from the hydroformulation reaction of use to the production of detergents in chemical industry.

One example is the hydrocyanation, as studied in Eindhoven. This uses a catalyst and a co-catalyst, for instance for the addition of hydrocyanic acid to alkenes. This reaction has found a large scale industrial application. Butadiene is the basis for the production of nylon. Many unresolved questions remain in this area. Such as the difficult addition of alkenes, which requires the presence of a Lewis acid as co-catalyst.

Using a supramolecular approach, concerted action of two reaction centers in a supramolecular catalytic complex has been realized. One example of this is seen in promising research in Amsterdam. Here, complex supramolecular bifunctional catalysts are developed. One side of these catalysts has an organometal center that binds a substrate, while hydrogen through a reactive center on the other side of the catalyst activates the same substrate. In this way, the synergy between the two sides leads to one unique reaction. This gives a very high reactivity, compared to that with enzymes. But they are still very specific for a single product

Several factors are important in the control and regulation of catalytic activity. The first consideration is whether a system should be under external control or whether it should be self-regulating. In case of external control, the experimentalist can up- or down-regulate the activity of one or more catalysts or change their reactivity to influence the system as a whole. In a self-regulating catalytic system one or more catalysts are capable of giving an autonomous response to changes and in this way optimal operating conditions can be maintained or a new product is produced.

A second point is that, in principle, a system can be made to respond to either physical or chemical stimuli. Physical stimuli for controlling catalyst activity include light, temperature; electrons/voltage, or even strain.

Sijbesma has used this principle to modify the reactivity of metal-organic catalysts by incorporating them in a polymer matrix. By straining the polymer, local stress is applied that deforms the ligands around the metal center of the catalyst.

Chemical stimuli are changes to the chemical environment of the system, e.g. changes in the pH or the presence of signal molecules, like intermediates in a multi-step reaction.

Although abundant in nature, responsive or adaptive designed catalysts, regardless of the type of regulation or stimuli, have gone largely unexplored until now. Therefore, a major effort is required to develop the principles of control and regulation in catalysis. Taking inspiration from nature, regulation of catalysis using intra- and allosteric control or covalent modifications of catalysts can be envisioned. Other feasible options include light or electrochemically switchable catalysts and control by modulation of the redox state of catalytically active metal centers.

Light-switchable systems are being developed in Groningen, where they have been applied to induce macroscopic changes in liquid crystals. It is a great example of macroscopic amplification of molecular local effects by use of supramolecular organization of the medium in which the molecules are embedded. Such catalytic systems can be integrated into a catalytic system for use in selective photochemical reactions.

## Biomimetics

The complexity and refinement of biological systems are a great inspiration for the development of novel man-made systems that emulate the action of biosystems. The benefit of the chemo-systems is that they can be used under completely conditions than the biological systems and for different reactions. It is also expected that the development of new hybrid systems of biocatalysts and the other inorganic, organic or metal-organic pillars of catalysis will generate valuable novel concepts and practical novel catalysts and materials.

Organic chemists have developed organocatalysts without any metal, that are of great use to organic synthesis in which complex molecules are made that often have several enantiomeric centers. One example is the use of quinine as a catalyst. In Amsterdam it is used for the reaction of nitromethane with benzaldehyde. Quinine can be modified by linking thio-ureum to the methoxy group. This results in a bifunctional catalyst with two active centers: basic nitrogen which removes protons from both nitromethane and thio-ureum (which is a Lewis acid). The positioning of the thio-ureum group on the molecule is important in the reaction.

In Amsterdam, there are plans to undertake new research in the development of catalysts for amide bond formation. Currently, amide bonds are made using very expensive stoichiometric reagents, for which, remarkably, no mild catalytic alternatives exist. We propose, inspired by nature's catalytic solution to this problem, via the His-Asp-Ser triade, the synthesis of catalysts displaying an alcohol, carboxylic acid and imidazole moiety, aptly positioned onto small cyclic (pseudo)peptide scaffolds. These molecules can be used as targets for the development of medicines and biologically active molecules.

Research in Groningen shows that the synthesizing process of complex natural substances can still be considerably improved. The synthesis of complex molecules is often hindered by an excessive number of reaction steps. Mimicking nature may reduce the number of steps. This will also offer greater insight into natural mechanisms. This is, for example, the case when using lipids such as those produced by the tuberculosis bacteria. The lipids in the cell membrane of the bacteria determine the virulence of tuberculosis. In order to know precisely how lipids act, it is important to be able to generate labeled natural substances and analogous substances. Recently, researchers in Groningen have succeeded in generating these complex substances with high selectivity using enzymatic catalysts.

As an example of bio-hetero catalysis integration, one can envision the combination of one or more enzymes with non-biological surfaces in order to add reactivity and control to a multi-component system. This concept has been explored to a limited extent over the past years in the form of redox potential control of oxidoreductases on solid electrode surfaces. However, many other possibilities are conceivable, including control via surfaces through other parameters, such as microwaves, or by making the surface an active non-biological catalyst in one or more steps of a cascade system.



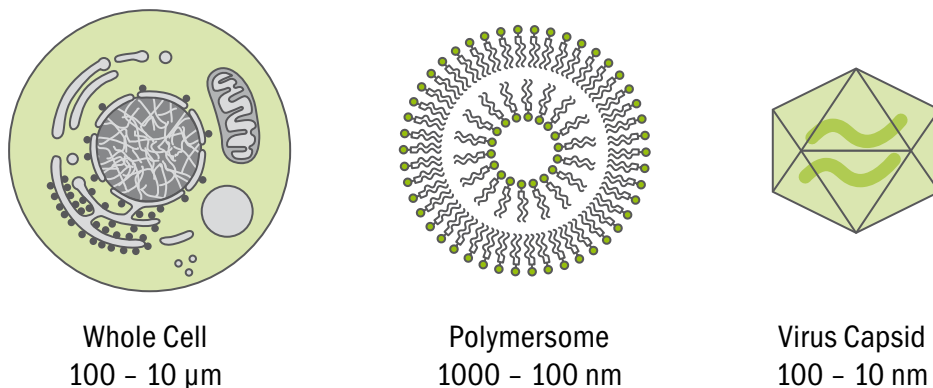


Fig. 5

Cellular structures appear at different scales. The catalytic reaction can be controlled by opening or closing the pores in the virus wall by changing the pH (Groep: Roeland Nolte, Radboud Universiteit Nijmegen)

Some of the catalysis in these complex hybrid systems will be inherently of a (semi-) homogeneous nature; i.e. in the enzymes' active centers, but also in/on newly formed, non-biological active sites of molecular dimensions. A formidable challenge of interpretation is to explore the extent of applicability of well established monodisciplinary catalytic concepts (i.e. from enzymology: Michaelis-Menten kinetics; allosteric regulation) to achieve understanding and control of these hybrid multi-catalytic structures.

Hydrolysis enzymes, which add water to double bonds, hold promise for industrial applications.

Directed evolution has also been carried out in Amsterdam on the phosphatase-enzyme. This research is particularly promising for the development of HIV blockers. Aldehydes can be coupled together, whereby ring closures are possible, which makes cyclical imides that block HIV. Also of interest are sulphate transfer reactions with recombinant transsulphatase, steroids sulphate with cheap sulphate donors. Carbon-sulphate compounds can also be generated using peroxidases.

Contrary to classic chemical synthesis, enzymes make use of friendlier reagents. The reaction is more subtle and subject to mild conditions. Reaction products can be used to generate biochemically interesting substances.

It is highly desirable to find better routes to catalyze enantiopure products. One promising approach, applied in Eindhoven, is the use of supramolecular organization for chiral selectivity. It is highly interesting to find out some general design rule to catalyze the formation of large chiral objects. This new research avenue may lead to the non-covalent synthesis of supramolecular systems.

Enzymatic processes also look promising. Chaperon proteins can be useful, too. These substances regulate proteins and can be regarded as catalysts. For example, you can stack molecules in a supramolecularly structured polymer. This is a racemic mixture, but if a

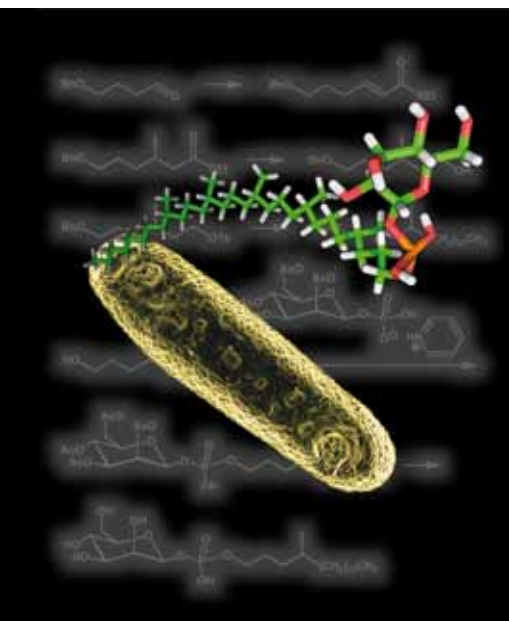


Fig. 6

This picture of a tuberculosis bacterium, *Mycobacterium tuberculosis*, has been made by an electron microscope. It shows the remarkable serpentine-like cell wall of the bacterium which consists of lipids with very long tails. As these lipids cause an immune response in human, the chemical synthesis of these lipids, thereby making them available for research, is very important. (Groep: Adria Minnaard, Rijksuniversiteit Groningen)

chiral monomer is injected, all polymers will be oriented in the same direction.

