

Splendid Science 2006

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Foreword

Professor K.Ch.A.M. Luyben - Dean, Faculty of Applied Sciences TU Delft - The Netherlands

The domain of science is often incomprehensible and impenetrable to outsiders. Even fellow scientists frequently have no idea what kind of research their colleagues from other fields are conducting. With this publication, the Faculty of Applied Sciences of Delft University of Technology (TU Delft) hopes to provide a look behind the scenes.

Splendid Science gives the floor to scientists of each of the faculty's six Departments who in turn shed more light on wonderful examples of inspiring research. The subjects range from the use of nanoparticles for hydrogen storage to bubble flows in fluid columns.



Not only do the articles illuminate examples of truly splendid science but they also show how the Faculty's research focuses on scales of increasingly smaller size. Scientists in the Departments of Nanoscience and Imaging Science & Technology concentrate on the nanometer level: the Nanoscientists study, and even manipulate single DNA molecules, whilst the Imaging Physicists hold a world record in fabricating structures at the scale of only one nanometer. The Radiation domain uses the smallest elements, positrons and neutrons, to study the composition and behaviour of complex materials. Researchers at the Department of Biotechnology investigate how biomolecules can be used as catalysts for chemical reactions. Taking the molecule as a starting point, the Chemical Engineers adapt them for large-scale industrial processes, drawing on nature for inspiration. Controlling industrial processes is also the goal of the Multi-Scale Physicists in studying the interactions of bubbles and their environment.

These articles show that gaining a better understanding of fundamental aspects leads to advanced insight and control of processes. I cordially invite you to join us and enter the magic of this small world.



Prof.Dr. Roger Sheldon - Department of Biotechnology

Revolution in green solvents

Many chemical reactions traditionally require volatile organic solvents that are hazardous, environmentally unfriendly or both. Enzymatic reactions, however, can very well take place in a much more friendly medium: ionic liquids. Advantages are plenty.

Almost ten years ago, Prof.Dr. Roger Sheldon attended a scientific lecture that not only triggered his interest, but also steered him onto a new path in his scientific career. It was during this lecture that Sheldon, head of the Section of Biocatalysis and Organic Chemistry (BOC) at the Department of Biotechnology of the Faculty of Applied Sciences, was introduced to the concept of ionic liquids as a medium for chemical reactions.

Ionic liquids are salts that are liquid around room temperature. They contain only ions – charged particles or molecules – and no water. The speaker, prof. Kenneth Seddon from the University of Belfast, announced that these ionic liquids could replace traditional solvents as a medium for chemical reactions. Sheldon immediately wondered if this would also apply to his own specialty: biocatalytic reactions. These use enzymes – proteins originally found in nature – as catalysts.

'The problem with traditional solvents is that they are often volatile as well as toxic, and often even hazardous,' says Sheldon. 'Chlorinated hydrocarbons are a notorious example. They end up in the air or in groundwater and pose a threat both to human health and the environment.' A logical

alternative would be to use water as a solvent. In water, however, the thermodynamic equilibrium of many industrially useful chemical reactions is unfavourable for practical purposes. In non-aqueous media, such as ionic liquids, the equilibrium is much more favourable. Moreover, as pointed out by the Belfast scientists, many reactions proceed faster in ionic liquids than in traditional solvents.

'I went up to Seddon after the lecture and asked him whether he'd applied this principle to enzymatic reactions as well,' Sheldon relates, 'but this wasn't the case. He did find it an interesting idea, and we decided to explore this question together.'

Dissolving power

The combined research soon produced promising results: enzymatic reactions did indeed proceed in ionic liquids. 'This was an amazing discovery,' says Sheldon. 'It appeared that our enzymes performed very well in a water-free ionic liquid.' He elaborates on several examples, including the esterification of sucrose, a common sugar. When sucrose molecules and fatty acids are chemically joined to form an ester, the

product functions as a bioemulsifier. Emulsifiers are used in many food products, such as creams and sauces, to suppress separation of the emulsion. Esters are traditionally produced using synthetic catalysts such as sulphuric acid. 'But in the case of sucrose these reactions yield products that are complex mixtures of esters. When catalysed by specific enzymes, on the other hand, the reactions yield a product that is much more pure.' Sucrose, however, is only sparingly soluble in most traditional solvents, which results in very low reaction rates that are not economically viable.

Putting two and two together, Sheldon first tried some simple esterification reactions using enzymes in water-free ionic liquids. 'And they worked extremely well,' he enthuses. The same was true for the actual sucrose esterification. 'It is possible to design ionic liquids that dissolve several hundred grams of sucrose per liter, which is quite remarkable. Furthermore, many other chemical compounds, even complex polymers, proved to be more soluble in ionic liquids than in traditional organic solvents.'

No reliable precedent

From an engineering point of view, Sheldon was amply satisfied with these findings, but from a scientific point of view his journey had only just begun. 'The more we experimented, the more the underlying scientific questions started to intrigue us,' he says. 'As opposed to the reactants, the enzyme is not usually dissolved in the ionic liquid solvent but rather suspended in it. When the enzyme dissolves, it loses its activity. I became very curious to see whether it would be possible to design an ionic liquid that would dissolve the enzyme while maintaining its functionality.' This proved to be possible indeed. Incorporating hydroxyl groups into the ions making up the ionic liquid, thus increasing its resemblance with water, did the trick.