Traditionally, synthetic molecules active as catalysts are merely designed to convert one molecule into another, with high chemo-, regio-, and stereo-selectiveness. Analogous with natural systems, it is of great interest to find catalysts that selectively form supramolecular and functional objects on all length scales. It will be highly interesting to find out some general design rule to catalyze the formation of large chiral objects. This will be a new research avenue for scientists in Eindhoven. Supramolecular catalysis will be used to catalyze the non-covalent synthesis of supramolecular systems. They also aim to design a supramolecular scaffold that will bring together building blocks into an assembly that is thermodynamically the most stable form within the scaffold. This will bring us to chaperon-like processes in the folding and self-assembly of supramolecular objects, which can be seen as catalysis in supramolecular synthesis, being different from supramolecularly formed catalysts.

In Nijmegen nano-sized architectures have been developed, that can be used as tiny reaction vessels. Naturally occurring cells, which are composed of double layers of phospholipid molecules, have been used as blueprints for its design. The idea was to construct cell-like assemblies from amphiphilic block-copolymers, which are more stable than phospholipids or synthetic surfactants. The work-horse in this line of research is a (chiral) block-copolymer composed of a polyisocyanopeptide and polystyrene, which on dispersal in water gives very stable hollow and porous capsules, i.e., polymersomes. A procedure has been developed to encapsulate enzymes at specific locations in these capsules, i.e. either in the inner aqueous compartments or in the double layers.

These systems have been used to perform cascade reactions. A combination of glucose oxidase in the inner aqueous compartment of the polymersomes, horseradish peroxidase in their bilayers, and Cal-B-lipase in the outer aqueous compartment was found to efficiently catalyze a three-step reaction. This is a 100 times more active than the reaction of a mixture of the three enzymes in solution.

Another promising research field is inspired by the so-called processive catalysis that is found in nature. The challenge is to mimic the machinery that is used to copy for example a DNA chain. Nature makes use of a template that contains the required information for the copying process. This may be mimicked by designing artificial processive catalysts that are composed of two catalytically active cage compounds that are held together by supramolecular interactions, e.g. hydrogen bond-

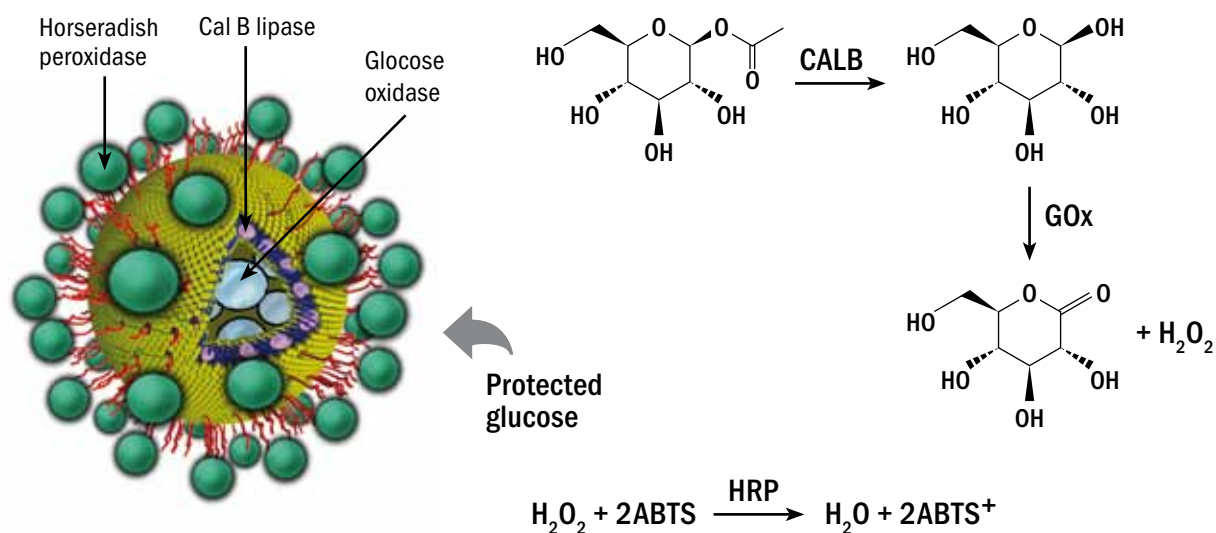


Fig. 7

(Left) Three enzymes anchored to polymersomes prepared from a block-copolymer of a polyisocyanopeptide and polystyrene. (Right) Cascade reaction in which the three enzymes are involved. (Groep: Alan Rowan, Radboud Universiteit Nijmegen)

ing. One cage complex will hold a polymer chain that acts as the template, while the other one binds the polymer chain that has to be modified. Information transfer between the two cage complexes will be achieved via allosteric interactions. Preliminary studies show that this concept is feasible.

Much catalysis research is focused on enzymes, but DNA too is an interesting catalyst, because of the enantiomeric characteristics of DNA. It gives an opportunity to provide information to the reaction through use of the stereo-selectivity of DNA or RNA molecules.

Recent research in Groningen shows that, in doing so, Diels-Alder reactions can be achieved with more than 99 % enantiomeric excess. The catalyst is a copper complex on the basis of dimethylbipyridine with a piece of DNA attached to it. It also shows that DNA can speed up the reaction by a factor of 100. In this way, other Lewis acids can enantioselectively catalyze in water, such as Michael additions to nitromethane or dimethylmalonate substrates.

It seems promising to elaborate on this concept for synthetic applications; e.g. to create a range of amino acids. The use of DNA is cheap since a lot of instruments for manipulating DNA are available, thanks to decades of biological research. Nevertheless, it remains difficult to selectively modify the chemical structure. It is favorable that the reactions take place in water at room temperature. Moreover, it appears that the catalyst is relatively stable. Reactions using DNA can also be used to store information. By linking a piece of oligo-DNA to a catalyst, a catalyst system can be put in place capable of generating a cascade

reaction. Analogous with DNA proteins and peptides also seem suitable for catalysts. In this way, it seems possible to provide peptide hormones with an active site.

Another example is the use of biomolecules as surfaces to guide the ordered nucleation and growth of non-biological materials. Recent results from Delft suggest practical possibilities for the formation of such diverse materials as palladium nano-particles, long carbon nanotubes, or molecular magnets on the inner surface of biological cages, such as ferritin. A variation is the use of ferritin, a globular protein complex consisting of 24 protein subunits and the main intracellular iron storage protein, in both prokaryotes and eukaryotes. This enzyme remains highly stable up to very high temperatures and pressure and can be easily produced using gene expression in *E.coli*.

Thanks to the spherical shape of ferritin, it is possible to fill proteins, so that superparamagnetic nanoparticles with a well-defined size and composition emerge. Carbon nanotubes can also be made in this regard. In this way, ferritin can be used for water purification.

Another exciting field of research is the mimicry of motions as they also occur in biological systems. Scientists in Groningen succeeded in mimicking the motion of bacteria using anisotropic parts. For example, directed motion can be achieved by glucose oxidase on carbon nanotubes in combination with the catalase enzyme. The catalysis is so active that oxygen bubbles are created which propel the system and create an autonomous motion. It is interesting to move such a system along a gradient or path. In a next step a load can be added to the system. The final challenge lies in moving such a system through a cell or a cell membrane.

Other molecular engines use light as a propulsion or other catalyst reactions. These kinds of engines mimic natural systems.

An exciting challenge for the future will be trying to emulate a natural cell. In doing so, attempts are now being made to artificially construct a cell membrane mimicking Archae bacteria. On the basis of this, vacuoles or capsules can be created.

Research in Groningen has shown that the aperture of a virus-like structure may be varied by integrating a photochemically sensitive molecular motor in it. In a next step, catalysis can be triggered in such a cell by linking an autocatalyst reaction to vesicles in membranes. The final goal is to build a microscopic factory that is self-sustainable and duplicates itself. This is not only an intellectual challenge but also offers interesting prospects for the pharmaceutical industry.

One of the main impediments for the further development of energy systems is the overpotential in the splitting of water. This is, for example, relevant when generating hydrogen or removing carbon dioxide. In this regard, there remains a lot to be learned from natural reaction. Research in Leiden focuses on enzyme lactase. Enzymes are often cheap and generate themselves over and over again. This is a source of inspiration for new energy systems.

## AREA 3: PREDICTIVE CATALYSIS

Increased understanding of catalysis leads to a more directed design of catalysts. The more we understand, the less trial and error is necessary. Computational chemistry and spectroscopy constitute the foundations of catalyst design. They have become an integral and indispensable part of modern catalysis research and development. Present-day spectroscopy offers unprecedented levels of experimental monitoring and insight at an atomic and molecular level. Computational chemistry and spectroscopy in accord have made it possible to explore and unravel complete reaction mechanisms, which in turn guide both academic and industrial experimental chemists in their quest to optimize syntheses of bulk and fine chemicals.

Of course, also other observational techniques are important, such as kinetic measurements. In order to design synthetic routes or catalyst materials or pharmacologically active molecules in a more rational fashion, it is crucial to combine accuracy with solid and profound insight into the underlying mechanisms in the electronic structure. This holds true also in the early stages of process and product development, where studies are nowadays often done in the form of computational chemistry as numerous properties can be computed with chemical accuracy. This makes it possible to study or predict quantities that are hardly or not all accessible through experimental techniques or are time consuming to obtain. Such insight can be obtained through detailed analyses of the computed wave function and bond energy, and the theoretical results have to be compared with those obtained by, for instance, spectroscopic means.

Only in a rather limited number of cases have we obtained detailed understanding that would allow prediction of the outcome of a catalytic reaction, despite the fact that many have worked for decades to “demystify” catalytic events. Understanding catalytic reactions at a fundamental level implies that the developed reaction network should be experimentally and theoretically tested in sufficient detail. This holds true in particular if one tries to use such understanding in a rational design. Only if we are able to further push both theoretical and experimental approaches to investigating catalytic processes in action, will we be able to arrive at the level of true predictive catalysis.

The key challenges of “Predictive Catalysis” for the coming decade are:

- (1) understanding of the mechanisms of many of our catalytic reactions;
- (2) rational design of catalyst, based on this understanding, for instance ligands, particle size, shape composition;
- (3) automated “transition-path finding;”
- (4) development of ultra-high spectroscopic and microscopic spatial and energy resolution with enough sensitivity to establish useful structure–function relationships under real reaction conditions.

The strengths of Dutch studies of “Predictive Catalysis” lies in the combination of different perspectives on approaches that characterize different research fields, such as homoge-

neous, heterogeneous and bio-catalysis, electrocatalysis and spectroscopy of catalysts in action. These fields are related and complement each other fruitfully. The favorable and rare mix of diversity and coherence of these fields makes “Predictive Catalysis” an indispensable leading player that can help develop any type of catalytic material, process or target molecule or material that is (or may become) important in a sustainable economy.

## Observing catalysis as it happens

Spectroscopic tools can increasingly be used to study catalytic materials in their working state. In the past, spectroscopy had to be used under conditions that often were far from true catalytic conditions. But new cell designs allow for more realistic temperatures and pressures. Also, [spectrometers??] can increasingly be used detached from its cells. The instrument may be brought to a proper catalytic reactor, guaranteeing that catalytic conditions are indeed met. This approach has given the opportunity to obtain more meaningful spectroscopic data, that can in certain cases even be used for kinetic analysis, enabling quantitative structure-performance relationships. These developments have seen in-situ spectroscopy blossoming in the last decade. Various in-situ spectrometers have become available, with much improved performance and at lower prices, making such instrumentation more accessible and easy to use.

The Utrecht research group in spectroscopy has a roadmap for in situ spectroscopy, heading towards the monitoring of single sites in a real catalytic system. The road goes from extrudate, via the observation of grains, to single metals.

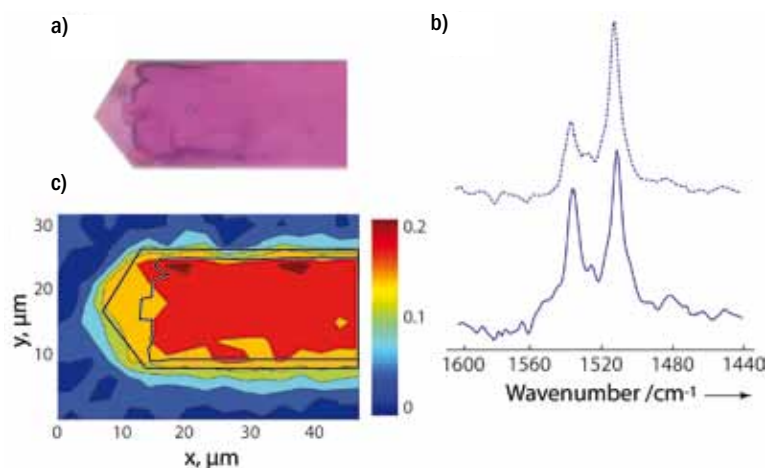
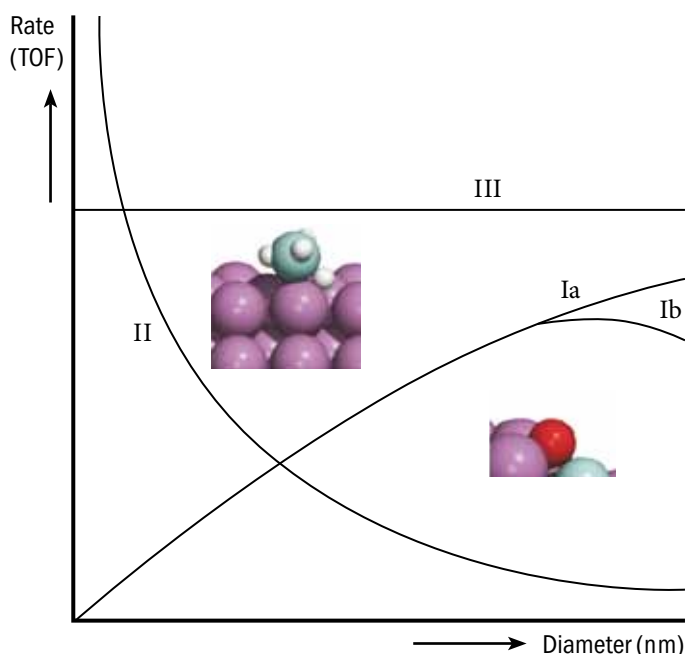


Fig. 8

a) Fragment of optical microphotograph of the H-ZSM-5 crystal after reaction with 4-fluorostyrene; b) Intensity of the IR band at 1534 cm<sup>-1</sup> mapped over the crystal after reaction; c) IR spectra taken from the edge (solid line) and the body (dotted line) of the crystal, demonstrating differences in the intensity ratio of the bands. (Groep: Bert Weckhuysen, Universiteit Utrecht)

## Structure sensitivity of catalytic reactions



**Fig. 9**

Catalytic reactivity can be a strong function of particle size and shape. Whether a reaction shows a maximum, increase with particle size or is not affected depends on the type of reaction catalysed. This we can predict due to computational catalytic chemist, who can predict the reactivity of surface intermediates as a function of catalyst structure (Groep: Rutger van Santen, Technische Universiteit Eindhoven)

In years to come, the challenge will be to further push the experimental boundaries of in-situ spectroscopic methods to increase their molecular sensitivity and spatial resolution. One would like to have both organic and inorganic information on the catalytic event. This implies that one should be able to visualize the single active site (e.g. metal nanoparticle) with a spectroscopic technique and at the same time visualize the organic transformation over this single active site (i.e. single catalytic event). Furthermore, we would like to visualize the orientation of the reacting molecules at the catalyst surface. Most of the information until now is focused around reaction intermediates and the coordination and oxidation state of the active site. The relationship between changes in the coordination environment and increased bond breaking and making should be further explored. In other words, how do changes in the local electronic structure result in changes in either activity or selectivity. This also demands that techniques should increase their energy resolution, as small changes in electron fluctuations should be made spectroscopically visible.

There are many questions that should be addressed for gas-phase observations as experimental conditions become harsher. But a growing number of scientists also started to develop instrumentation that can observe liquid-phase catalytic reactions. The challenge is to deal with solvents, mostly water or organic solvents. A valuable technique in this respect is attenuated total reflection IR spectroscopy, that may observe the interface of catalytic solids reactants, reaction products, and sometimes reaction intermediates.

Another development is the improvement of spectroscopy for solids. This has become possible through a sensitivity at a molecular level, for instance by fluorescence or surface enhanced Raman. These techniques enable spatially resolved observations in catalyst grains or crystals. It is a challenge to observe how molecules make their first docking on zeolite pores. Such experiments are now being planned in Utrecht. X-ray microscopy also looks promising in this regard. At present, 25 nm details can be made visible. The technique is now being downscaled to 0 nm resolution. A 1 nm resolution should be achievable in five years.

These techniques are sensitive for only certain types of molecules. An important challenge is to develop useful reporter molecules, which may be observed and have catalytic resemblance to true reactant molecules. Another challenge is to extend the observation window to include other molecules.

A next step involves work on three-dimensional spectroscopy. In Utrecht, steps are being taken to use an X-ray detector for this purpose. The use of such detectors allows three-dimensional tomography. It seems possible to improve the time and space resolution. Dispersions of metal ions should also be measurable with these detectors.

The space resolution of time-resolved STM-measurements extends to an atomic level, but the time resolution is still so low that it is difficult to follow dynamic processes. Techniques are now being developed to gain information about shorter events using noise measurements

We would like to extend the capabilities of spectroscopic techniques further, to monitor an even wider variety of catalytic events. More specifically, three phase types of reactions should be studied. Attention should also be further directed towards pushing the pressure and temperature limits. And finally, efforts should be made to limit the contribution of the solvent to spectroscopic data. New methodologies should be developed to make this possible. Non-linear optical techniques, such as Sum Frequency Generation, are particularly promising, especially at the electrified catalyst-solution interface, as this allows electrode potential modulation leading to additional sensitivity enhancement.