'The advantage is not immediately clear,' he admits, 'because it makes it harder to separate the enzyme from the solvent during recycling. There are instances, however, when dissolving the enzyme could present an advantage. For example, when the product precipitates from the reaction medium, as is the case with certain polymers, separation of the enzyme from the product would be facilitated.' Separating the reaction's end product from the ionic liquid is a challenge in its own right. When the end product is volatile it can be distilled; when it is insoluble it is easily isolated as well. The problem arises when the product is dissolved in the ionic liquid. 'There are several ways of tackling this problem,' Sheldon explains. 'One involves extraction with supercritical carbon dioxide - carbon dioxide at high pressure and slightly above room temperature. This is a technique also used to extract caffeine from coffee. It can be performed in a continuous operation whereby the ionic liquid is the stationary phase and the supercritical carbon dioxide is the mobile phase. The product is recovered from the supercritical carbon dioxide phase by depressurisation.'

Sheldon is collaborating with colleagues Cor Peters and Geert-Jan Witkamp at Delft University of Technology's Department of Chemical Engineering on an innovative elaboration of this methodology, in which the reaction is performed at a pressure where the carbon dioxide and ionic liquid are miscible. After completion of the target reaction, this homogeneous system is depressurised and separates into a two-phase system: the product is dissolved in the carbon dioxide phase and the enzyme in the ionic liquid phase. Separation of the two phases is relatively easy. Upon further depressurisation, the end product can be separated from the carbon dioxide. 'This method employing a so-called 'miscibility switch' is still in its infancy,' says Sheldon. 'We are trying to find funding for further research, but an inherent problem with innovative research is that there is no literature precedent. And that is what, incredible as it may seem, referees of research proposals often require.'

Perfect recipe

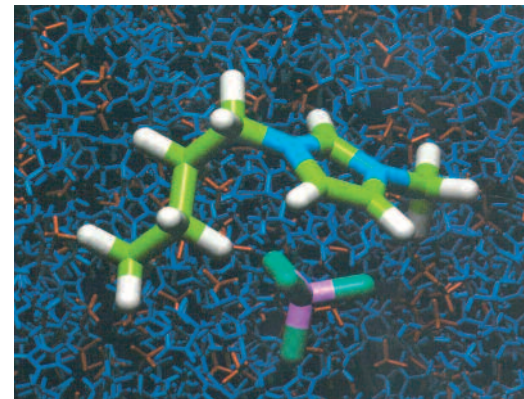
Sheldon points out some other advantages of ionic liquids as green solvents. 'Enzymes are very selective in the reactions they catalyse. They often even distinguish between different enantiomers: mirror images of molecules that are otherwise similar. In ionic liquids this selectivity is sometimes even better than in organic solvents.' Enzymes also appear to be more stable in ionic liquids. 'Enzymes are large protein molecules that are folded in a particular way,' he explains. 'Their folding pattern determines their functionality. In some organic solvents, however, enzymes are easily unfolded, which alters or even destroys their activity. Ionic liquids seem to prevent, or even reverse unfolding.' Exactly how this works is a mystery that Sheldon would love to unravel.

The advantages appear too good to be true. Some aspects, however, remain to be improved. Sheldon: 'Although enzyme activity is much higher in ionic liquids than in organic solvents, it still doesn't approach enzyme activity in water. It is a problem that keeps challenging us, but I am convinced that we'll succeed in improving the activity even further.' Another challenge is purifying and perfecting the ionic liquids themselves. 'It is really a question of mixing different ingre-

dients in the appropriate quantities,' Sheldon points out. 'We're still looking for the perfect recipe for each of our target reactions. The choice of the ionic components determines parameters such as activity, viscosity and environmental sustainability. It also determines the price, which in turn predicts whether an innovation will be a commercial success. But with an increasing demand the price is bound to become less of a problem.'