None of the spectroscopic techniques gives a complete picture of the catalytic event. To observe the full process, it is necessary to make a smart combination of different spectroscopies, each with their own sensitivity and typical length scales. Monitoring catalytic phenomena at different length scales, with different agents, in different phases, involves different techniques. A proper mix of them makes it possible to obtain a more detailed understanding of catalytic mechanisms. Several combined spectroscopic set-ups have now been developed. This trend is now also in evidence at various synchrotron beam stations, where different spectroscopic and diffraction techniques are combined. The advantage of such an approach is that it also allows assessment of the influence that a measuring technique has on the catalytic reaction.

In Utrecht, for instance, a cell has been built in which Raman microscopy is combined with atomic force microscopy (AFM). The combined instrument can make 20-30 nm details visible. This technique is now being used for zeolite crystals.



We would like to integrate the different steps of heterogeneous catalysis by visualizing diffusion, adsorption, reaction, desorption and diffusion. This requires employment of various methods on different length scales and subsequent transformation into a kinetic model and reaction scheme. Most of the efforts until now focus on specific steps of catalysis, but if one wants to design new catalytic materials, we need to gain a better understanding of the links between the individual steps. This certainly also requires a further integration of spectroscopic and microscopic methods down to the nanoscale; i.e. in-situ nanoscopy. Most of the spectroscopic species observed, besides reactants and reaction products are unknown, which restricts interpretation of experimental spectroscopic data. In other words, a better interface between experimentalists and theoreticians is desirable if we are to lay a solid foundation for the interpretation of in-situ spectroscopic data. Spectroscopy is not only a technique that enhances the understanding of catalytic processes, it also presents the possibility to control a reactor on the basis of in-situ spectroscopic measurements. This technique can be used as a practical tool for regulating reactors. This idea is now being tested in Utrecht, with alkylating zeolite reactors.

Spectroscopy is a science in its own right. But by working on the frontiers of instrumentation, one often gains a greater understanding of the systems under study. That's why many groups within NRSC Catalysis are trying to push spectroscopic techniques further, as part of their study of catalytic systems, often in close concord with computational chemistry.

## Predicting catalytic behavior

Computational catalysis plays a huge part in the development of catalysts. New methodology, better software and the ever-increasing power of supercomputers have given this field a gigantic performance boost. Examples include the refinement of parallelization and linearization techniques, and progress in multi-scale modeling. The challenge is to explore in detail all routes on the potential energy surface of the catalytic process, both the viable ones (which can then be optimized) and the a priori plausible but in reality inaccessible pathways (which can then be ignored in further work).

Calculations may already elucidate complete networks of intertwined reaction mechanisms that are active in complex catalytic cycles. This reveals to an experimental chemist which intermediates exist, how they are connected, and where the rate-determining step is located. With this knowledge the catalytic process may be tuned and optimized. A second important challenge is the modeling of the shape of the potential energy surface along the reaction coordinate. This realm of chemical reactivity is comparatively poorly understood, in contrast to our understanding of chemical structure, which has for decades offered a rich conceptual framework for bonding theory. The recent qualitative physical understanding of chemical reactions (e.g. by the activation strain model) is an important step in a more directed design of catalysts.

Major progress in his field has been made in Amsterdam, applying DFT methods. The study of oxidation by iron was done in great detail. This work helps in the search of new catalysts to enable the important production of methanol.

Presently, computational bio-catalysis is an emerging activity. Work should be done to extend the number of factors that may be incorporated in the computational treatment. Calculations are currently limited to the local environment or a single step in the catalytic cycle. It is a great challenge to expand this for more realistic biological systems. In biological systems, different reactions often work in concert to bring about high activity and selectivity. A concrete example of a bio-catalytic reaction is the polymerase-assisted replication of DNA, as is currently being researched in Amsterdam. It remains a major challenge to consider gene expression at a molecular level in order to determine the mechanisms of DNA-duplication. The different factors which influence activity and selectivity may be determined separately. Covalent,  $\pi$ -stacking, solvation and steric factors determine the activity and selectivity. The challenge now is to combine these in a single model.

DNA replication is also a good model for template-assisted synthesis in general, as well as for supramolecular catalysis (H-bonding directed recognition). These and other bio-inspired phenomena constitute valuable input for the non-natural catalytic processes that are required to achieve sustainable industrial catalysis. Further expansion of this insight could shed greater light on the unsurpassed performance of catalysts in biology. Typically, the unprecedented selectivity of enzymes stems from specific, directed interactions, such as hydrogen bonding. Functional principles of these natural catalysts can be mimicked. This often involves supramolecular, hydrogen-bonded complexes. An intricate aspect are the fluctuations that may occur here due to the thermal motion of the environment. This makes it necessary to incorporate large length and time scales. Thermal fluctuations involve both small ligand or solvent molecules as well as large-scale conformational changes of the embedding protein.

For heterogeneous catalysis, one of the major challenges is to predict how surfaces change during catalytic reactions. Surface structures may change as a function of coverage, and there is a need to predict such structures as well as the rates of change between metastable phases. These calculations require a smart combination of different models. The challenge here is to integrate molecular quantum-chemical methods, solid state simulations, and molecular dynamics methods.

These predictions are important to be able to interpret the surface data that come from e.g. Scanning Tunneling Microscopy (STM). Computational studies are essential to unravel the structure sensitivity and insensitivity to chemical reactions.

An illustration of this is the recent understanding of particle size effects in surface layers. Whereas the activity of molecules such as CO and N<sub>2</sub> rearranges surface atom arrangements as edges and kinks, activation of molecules as methane and ethane occurs by single atom centers. This provides the basis for the classification of structure-sensitive reactions.

Progress has been made in predicting the overlayer structure of surfaces that rearrange during catalysis and in calculating the rate of these processes. Successful cases include the surfaces of sulfides and some of the oxides. Predictions are made on acidity and basicity, as well as surface reactivity. Dynamic studies become possible when Car-Parrinello type

quantum chemical procedures are used. Also much progress has been made to predict the overlayer structure or coadsorbate layers as a function of coverage. Other key insight includes the realization that the reactivity of adsorbates or adatoms on surfaces may be a strong function of overlayer concentration, as is for instance the case for ethylene hydrogenation or ethylene epoxidation.

This is only one example where different models have to be combined. One of the great challenges of computational chemistry is to integrate the models that are developed for different aspects of catalysis. There are electronic structure methods with quantitative accuracy, tracing methods for reaction pathways, a conceptual framework for understanding why reactions do or do not take place, and there are methods for incorporating fluctuating environments, such as solvents, proteins, or supramolecular structures. For a proper and complete understanding of the catalytic cycle, these methods should be applied in concert. To date, however, these have been mostly applied separately. We are now at the level where we can make a next step, integrating some of these models. The ultimate dream is making a comprehensive model, covering all aspects of catalysis and making it available as a standard research tool in catalysis.

Before such a model can be routinely used, we need to extend our computational methodologies to the more macroscopic time and length scales on which catalytic events really occur.

It is important to realize that the overall time scale of catalytic events is typically  $10^{-1}$  s and the corresponding length scales are those of a micron. Our calculations using state-of-the-art DFT methods produce results on a picosecond time scale, which may be extended to a scale of some  $10^{-5}$  s, using transition state theory expressions. But there is currently still a time- and length-scale gap between simulations at a molecular level and macroscopic catalytic systems.

By extending length and time scales, we can include more relevant physical structures that feature in the catalytic process, including its dynamics. A great step forward would be a routine treatment of solvent and other environment effects. This is especially important when solvent molecules are actively involved in the reaction mechanism. One approach is the coupling of various quantum chemical and classical techniques in so-called multiscale modeling approaches. The idea is to use detailed calculations where the action really occurs, and more coarse-grained techniques for slowly varying or distant parts of the system. An example of a multiscale strategy is to apply density functional theory (DFT) on a part of a model, to conduct quantum mechanical calculations on the chemical bonding and reactivity at crucial places. The larger system may then be described with a classical approach, such as molecular dynamics (e.g. Car-Parrinello MD), to account for the thermal fluctuations of the local, chemical environment due to solvents and ligands. On a third level, this may be incorporated in a larger system still, with an even more coarse-grained method that offers a good approximation of the chemically inert and more distant groups, such as the outer part of (supra-molecular) ligands or the protein. Force field calculations using molecular mechanics may be used for that. Finally, slow processes or large conformational changes in the environment may be accounted for by Monte Carlo methods and transition-path search methods.

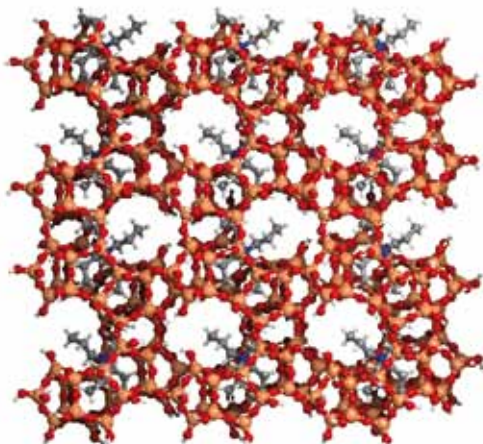


Fig. 10

Zeolite synthesis intermediates can be modelled using Molecular Dynamics tools. The formation of zeolitic precursor intermediates in contact with structure directing organic template in solution is shown. After synthesis the template becomes incorporated in the zeolite micropore (Ook weer ik weet niet hoe te refereren, R.A. van Santen et.al. Topics in Catalysis (Groep: Rutger van Santen, Technische Universiteit Eindhoven))

Very often such methods require the use of assumptions to integrate one level into the next, creating unwanted artifacts in the calculations. There is a need for methods to improve this.

This is even more important as long as we do not have methods available that are able to predict the Van der Waal interactions, often relevant for conformational changes. In such a case, Quantum Mechanical (QM) and Molecular Mechanics (MM) procedures have to be combined (QM/MM).

Models with extended time and length scales are relevant for the design of optimum circumstances for a catalytic system. Catalyst preconditioning, size effects of dispersed particles, and the morphology of microporous systems are all important for catalytic action. But this area is little explored in terms of computation. Molecular Dynamics (MD) methods based on force fields can be used when adequate potentials are available. Otherwise Car-Parrinello Molecular Dynamics (CP-MD) methods are useful. These can be used to compute the rates of condensed-phase reactions. Another important area of attention is the interaction of organic structure directing molecules with inorganic cluster precursors for zeolite synthesis. For the preparation of nanoporous materials with pores of larger dimensions, self-assembly of SDA lipophilic molecules is relevant. Here, coarse-grained methods can be usefully applied to extend length and time scales.

It is interesting to note that nature itself sometimes takes a multi-scale approach. Synthesis may proceed from the molecular to the nanoscale. At the intermediate level, aggregates may be formed undergoing preannealing processes before crystallization eventually occurs. These are complex reaction sequences in which dynamic events of different time and length scales play a role. Colloid chemical aspects are now becoming increasingly important too.

Also for metal-mediated catalysis the fine details of coverage dependence, surface reconstruction and, generally, the effect of particle size are little understood. Molecular models of the action of promoters are even more scarce. The challenge now is to computationally explore in full detail the integrated, complex features that control heterogeneous reactions. Relevant catalytic reactions of great interest are all the reactions steps and materials that relate to the Fischer-Tropsch reaction. Hydrocarbon activation on many catalytic systems are now open for theoretical exploration. Also, the realm of catalyst synthesis is now ready for computational study. This implies again, as a great challenge, the extension of the computational methodology to more macroscopic

time and length scales on which catalytic events really occur.

In the case of catalyst systems in a solution, quantum mechanical calculations can be linked to particle motions. This is complicated if the solvent is part of the reaction. Systems of this kind are studied in Amsterdam. One example is the absorption of a hydride in an aldehyde. In this process, a proton is bound to oxygen. This proton does not come from the catalyst, as is the case during the gas phase, but from the solvent. In the event of a proton transfer, the influence of the solvent may be well described in quantitative terms. In such instances, the Van der Waal interactions can also be integrated into the model.

An important challenge lies in the prediction of enantio selectivity. This would constitute an important advance in the more efficient production of stereospecific medicines.

Arithmetic power is a limiting factor, too. A smart combination of various arithmetic methods should therefore be developed. For instance, quantum mechanics may be limited to the reactive part of the system.

For electrocatalysis, the key challenge remains to develop a first-principles simulation of an electrochemical reaction in which all aspects of the electrochemical interface are treated consistently and accurately. This also implies the integration of different aspects of catalysis. It is necessary to control the electrode potential with respect to some well-defined reference. This is, of course, inherent to electrochemistry. It essentially entails setting up a non-equilibrium simulation in which there is a continuous gradient of electrochemical potential, either by artificially separating charge or, preferably, by creating two regions in the simulation cell with different (but controllable) electrochemical potentials. It would be a considerable breakthrough to find an accurate but not very computationally intensive way to achieve this. Also a full and consistent treatment of the solvent (water) is necessary, in order to probe the role of the aqueous environment on various types of reactions, ranging from “simple” electron transfer chemistry (Marcus theory) to electrocatalytic reactions in which water acts as hydrogen or oxygen donor. This also concerns the accurate calculation of redox potentials. The role of the solvent and double-layer ions demands extensive computer time to ensure good statistical sampling. There have been calculations of electrocatalysis in the presence of water, but they are a far cry from the actual reactions that occur. Mapping out reaction paths in the presence of water, at finite temperature, would be a very important next development, but will depend heavily on method development in a computational chemistry community. At the same time, smart ways should be devised to systematically probe the fundamental role of water and screening ions without having to resort to large-scale, brute-force calculations. The exploration of model systems of increasing complexity is an important approach in this regard. Another important area of attention for electrocatalysis involves modeling screening by the double layer ions, and its effect on reactivity.

First-principles calculations will offer more realistic molecular modeling of electrochemical reactivity. But this is only the first step. The next major challenge is to derive voltammetry observables from it. This includes the calculation of thermodynamic quantities such as redox potentials, (potential-dependent) binding energies, and electrosorption valencies,

as well as non-equilibrium observables such as voltametric curves. Kinetic Monte Carlo simulations provide the statistical-mechanical link between first-principles calculations and voltammetry, but developments in this area have stagnated, primarily because there is a lack of good model systems, and because it is costly to conduct accurate calculations involving water and double-layer ions. Nevertheless, this is a field where important advances may be expected in the coming years.

Another obstacle on the way to more comprehensive models for different types of catalytic systems is the determination of the pathways and transition states that connect the educts, intermediates, and products. This is still labor-intensive and time-consuming handcraft that involves much experience, skill, and chemical intuition, in combination with many trial-and-error cycles.

Very few reactions have been described in conclusive detail in this manner. One of the best examples involves zeolite proton-catalyzed reactions, such as isomerization and cracking. Even for these reactions, there is still a debate on how to understand in detail the role of the zeolite lattice or cavity. This question is even less resolved when cations are used as promoters.

It would be a great leap forward if we could automatically evaluate all reasonable competing pathways that lead from educts to products. A promising development in this respect are approaches such as the Nudge Elastic Band (NEB), transition-path sampling, meta-dynamics, and parallel tempering. An exciting contribution is also the use of Configurational-Bias Monte Carlo (CB-MC) methods that predict the conformation and chemical potentials of adsorbed phases as a function of pore filling. These and yet unknown techniques must be further developed and validated. Also potentials for complex systems are not yet fully available.

There is a need to improve these simulations using combined scaling methods. This would bring us closer to the final goal of automated “transition-path finding”.

As our analysis tools and models gain more qualitative physical understanding of catalysis, we are now about to take the next step. Once we understand, we can also create. Our knowledge has matured to such an extent that we can use it for a rational design of functional agents and materials, as we can identify the essence of what causes catalytic activity and selectivity. This opens routes to completely new principles of catalyst design. It also allows more efficient cross-coupling of insights from homogeneous and heterogeneous catalysis and physical and synthetic organic chemistry. This novel rational computational design may be combined with existing experimental techniques, such as high throughput screening, where dozens of automated experiments are performed in parallel. Calculations may make those experiments more directed. This may boost the speed with which new catalysts, processes and materials can be developed.

Experimental results in turn may provide validation of the models. It is therefore desirable for the simplest possible model systems to help provide testable data. This experimental feedback supports the development of theoretical models and will also speed up more

applied experimental and industrial catalysis.

These challenges apply to all types of catalysts, be it homogeneous, heterogeneous or biologically inspired. In all fields, it is important to work on automated “transition-path finding,” rational design, and extension of time and length scales.

It is important to note that computers are not the only factor dictating theory in catalysis research. There is a continuous need to work on analytical theories of catalysis.

Theories are emerging that relate trends in activation energies as a function of substrate bond type with the topological structure of the reactive centers. Theories are available that relate electronic structure of catalyst with trends in interaction energies as well as activation energies. Bond order conservation rules can be used to study lateral interactions between coadsorbed overlayer species. In concreto, it is promising and highly interesting to extend the Activation Strain Model for homogeneous and bio-catalysis to the realm of heterogeneous catalysis.

This implies that is becoming possible to apply modeling approaches, using parameters available from such theories, in making predictions for designed complex catalysts.

## AREA 4: NEW CATALYTIC CONVERSIONS

The past decade has seen rapid development in rendering chemical processes more benign. A lot of catalytic ingenuity was invested in de-NO<sub>x</sub>-ing, N<sub>2</sub>O-decomposition, desulphurization, etc. Catalysis was effectively applied in cleaning up waste streams.

Next to these developments, highly selective reactions have been developed for hydrogenation, cross coupling and metathesis reaction, improving the efficiency the production of fine chemicals in a dramatic way. In addition to these developments, the challenge of the next decade will be to increase sustainability, towards an improved and durable quality of life. This will require a fundamental approach and invention of net catalytic processes that actually prevent further changes to our environment.

Global development has reached a stage where the limits of natural resources as well as the environmental impact of human activity also present clear boundaries for future development.

The reduction of carbon dioxide emissions and the reduction of carbon content in the earth's atmosphere, requires more than end-of-pipe solutions. There is a clear need for energy sources with reduced carbon emissions or even processes that remove carbon from the atmosphere.