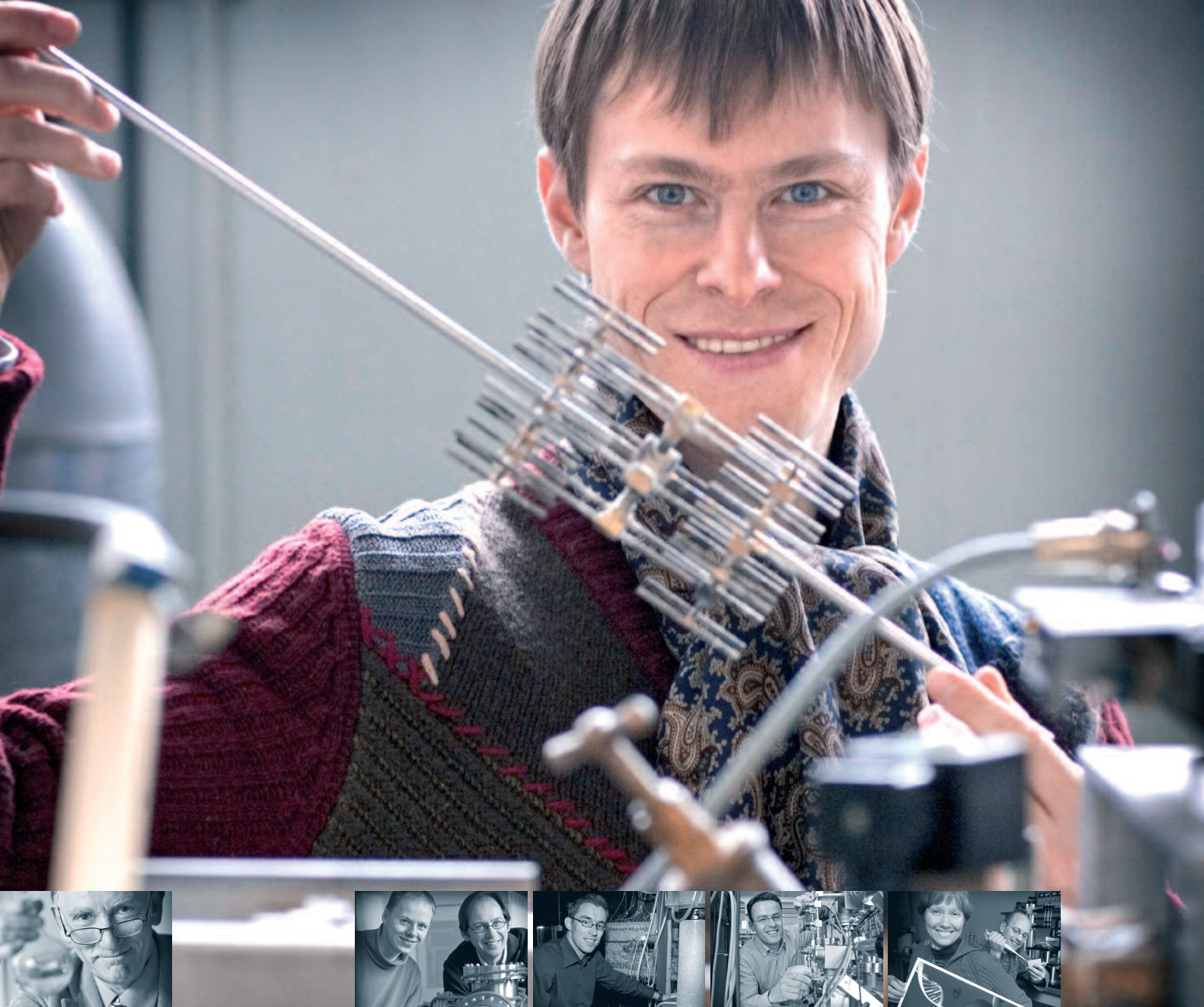
Sheldon and his colleagues are also planning on extending their scope to include different kinds of enzymes, targeting not only hydrolysis, but also oxidation and reduction reactions. 'We are even looking at what is possible in relation to fermentation, a biological process performed not by separate enzymes but by entire living cells. Letting part of the fermentation process take place in ionic liquids might eliminate the need for distillation of the end product, for instance ethanol. This would save considerable amounts of energy, something that might prove to be a decisive factor determining the potential of ethanol as a biofuel.'

Applications abound. As the technology is still new, it is difficult to predict which way it will go. In any case, the total number of publications on ionic liquids has risen dramatically over the past few years, and applications are already gradually finding their way into industry. 'Ionic liquids will certainly not solve all of our problems,' Sheldon concludes, 'but they will absolutely find their niche.'



Ionic liquids are salts that are liquid around room temperature. They consist of charged molecules, in this case 1-methyl-3-butyl-imidazolium tetrafluoroborate. Credit: TU Delft/BOC and the Royal Society of Chemistry





Prof. Dr. Ir. Mark-Olivier Coppens - Department of Chemical Engineering

Inspired by nature's chemical machinery

Nature displays an amazing array of pathways and processes that are brilliantly organised and highly efficient. Chemical engineers at Delft University of Technology try to use these natural principles to optimise industrial processes.

Concepts from nature have inspired engineers since time immemorial. Leonardo da Vinci studied birds and bats to improve his aeroplane designs, and Gustave Eiffel derived the architecture of this famous tower from the internal structure of the human hip. Many of nature's principles have led to technological applications, ranging from machines to materials to industrial processes. Nature implements countless concepts that surpass man's current designing ability and trigger the imagination.

'Chemical engineers have taken remarkably little advantage of these insights,' says Prof. Dr. Ir. Marc-Olivier Coppens. A champion of nature-inspired chemical engineering, Coppens is conducting pioneering research at the Faculty of Applied Sciences' Department of Chemical Engineering. 'Aided by chemists and physicists, chemical engineers know increasingly well how to design and optimise processes down to the molecular level, but when translating these to a larger, industrial scale, they typically abandon the rational approach and proceed empirically.' Their method of trial and error hardly ever yields the most efficient solution. Looking at nature, however, offers an opportunity to discover intricate ways of scaling up chemical processes. This is the ap-

proach Coppens advocates. 'Nature's way is not a dogma. It is just a tremendous source of inspiration.'

Trees, lungs and rivers

'Just look at a tree,' Coppens says. 'A tree is in fact a large chemical reactor: it converts water and carbon dioxide into sugar and oxygen, while growing at the same time. At the cellular level, the reactor is both complex and efficient. Specialised organelles each perform their own step in the reaction chain. However, the system only functions if the necessary chemical compounds, the building blocks, are transported to the right places, while the waste products are effectively removed.' This is done by the tree's circulatory system. The roots as well as the tree crown consist of a repeatedly branching network of channels linking the trunk to the thinnest roots and the finest twigs. The branching pattern, as Coppens points out, has a unique characteristic. 'It shows a so-called fractal symmetry, at least in a statistical sense: the shape of each part is indistinguishable from a larger part, only at a different scale. The pattern looks the same under any magnification.' The interesting thing is that

this pattern is universally present in nature, as Benoit Mandelbrot discovered in 1975. Our lungs, our vasculatory system, our kidneys, and even a river branching off and atmospheric eddies breaking up: all show a fractal symmetry.

'Chemical engineering has neglected this principle,' stresses Coppens. 'Look for instance at the pipes that are used to inject a chemical into a reactor. They do split up, but always like a multi-toothed fork and never like a river. The result is that the distance between the inlet and the point where a chemical is actually released, is different for each pipe. Consequently the pressures are different for each of them, and the chemicals are never evenly distributed - unless a high inlet pressure is used to overcome maldistribution, which is costly and inefficient.' When a branching distribution system is used, it is built in a purely empirical way. However, if these pipes were divided in a fractal way, the pressure would be equal in all pipes, even if one of them were broken or clogged, and even at lower upstream pressures. 'A reactor using fractal injection is therefore not only more robust than a traditional one, it also requires considerably less energy. And that is what we need for sustainable engineering.'

Most importantly, however, fractal injection allows chemical reactions to proceed more efficiently. The injector can release a chemical evenly throughout a reactor, which avoids local concentration differences that hamper the reaction. 'A good industrial example is a gas-fluidised bed of solids,' says Coppens. 'This type of reactor contains reacting or catalytic solid particles through which a gas is injected at the bottom. When this upward flow is sufficiently high, the solid particles start behaving like a liquid and the gas will form bubbles. As these bubbles rise, they merge to form larger bubbles.' Local conditions therefore differ, which affects the associated chemical reactions. This makes it difficult to predict and control these reactions, and to scale up the industrial process. 'All of this is a lot easier when gas is

injected not only from the bottom, but throughout the reactor by fractal injection,' notes the chemical engineer. 'For the same total amount of gas, the bubbles are smaller and more homogeneously dispersed, which improves contact between gas and solids.'

Theoretically, scale-up will not affect the nature of these reactions, since the distance between the outlets is kept constant. Only the number of 'generations' in the hierarchy is increased. Whether this will be true in practice remains to be tested, but Coppens is optimistic, based on running experiments and calculations. The next step is to identify the optimal hierarchical structure for different technological processes. Having a different function, for instance, lungs and kidneys require different fractal geometric parameters. These also differ among animal species. In chemical engineering this will be similar: different functions require different structures. The Delft engineers are now trying to design simulations to compute optimal structures for different reactions. These include not only fractal symmetry, but also other kinds of functional design that determine the efficiency of systems as a whole. Again, nature is used as an inspiration. 'Lungs, for instance, are so incredibly efficient, also thermodynamically,' Coppens enthuses. 'The particular ratio between a capillary's diameter and length yields a constant pressure drop across each individual tube, minimising the overall loss of energy. At the very end of the chain the fractal symmetry makes way for a division into multiple alveolar sponges, to optimise the transfer of compounds. It's fantastic. This could be very useful in chemical engineering.' The Department of Chemical Engineering uses such insights to design not only distributors, but also porous catalyst particles with an optimised hierarchy of pore channels, to rapidly bring the molecules to where they react, and allow products to quickly diffuse out. Similar concepts could lead to better sensors and porous matrices for the controlled release of pharmaceutical compounds.

The distance from the main pipe of this fractal injector to each individual outlet is the same. The outlets are spaced evenly apart. The result is a very uniform injection.