This requires a fundamental transformation of today's industrial processes, leaving resources for future generations. Our success will strongly depend on catalytic technologies. We need to diversify our carbon feedstocks, including efficient biomass conversion, but we also need to make chemical transformations more atom- and energy-efficient. There is a clear need for new catalytic conversions that will allow more efficient transformations, some of which are simply impossible or unknown today, and others that are known but that at present only work in a stoichiometric fashion. This is the field which is addressed by this

working program. A concerted effort should be made, applying the combined knowledge on catalysis and chemistry, to design and develop new catalytic transformations.

## Atom efficiency

An important key to the effective use of feedstock and minimization of waste is the substitution of classical organic syntheses, employing stoichiometric amounts of reagents, with cleaner catalytic alternatives.

There are many areas of improvement, especially in the downstream processing of fine chemicals and pharmaceuticals. The ratio of waste (and byproducts) to product is typically 20:40 in these production areas (by weight, this is the so-called E-factor). The development of catalytic versions of such stoichiometric transformations would significantly increase the sustainability in this branch of chemical production. Significant improvements could be made especially through circumvention of stoichiometric protection and deprotection steps, implying and underlining the need for protective, group-free conversions. Similarly, significant improvements could also be achieved through in-situ regeneration of protective reagents and leaving groups. The combination and integration of several catalytic steps and the introduction of additional redox steps can help the solution achieve this goal.

A number of existing catalytic processes would benefit from radical improvement. Many fields would benefit from more efficient and selective catalysts. The development of such systems is based on new chemistry, as well as detailed insight and understanding on the molecular level. This insight is generated by cutting-edge, fundamental research. Experimental and theoretical studies have to be combined in order to understand what really happens, thus ensuring reliable prediction of the properties and performance of catalysts. This demands the development of better and new analytical tools.

Especially in areas where consecutive reactions of target products may generate a selectivity issue, the combination of catalysis and innovative reactor and engineering concepts can bring about significant improvements. Microreactors, for example, offer a number of advantages that may be beneficial for catalytic reactions:

- High surface to volume ratio, allowing for a highly efficient removal of heat for exothermal reactions;
- Short diffusion distances, allowing for higher selectivities in the case of competing reactions, and higher conversions in the case of mass transfer limitations;
- Ideal plug flow behavior, allowing for precise control of residence times, which can be utilized to “stop” a reaction at the right time and prevent over-reaction. This also allows the linking of sequential reactions over different catalysts in the same operational unit;
- Low thermal mass of the unit as a whole, while having a very high thermal mass of the unit as such in relation to the fluids it processes, allowing for temperature steps of the reactants at different stages in the microreactor unit.



The simultaneous use of two immiscible fluids in a microchannel offers new possibilities to reach higher conversion rates and may prevent consecutive reactions. One channel is used for the catalytic reaction and one for the immediate product extraction. The combination of reaction and product separation/extraction may be a major advantage in equilibrium reactions.

For example, the production of primary amines by reductive amination of carbonyl compounds or the hydroaminomethylation would benefit from this latter approach. In hydroaminomethylation, ideally an alkene would be converted with syngas (CO/H<sub>2</sub> 1:2) and NH<sub>3</sub> to a primary amine. However, the primary product amines are considerably more nucleophilic than ammonia, as are the resulting secondary amines. This typically leads to tertiary and secondary, rather than primary, amines. Decoupling of residence time and concentration/location of intermediates, by transferring the reaction into a microchannel, can bring about extended selectivity control. In highly exothermal reactions, the excellent temperature control could allow safe and complete conversion; e.g. in the hydrogenation of dinitrotoluene to form diaminotoluene.

Another example of radical improvement of catalytic reactions is the replacement of expensive noble metals or toxic catalyst metals with inexpensive, non-toxic metals. Recently, it was shown that Pd and Ni can be substituted with cobalt in the codimerization of vinylarenes and ethene. This has the added advantage that, in the case of these unprecedentedly active and chemoselective catalysts, bidentate and even multidentate ligands may be used, unlike when using Pd and Ni.

The hydrocyanation of alkenes is, to date, more or less limited to 1,3-dienes, and DuPont's adiponitrile process is the only larger scale application of this reaction. The reductive elimination of the product from metal alkyl (cyano) species is typically the rate-limiting step in this conversion. Simple alkenes react only in the presence of a Lewis acid co-catalyst, and give only low turnover numbers. New types of bifunctional catalysts, with a Lewis acid center positioned next to the catalyst metal, might result in significant improvement of this reaction.

In the case of alkene epoxidation using air/oxygen, it is currently only possible to selectively and directly epoxidize ethene using air/oxygen, primarily because of the reactivity of the gamma-hydrogen atoms of larger alkenes. Recently, it has been shown that gold/carbon or copper are good candidates for the direct epoxidation of propene and larger alkenes. This may be considered a major breakthrough. The mechanisms of both these systems are, however, only poorly understood and the performance and stability of both these catalysts need to be improved significantly.

There are many more examples of potential reactions that would be of major benefit to many chemical applications:

- Specific catalysis for fine chemical specialty and pharma intermediate production;
- New catalysts for the development of new functional polymers with unique properties, for electronics, light emission, etc;

- Further development of organic catalysts for complex natural products with application to pharmaceuticals;
- The development of manmade selective iron catalyst for the selective oxidation in order to convert natural gas;
- Enantioselective catalysts for the production of pharmaceuticals.

## CO<sub>2</sub> capture and conversion

One of the greatest challenges of our century is to reduce carbon dioxide emissions and to lower atmospheric concentrations of this gas. Carbon capture at the source implies the large-scale production of hydrogen out of fossil fuels, leaving the carbon at its source. Hydrogen is a promising fuel for the transport industry. The current method for producing hydrogen from methane gives off CO<sub>2</sub>, which is still released into the atmosphere, where it contributes to the greenhouse effect. We may be able to capture and store the CO<sub>2</sub> at the source. This may be achieved by way of CO<sub>2</sub> capture at power plants, but it would be fantastic if we could perform this transformation literally at the source, being underground in oil fields, or maybe even in coal seams. The challenge to gasify the oil or coal in situ is to lower temperatures at which gasification can occur. This may be done using catalysts. The required efficiency of the process makes it necessary to shift the equilibrium of the conversion processes at high temperature. This requires the development of new catalysts, new process technology, and possibly also new membrane technology. The hydrogen may be used to generate power in a central plant, or as fuel for transportation. A breakthrough is required in hydrogen storage. Hydrogen can form compounds with metals, resulting in hydrides in which the hydrogen is taken up. Catalytic knowledge may lead to the design of materials that can reversibly store enough hydrogen at a temperature that isn't too extreme.

## Electrochemistry for our energy supply

Another way of producing hydrogen is by electrolysis. But this is not particularly efficient, as 30–40% of the energy is lost in the process. Electrolysis currently costs about three times as much as chemically producing hydrogen from methane. The electrochemical reduction of oxygen is also very costly in terms of energy.

The same limitations hold for fuel cells that generate electricity from hydrogen. Lack of recent progress in this field presents a severe obstacle in developing hydrogen infrastructure. New electrocatalytic materials are needed to reduce the current overpotential of these processes. Also, the limited supply of platinum requires finding a replacement. New catalysts should be developed that can be employed on a large scale without depleting raw materials.

A major advance will be needed to improve fuel cells, ensuring that they are available for about a tenth of their current price. The current high cost may be partly attributed to the fact that the cells require platinum. The challenge is to develop catalytic techniques that make better fuel cells.

There are many fundamental questions to be answered. What is role of water in the case of a reaction during the liquid phase? How does water work as a co-reactant or oxygen? How does water decomposition take place? How does water stabilize hydrolytic reaction paths and other steps in which ions play a part? What is the effect of pH? What role does the potential play? How can this be used in order to control heterogeneous catalyst reactions during the liquid phase? What can be learned from natural reactions in this respect?

## Liquid fuels and bulk chemicals

Our transport and petrochemical industries are largely based on the use of olefins and aromatics derived from fossil feedstock. Switching to other feedstock, such as natural gas, coal, and biomass, requires fundamental changes.

The abundance of coal makes it an attractive feedstock to make liquid fuels. However, the processes involved are not very efficient at present. First, in an endotherm process, coal is converted with steam to a syngas at high temperature. Coal is broken down into carbon monoxide, hydrogen, and lots of carbon dioxide. This process can be improved, increasing the hydrogen yield, with the aid of membranes, for instance. It is important to test these techniques. In a second step, these gases are recombined subsequently to give liquid hydrocarbons. This Fischer-Tropsch process is a complex combination of catalytic reactions. One of the mayor problems is the lack of selectivity. The process usually gives a mixture of different products. We already know how to tune the process to obtain a maximum yield of methanol, but it would be great if we could tune it to other products as well. This may be done now that we are able to produce catalysts with nanoprecision. The challenge is to reach the same level of selectivity, efficiency and flexibility that we have accomplished in a century of development of fossil-based petrochemistry. But we lack insight as to how catalyst nanostructure influences the efficiency of the process. We also don't know which surface properties of the catalysts are responsible for extracting carbon out of carbon monoxide in syngas. This requires intensive research.

Syngas can also be produced from natural gas. Because of the higher hydrogen content of natural gas, making this syngas involves significantly less carbon dioxide production. Again, there is a need for improved and more stable catalysts.