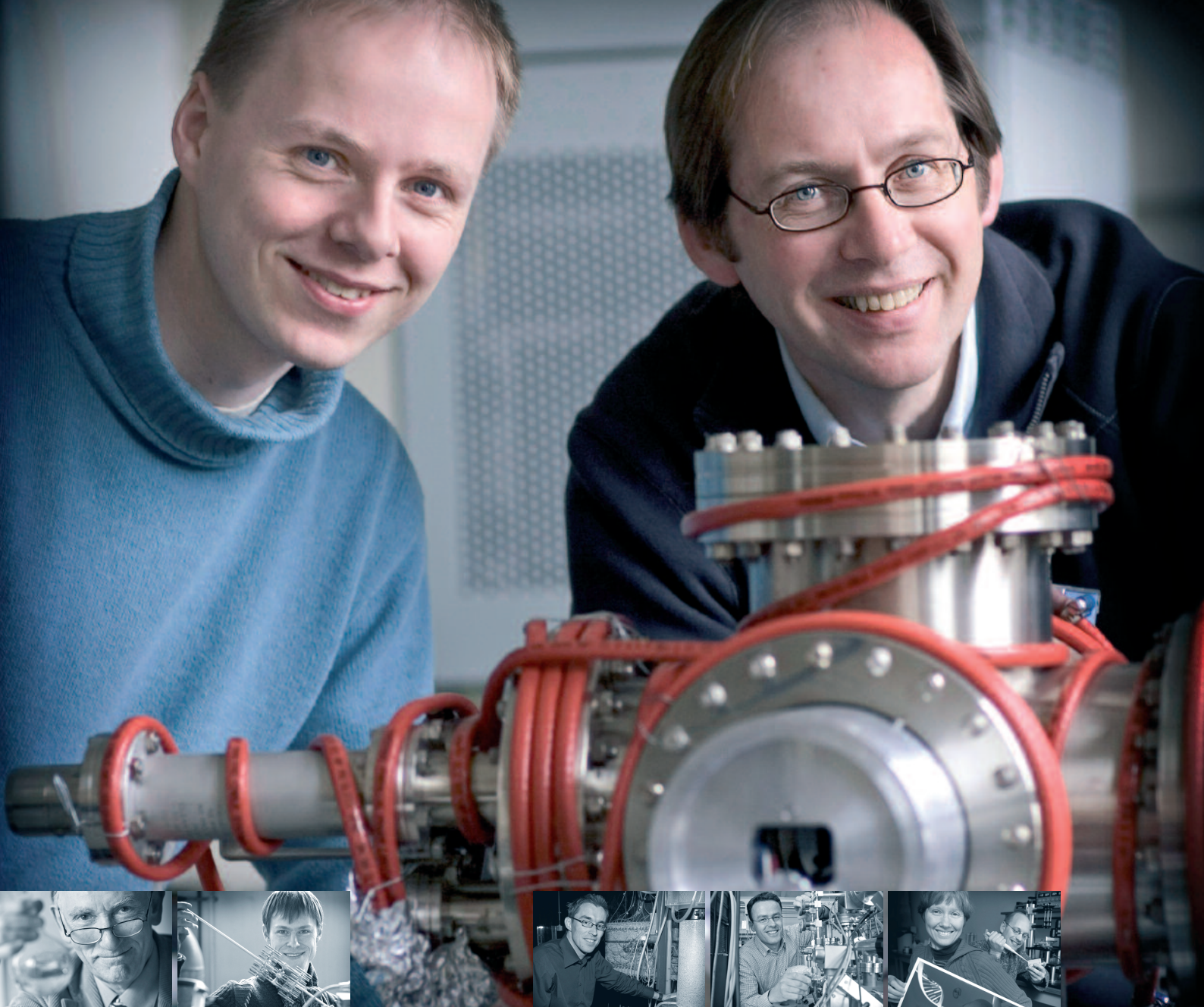


Sustainability is key

Fractal symmetry is just one of Coppens' sources of inspiration. In his mind he is constantly looking for natural principles and processes that can benefit chemical engineering. 'A virus, for example, consists of genetic material surrounded by a self-assembled protein mantle,' he highlights. 'Once inside a host cell, the mantle is broken down and the genetic material is released. Think of all the possibilities that this principle offers to the pharmaceutical industry! Think of packing a medicine inside a mantle mimicking these properties, and having the mantle disassemble under the right circumstances in a target cell! This would be an ultimate form of controlled release.'

One of his current projects focuses on nature-inspired porous membranes. Living cells communicate with their external environment through specialised nanoscale protein channels that transport chemical compounds both actively and passively. Coppens' student Vincent van Hijkoop has made progress in identifying such transport mechanisms that could be useful in chemical engineering, and in modelling their functionality. 'These molecular dynamics simulations help to reveal how the extremely high flux and selectivity of ion and water channels is achieved in the membranes of living cells. We intend to design artificial membranes that approach this high performance,' says Coppens. 'The potential is endless. Imagine nature-inspired water purification and desalinisation, and many other kinds of chemical filtration. These will pave the way for industrial solutions that are both economically and ecologically sustainable. This will be one of the world's major challenges in the near future. It is very rewarding to be able to work towards these goals.'





Dr. Kees Hagen (right) and Ir. Willem van Dorp (left) - Imaging Science & Technology

Writing with electrons

A focused beam of electrons can be used to deposit solid materials on a surface at nanometer scale. Scientists from the Delft University of Technology have refined this technique, and produced the world’s smallest electron-beam-induced structure.

The Delft University of Technology boasts an impressive historical collection of electron microscopes. The shining, sophisticated machines give the hallway of the Department of Imaging Science and Technology (IST) of the Faculty of Applied Sciences the appearance of a science museum. This is hardly a coincidence: this lab is the cradle of advanced electron microscopy. It was here that scientists developed the technique of directing electrons through a strong magnetic field that acts like a lens, thus improving its focusing ability. While conventional microscopes use a beam of light to study objects, an electron microscope uses a beam of electrons. ‘Electron wavelengths are much smaller than the wavelengths of visible light. This allows us to study objects in much more detail,’ says Dr. Kees Hagen, senior physicist in the Charged Particle Optics (CPO) group of IST. ‘The study object is placed in a vacuum chamber where it is examined by an intensive electron beam. If the instrument is a Transmission Electron Microscope, it detects the electrons that originate from the beam and are scattered by the study object. If it is a Scanning Electron Microscope, it detects the so-called secondary electrons, which are released from the object’s material itself under the influence of the electron

beam. In both cases the detected electrons provide detailed information about the study object. A computer can turn this information into a usable image.’