It would be even more desirable to skip the syngas step completely. This would allow the processing of saturated hydrocarbons, such as alkanes, to make chemicals. It would be fantastic if we were able to use more direct conversion routes circumventing the intermediate production of olefins. For instance, we would like to convert methane to methanol and ethane directly into alcohol with the same ease with which we now convert ethene into alcohol. Such processes would give a more direct route, with less energy loss, to make chemicals and liquid fuels out of natural gas. In the same way, we would like to use butane to make maleic acid, instead of benzene. Or propane to make acrolyne. That would open the door to a wide range of petrochemical applications.

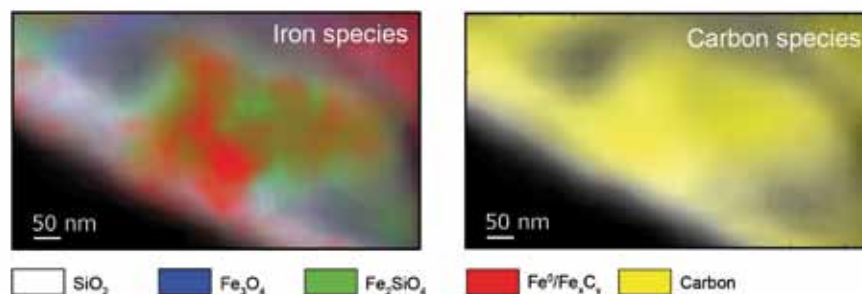


Fig. 11

Chemical maps showing the location of iron species (top) and carbon species (bottom) present on a SiO<sub>2</sub> supported iron-based catalyst after 4 hours of Fischer-Tropsch synthesis. (Groep: Bert Weckhuysen, Universiteit Utrecht)

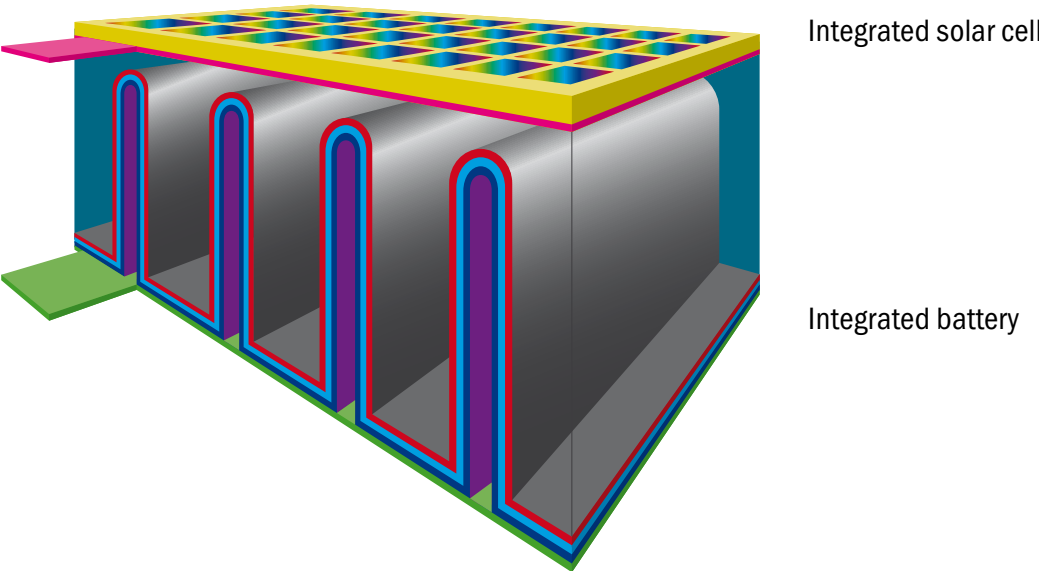
## Biomass processing

Biomass contains various materials, including fats, cellulose, and lignin, that may serve as fuel or as feedstock for further chemical processing. All over Europe, new installations are being built to process the fats contained in biomass, encouraged by European legislation promoting the use of biofuels. Fats were the easiest components to process, but catalytic optimization is needed to make it more efficient and cleaner. Even then, it is not always a good idea to focus on the conversion of fats. In principle, all fats are edible. Using them for other purposes always competes with food production. This is not the case with cellulose and lignin. These are too solid to be digested, with a lot of woody or fibrous biomass. This makes them more difficult to handle in chemical processes. Finding the right catalysts for these conversions is the real catalytic challenge for biofuel production.

## Photocatalysis

Many other alternative energy sources require some form of catalysis. The catalytic capture of energy from light in chlorophyll is an alternative to the present photocells based on semiconductor technology. Study of photocatalysis promises to generate novel devices that produce hydrogen out of water or fixate carbon dioxide.

### Energy scavenging/ storage system



**Fig. 12**  
A device that collects solar energy and connects with microbattery system. It stores the electricity generated in the activated microchannels of a Si waver (Groep: Peter Notten, Technische Universiteit Eindhoven)

## LOOKING AHEAD

We are entering a new era in Dutch catalysis research. During the coming decade, we will encounter and surmount new barriers. The 21st century demands technology ensuring cleaner and more sustainable production methods. We can gain inspiration from the natural environment we want to protect. Catalytic processes in nature are often more benign than in industry. There is plenty of room for improvement. Our dream is to bring about chemical production methods in which all aspects are fully controlled and coordinated, with no by-products and no excess or wasted energy, using small chemical plants that automatically adjust to the conditions in which they operate, located in close proximity to users. Energy consumption would approach the minimum required to bring about the chemical reactions.



## PARTICIPANTS AND CONTACTS

### Research groups



#### Radboud Universiteit Nijmegen

##### Prof. dr. F.P.J.T. Rutjes

Synthetic-Organic Chemistry. The group synthesizes highly functionalized bioactive compounds. To this end various catalyst materials are used such as metal catalysts, organocatalysts and enzymes. Besides this, the group focuses on fundamental catalysis. Recently the group carried out research on heterocycle-synthesis, enzymatic peptide synthesis, specific ligand synthesis for C-C-binding reactions and metathesis.

##### Prof.dr.ir. J.C.M. van Hest

Bio-organic chemistry. The research within this group is positioned at the interface of 3 disciplines: organic chemistry, polymer chemistry and molecular biology. Inspired by concepts found in Nature, biomimetic materials and processes are developed by applying advanced synthetic techniques. Four lines of research have been set up, based on this common theme: peptide-based materials, functionalized liposomes, nucleobase polymers and miniaturised reaction systems, also known as process on a chip.

##### Prof.dr. A.E. Rowan

Molecular Materials. The group focusses on the construction of a variety of catalysts. The aim of the group is the design and synthesis of novel polymers, self-organizing molecules and ordered crystals and the subsequent investigation of their properties. The relationship between the molecular structure and architecture at the nanometer level and the material properties are be studied.



#### Rijksuniversiteit Groningen

##### Prof.dr. B.L. Feringa

As head of the Stratingh Institute of Chemistry and Technology Feringa leads the way in the field of research of molecular anorganic chemistry, bio-organic chemistry and the making of organic materials. His research focuses on organic synthesis and in particular supramolecular systems, for example molecular machinery. Important related phenomena like self-organization and selfrepair are also studied.

##### Dr. G. Roelfes

The group uses a combination of organic, molecular inorganic, and bio-chemistry to develop new concepts in (bio-)catalysis and obtain new insights into how the catalysts from nature work. The main research themes in the group currently are: "DNA as a scaffold for new (bio-)catalytic systems", "development of new DNA cleaving agents", and "semi-synthetic proteins".

##### Prof.dr.ir. A.J. Minnaard

Bio-organic chemistry. His group develops new organic reactions for the synthesis of complex molecules. He hereby focuses on the synthesis of very complex natural substances (lipides, carbohydrates). In doing so, enantioselective carbon-compounds are used.



## Technische Universiteit Delft



### **Prof.dr. F. Kapteijn**

Precise synthesis of catalysts. The group focuses on catalyst engineering by applying chemical engineering to catalysis.

### **Prof.dr.ir. M.T. Kreutzer**

Microfluidic devices are used to control kinetics and dynamics. Parallelizing is an important strategy for scaling up. These kind of reactors are also used for making photocatalytic devices.

### **Prof.dr. I.W.C.E. Arends**

Biocatalysis. The group has a vast laboratory at its disposal for stabilizing and immobilizing natural enzymes. Recent research has focused on nitrile hydratase, hydrolase and oxyde reductase enzymes. The emphasis is on the integration of catalysis in synthesis, novel conversions and directed evolution of enzymes.

### **Prof.dr. W.R. Hagen**

Enzymes. The group carries out fundamental and applied research in the field of enzymology: the bio-chemistry, biophysics and molecular biology of enzymes in living cells and as purified chemical compounds. Emphasis is on the bioconversions by redox enzymes, in particular metalloenzymes, from extremophilic organisms, i.e. with a putative, intrinsic added value of stability under typical operational conditions for practical applications. A general Leitmotiv is the study of physiologi-cally related proteins (e.g., metallo-enzymes, metal transport, metal insertion) as elements of a sub-network of the cell machinery with the objective to gather an understanding of integrated biological functioning.