A commonly encountered problem with this technique is the fact that the vacuum chamber’s inside is often slightly contaminated. It may contain chemical compounds from the microscope itself, or from the slightly oily hands of the researcher who placed the object in the chamber. ‘It is impossible to keep the chamber absolutely clean. The problem arises when the electron beam hits these unwanted molecules - often carbon compounds: it ‘glues’ them onto the surface of the study object. This obscures the image and distorts the measurements.’

Scientists have found a way to put this phenomenon, called electron-beam-induced deposition (EBID), to good use: they use EBID to produce tiny functional structures. They purposely release metal-containing gas molecules into the chamber. The electron beam cracks these molecules, leaving small metal deposits on the surface, which in this case is a thin silicon-nitride membrane. The structures can be used for instance in nanoelectronics, and hold promising prospects for computer chip technology.

The structures commonly produced have a typical size of at least twenty to thirty nanometers (millionths of a millimeter). 'The fabrication of smaller structures was assumed to be theoretically impossible,' says Hagen. 'The smallest dots that we produced, however, have an average size of only one nanometer. This is the current world record for this technique.'

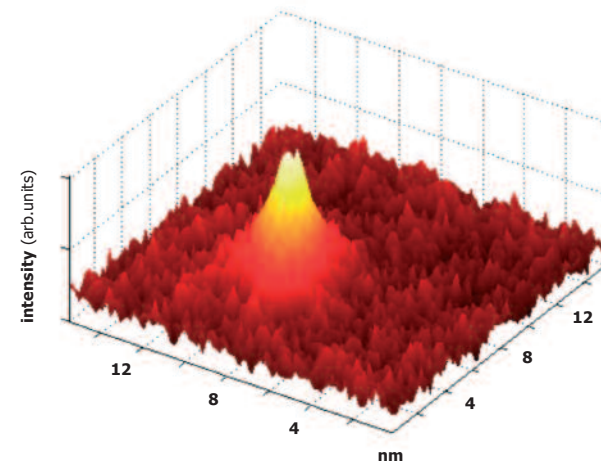
Computer simulation

The size of a single atom is around 0.3 nanometer. Scientists' ultimate dream is to be able to deposit structures that are only one atom wide. 'The possibility of actually achieving this has been thought to be limited by the underlying mechanism of atom deposition,' explains Hagen. 'Deposition takes place because some gas precursor molecules are adsorbed onto the surface. Once these are hit by the electron beam, they are cracked. They decompose into volatile parts, which are pumped away by the vacuum system, and metal atoms, which stick to the substrate. This decomposition process is mainly governed by the secondary electrons: electrons that originate from the interaction of the electron beam with the precursor molecule that is hit.' The behaviour of these secondary electrons determines the minimum width of the deposit. However, when the deposit starts growing, secondary electrons will also be created in the deposit itself, thus causing the deposit width to increase. All in all this leads to the formation of a cone-shaped deposit. The cone will continue to grow as long as it is hit by the electron beam, although its width saturates at a constant value.

Until recently, no-one had ever simulated the precursor dissociation process. Hagen and his colleague Ir. Willem van Dorp were the first to conduct these so-called Monte Carlo simulations. 'These simulations assess the probability that secondary electrons will be released,' Hagen explains. 'When an electron hits an atom, the collision can be either elastic or

inelastic. In the first case, no energy is lost, and the electron is only diverted. In the second case, some of the electron's energy is used to generate secondary electrons.' Some of these electrons may actually escape through the specimen surface. These electrons are counted and their energy is recorded. Then the probability is calculated that an adsorbed molecule is dissociated by these low-energetic secondary electrons.

'Our simulations showed that it should definitely be possible to produce sub-five nanometer structures,' says Hagen. 'The reason why these had never been produced before is purely practical. People simply focus the beam onto the substrate too long, allowing the cone to grow to a larger size.' Producing one-nanometer structures by using their beam no longer than fifty milliseconds, Hagen and Van Dorp proved their theoretical predictions to be accurate. In fact they believe that it should be feasible to produce even smaller ones. 'In theory the minimum deposit is one atom.'



EBID results in a cone-shaped deposition of metal atoms. Simulations reveal that sub-five nanometer structures are feasible.

Multi-beam technology

For the time being, the nanophysicists in Delft are limited in their ambitions by the possibilities of their electron microscopes. 'Electron microscopes with a sufficiently high resolution and the necessary gas-handling facilities do exist,' says Hagen, 'but only abroad. Worldwide there are only three of these instruments that are designed especially for EBID. Generally electron microscopes are too costly to purposely contaminate their vacuum chambers for deposition experiments.'