## Technische Universiteit Eindhoven



### **Prof.dr. E.W. Meijer**

Supramolecular organic chemistry. The research program is aimed at the design, synthesis, characterization and possible applications of complex (macro)molecules with unconventional properties. Combining supramolecular architectures and knowledge of chirality results in novel concepts in catalysis. Emphasis is on self-replication and the mechanisms of selecting right- or left-handed chirality on all length scales. Emphasis is also put on enzymatic catalysis to make polymers and to use enzymes for biomedical assays.

### **Prof.dr. R.A. van Santen**

Computational and spectroscopic analysis of complex catalytic systems. The group focuses on the theoretical analysis of reaction kinetics, using calculations of transition states, reaction rate constants and time dependent Monte Carlo methods. Also in situ spectroscopic techniques are developed, such as positron emission profiling. Biomimicry and systems for our energy supply are important themes of the group.

### **Prof.dr. D. Vogt**

Complexity in organocatalysis. Examples of research include corporate activity in bi- or multimetal catalysis and efficient carbon-nitrogen binding compounds. The group also examines non-noble metals which can replace scarce noble metals as catalysts.

**Prof.dr.ir. J.C. Schouten**

Microfluidics for gas-liquid systems. The research is focused on polyphase reactors, whereby techniques are developed to optimize the lingering period, thermal management and the dynamics at interfaces. Recent research has focused on spinning disc reactors, reactors using foams and microchannels.

**Prof.dr. J.W. Niemantsverdriet**

Physical chemistry of catalytic surfaces. The group relates the structure and composition of surfaces in atomic detail to their reactivity, by exploiting a range of advanced surface sensitive tools, kinetic analysis and computational methods. Main subjects of study are the interactions between adsorbate species and kinetics of elementary reactions on metal surfaces, modeling of supported catalysts (in polymerization catalysis, the hydrodesulfurization of hydrocarbon feed stocks and Fischer-Tropsch synthesis), and surface characterization of polymers, coatings and natural fibers.

**Prof.dr. R.P. Sijbesma**

Supramolecular polymer chemistry. In the group, the application of hydrogen bonding takes a central position. The design of synthetically accessible hydrogen bonding units has played an important role in the development of 'supramolecular polymers', polymers in which the monomeric units are held together by non-covalent interactions. The ready availability of these hydrogen bonding units and their extremely high binding constants allows the study of many fundamental aspects of supramolecular polymers, as well as the development of this novel type of polymers as promising 'smart' materials with commercial applications.

**Universiteit van Amsterdam****Prof.dr. J.N.H. Reek**

Supramoleculaire homogeneous catalysis. The group aims at the development of novel concepts for catalysis. Bio- inspiration is often an element in the new approaches. Influencing catalyst performance via secondary interactions between ligands and activating auxiliaries or substrates is one approach. Ligand formation by assembly to form new catalyst is an interesting new development, as well as DNA and peptide based ligands. The creation of local environments that may induce specific selectivities or high reaction rates is an important goal.

**Prof.dr. H. Hiemstra**

Organocatalysis. The group works on enzymes which are modified by directed evolution in order to carry out new reactions. Recently, research was conducted on the enzymes phosphatase and sulphatase. Besides this, research is conducted on precursors for iminium ions in view of pharmaceutical and biological applications. In addition, click chemistry using for instance copper catalysts and cyclical peptides is researched.

**Prof.dr. R. Wever**

Biocatalysis. The group focuses on the use and development of biocatalysts in synthetic organic chemistry as a green alternative for existing chemical procedures. The group members discover new enzymes, modify others and test their potential use in novel synthetic procedures. Suitable expression systems with convenient hosts are developed for enzymes of interest. After purification and characterization the recombinant enzymes are subjected to screening of their substrate specificity, regioselectivity, enantioselectivity and their potential application. Directed evolution is used as a tool to optimize and improve selected enzymes. In general organic conversions with enzymes are performed in aqueous media.

**Prof.dr. C.J. Elsevier**

The group focuses on fundamental research in coordination and organometallic chemistry, notably the synthesis, characterization and application of organometallic compounds and homogeneous catalysts. The reactions concerned are mainly bond-forming and bond-breaking reactions between carbon and the other elements, with emphasis on carbon, hydrogen, and late transition metals. Processes studied are, e.g., hydrogenation, hydrosilylation, and C-C coupling reactions. Several of these are studied under pressure and in neoteric solvents, e.g. supercritical fluids. Spectroscopic studies of reactions under pressure are carried out to evaluate the reaction and intermediates under conditions similar to those in the catalytic reactions studied.

**Prof.dr. G. Rothenberg**

The research of this group focuses on finding and optimising new catalysts and materials for a range of applications in the areas of sustainable chemistry and sustainable energy. Specifically, the group develops methods focused on the combination of experimental and computational tools.

**Universiteit Leiden****Prof.dr. M.T. Koper**

Electroanalysis and catalysis of electrode reactions. The group examines inter alia water splitting, one of the main challenges in the catalysis of energy provision. Oxidation of water constitutes the bottleneck in this process. In addition, the research is focused on ethanol oxidation which is important to fuel applications. In this context the electroanalysis of the nitrogen cycle (for removing nitrate from waste water) is to be mentioned too.

**Prof.dr. J. Reedijk / dr. E. Bouwman**

Bioinorganic chemistry for new systems. Fundamental research in the synthesis, characterisation and application of coordination compounds in (biomimetic) catalysis, materials and in medicinal applications of such compounds. The design of the ligands, with their steric and electronic constraints is a main starting challenge, and from here the prediction of the coordination geometry and intramolecular interaction and reactivity is a major goal. Themes include the activity, selectivity and mechanistic details of oxidative phenol coupling, bio-mimetic oxidations of organic compounds and chelating imidazoline-based Carbenes in homogeneous catalysis.

**Universiteit Twente****Prof.dr.ir. L. Lefferts**

Catalytic systems and micro devices. The group examines new materials in order to improve the accessibility of catalysts and their active sites in liquid phase processes. Ideally packed beds, microplasmareactors and high-pressure reactions are also produced. In addition, techniques for characterizing the interface of fixed catalysts in the liquid phase are developed and micro-NMR is applied.





## Universiteit Utrecht

### Prof.dr. B.J.M. Klein Gebbink

Biological and synthetic chemistry of transition metals. The group focuses on organometal fragments, new catalyst structures and the use of biorenewables. Non-heme iron enzymes, a very reactive catalyst, are also being investigated. In this research extra attention is paid to immobilizing catalysts using for instance large dendrimers. Another focus is on artificial metallo-enzymes (serine hydrolases).

### Prof.dr.ir. K.P. de Jong

The group carries out research in the field of catalysis, gas adsorption, hydrogen storage and CO<sub>2</sub> capture, with an emphasis on processes determined by the nanometer scale, such as particle size effects in catalysis and the changes in gas sorption due to cluster size. Recent research has focused on nanostructured carbon using chemical vapor deposition. Hydrogenation catalysis is an important focus, and relevant for the Fischer Tropsch process. Systems for hydrogen storage, for instance on the basis of magnesium and sodium alanate, are also researched. Precision in the synthesis of nanostructured materials is a key element of the research.

### Prof.dr.ir. B.M. Weckhuysen

Spectroscopy. The central research theme of this group is the development of structure-activity relationships and expert systems in the field of heterogeneous catalysis and materials science with special emphasis on the development and use of advanced in situ characterization techniques. Another area of interest is the molecular design of transition metal ion complexes in inorganic hosts for catalytic and sensor applications. Enzymes, the most effective catalysts in nature, are the inspiration source for this research.



## Vrije Universiteit

### Prof.dr. E.J. Baerends

Computational chemistry. The group is primarily involved in the development of density functional theory (DFT) and quantum chemical methods and codes based on DFT and in the application of these methods for developing chemical theories and concepts. Recent research results inter alia focus on the functional design of catalysts, DNA-duplication and oxidation catalysis.

### Prof.dr. F.M. Bickelhaupt

Theoretical chemistry. The group aims at developing chemical theories and methods for rationally designing molecules, nano-structures and materials as well as chemical processes toward these compounds, based on quantum mechanics and computer simulations. An essential part of these efforts is the application of theories and models in cooperation with experimental groups. The four main directions of research of the group are intimately connected and reinforce each other: structure and chemical bonding in Kohn-Sham density functional theory (DFT), molecular recognition and theoretical biochemistry, elementary chemical reactions and fragment-oriented design of catalysts.

### Prof.dr. K. Lammertsma

(Bio-)organic catalysis. The group is currently focusing on phosphorous chemistry, whereby artizymes constitute an interesting alternative to the production with minerals. Other bio-inspired synthesis is being developed to create new applications for the pharmaceutical industry. The group develops multicomponent synthesis and tandem processes and incorporates biocatalysis in multicomponent synthesis.

**Prof.dr.ir. R.V.A. Orru**

Bio-organic synthesis. The main focus of the group is the development of highly efficient, asymmetric synthetic methodologies and their application to the synthesis of diverse, biologically relevant compounds, with an emphasis on atom and resource efficiency. The group studies the rational design and development of flexible novel multicomponent reactions (MCRs), the use of biocatalysts for the production of enantiopure building blocks and resolution of racemic MCR products, and the development of asymmetric versions of MCRs and related processes using biocatalysis and/or homogeneous catalysis.

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