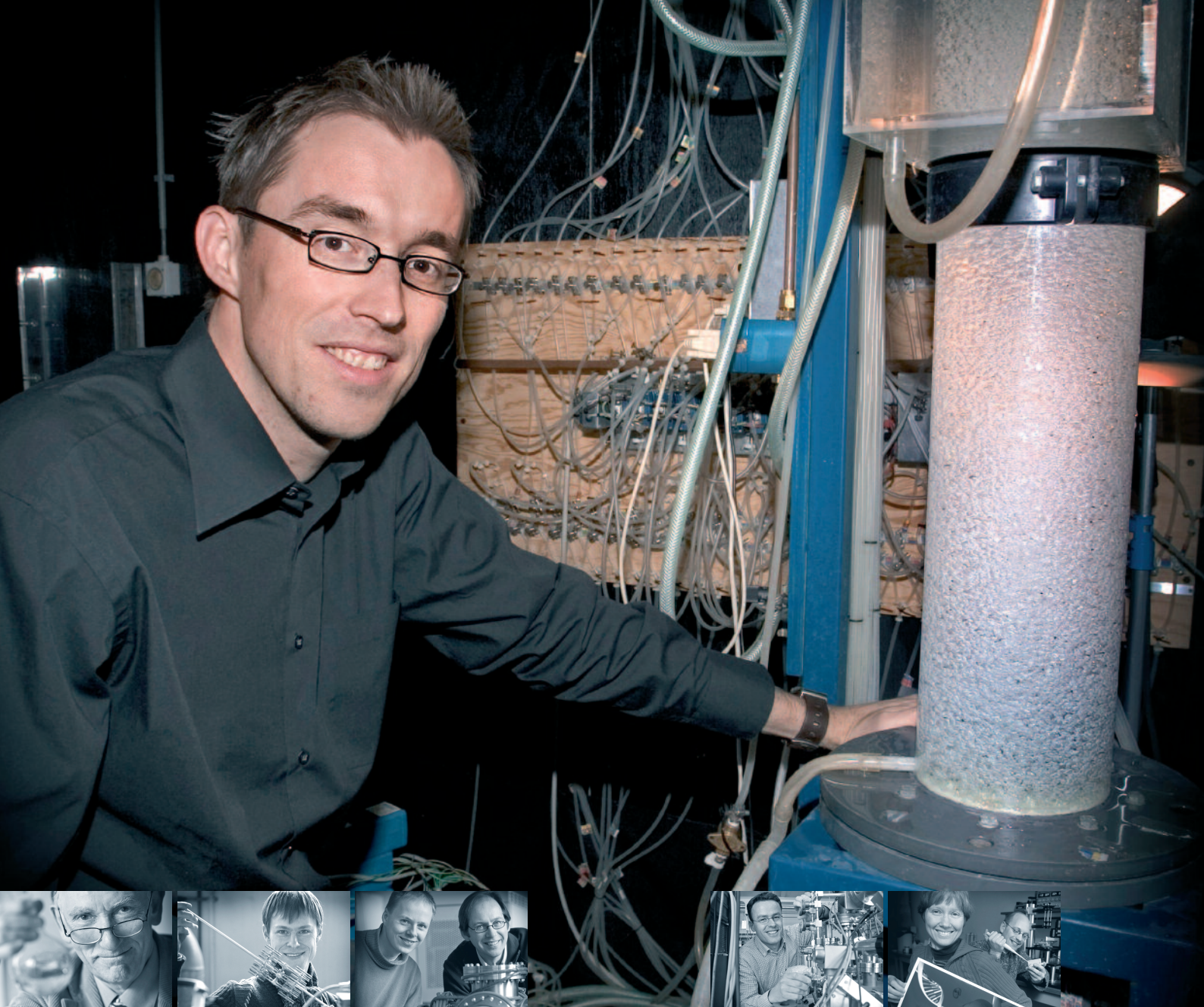
Hagen's group is currently building its very own EBID microscope. Its construction will take a few more years, and the instrument will be dedicated entirely to nanoscale EBID processing. 'It is our specialty to design high-tech instrumentation,' Hagen notes. 'That defines our work here at the University of Technology: we combine advanced engineering with the underlying science.' He has no doubt that the new instrument will make Delft the world centre of EBID technology.

CPO is also working on ways to increase the speed of structure fabrication. 'It is difficult to increase the number of electrons without increasing the beam size,' he points out. 'One solution would be to increase the brightness of the electron source, which is one of the group's challenging research issues. Another solution is to parallelise the deposition process by developing multi-beam technology, which simultaneously employs one hundred beams that can be individually controlled.'

The application potential, stresses Hagen, is endless. In the long run, EBID could play a role in the semiconductor industry, allowing chips to become more compact. This feeds into the trend of housing more functionality in a smaller object. 'Immediate applications,' he adds, 'can be found in the field of nanoscience. For instance, measuring the conductivity of single molecules, including proteins and DNA molecules, requires nanoscale electrodes. These can be made by EBID.'

Hagen can't wait to see the societal implications of these developments. 'EBID is still in its infancy,' he says. 'The pace of change will undoubtedly increase over the next decades.' People around the world agree on this and are working hard on EBID's advancement. The Dutch Ministry of Economic Affairs is very interested, and is co-funding this research. Hagen: 'We don't even know what is ultimately possible. That is what makes our work so exciting.'





Dr. Ir. Wouter Harteveld - Department of Multi-Scale Physics

Bubbles abound

Bubble flows in fluid columns can be much more stable than generally assumed. Perfectly uniform gas injection does the trick. Even in columns containing more than fifty percent gas bubbles, the flow can be stable.

'Bubbles are useful in many ways,' says Dr. Ir. Wouter Harteveld as he sips a glass of coke. 'Countless industrial processes depend on bubble flows. Bioreactors in wastewater treatment are a common example. Wastewater needs to be oxygenated continuously to ensure the effective breakdown of pollutants by bacteria.'

Currently working as a fluid flow engineer at Shell, Harteveld recently obtained his PhD from the Department of Multi-Scale Physics (MSP) of the Faculty of Applied Sciences. His experiments, aimed at validating current models on bubble flows, yielded some interesting new insights.

'A bubble flow is a very efficient mechanism to optimise the chemical reaction between a gas and a fluid,' Harteveld notes. 'Yet bubble flows have always been poorly understood. The exact gravity-driven interactions between the bubbles and their environment are very difficult to model.' Understanding these interactions, which determine for instance how fast bubbles rise through a vertical column, is crucial for controlling industrial processes. Models that are used to describe this behaviour are usually based on the behaviour of a single bubble. Harteveld: 'The challenge is to translate these calculations to the larger system without making too many simplifications.' In order to tease apart the

different factors determining bubble behaviour, Harteveld conducted some highly controlled experiments and proved some prevailing assumptions to be incorrect.

Six hundred needles

'Several parameters affect bubble behaviour,' he explains. 'The fluid's viscosity plays a role, as well as the local number of bubbles, bubble size, and column diameter.' Different combinations of these factors result in different flow regimes. Small bubbles rise relatively slowly and cause little turbulence in the column. Larger bubbles disturb the regular flow and cause more mixing. An excessive number of bubbles results in a swirling mass in which bubble movements - which are sometimes even directed downwards - are very unpredictable.

The industrial application determines which regime is preferable. Wastewater plants, for instance, aim for optimal oxygen uptake by the water. They function best when bubbles rise slowly and uniformly through the reactor. In some industrial processes, however, local temperature increases hamper the chemical reactions. These processes benefit

from stronger turbulence to enhance mixing and smooth the temperature distribution. Hartevelde's research aimed to use an experimental set-up to validate current theories, thus improving the predictability of industrial flow regimes.

'One factor that has hardly been experimented with is the pattern in which the bubbles are injected through the bottom of the column,' says Hartevelde. He decided to experiment with different bubble injection patterns: either coming through the centre of his fifteen-centimeter diameter column, or throughout the entire bottom. 'One thing we wanted to measure exactly is the point at which a certain bubble flow loses its stability and becomes turbulent. We express the amount of bubbles as a gas fraction: the percentage of the total column volume consisting of gas.' As had been expected, the experiments proved that the more uniform the gas injection, the higher the gas fraction could be without losing the flow's stability. However, Hartevelde proved that a perfectly uniform gas injection allows for a critical gas fraction almost twice as high as generally assumed: fifty-five percent. In other words, even when the bubbles make up more than half of a column's volume, the flow can still be non-turbulent.

Hartevelde's secret was a gas injection system using six hundred hollow needles, spaced evenly apart across the entire bottom of the column, and connected to an air supply by narrow tubes. He used more than a year to perfect his sparger, constructing it in such a way that he could control the gas flow through each needle independently. 'This work was sometimes really frustrating,' he laughs. 'It is extremely difficult to ensure that each needle produces bubbles of equal size.' The sophisticated system allowed him to experiment with different flow regimes and to determine the critical gas fraction for each of these regimes.

'Our findings are really quite remarkable,' says the engineer. 'Several people have suggested that large-scale turbulence, at the scale of the diameter of the column, exists irrespectively of the flow regime. We proved this to be incorrect.

I guess that no-one ever succeeded in achieving a perfectly uniform gas injection before.' Other systems include ones that are based on air being forced through a porous plate. It is impossible to ensure that all pores are equally permeable, as water and dirt easily clog them.

Yet to be solved

Using practical findings to adjust computer models, as well as understanding the underlying physical principles, requires accurate measurements. 'There are several parameters we need to know,' says Hartevelde. 'How fast does the liquid flow? How many bubbles are there and what is their size? How fast do they move and in which direction?'

Bubble flows are practically opaque, especially at larger gas fractions. Taking pictures from the outside gives little information on the column's inside. Sticking an instrument into the column is not an attractive option either, since it influences the flow. 'The solution is a combination of measurements on the outside and on the inside,' explains Hartevelde. 'To measure liquid velocities, we use a system that employs two laser beams. At the point where the beams cross, they interfere with each other. We analyse the light scattered by particles in this interference zone.' The measurement is based on the Doppler effect: particles moving faster scatter light with a higher frequency than particles moving more slowly.

Bubbles, however, interrupt the laser beam. It is almost impossible to conduct measurements towards the centre of the column, because the laser hits too many bubbles on its way. 'When the gas fraction is fifty percent, you can measure at the most three centimeters from the side. And even then the laser is interrupted 99.9 percent of the time. This is indeed a problem that has yet to be solved. You can't have everything.'



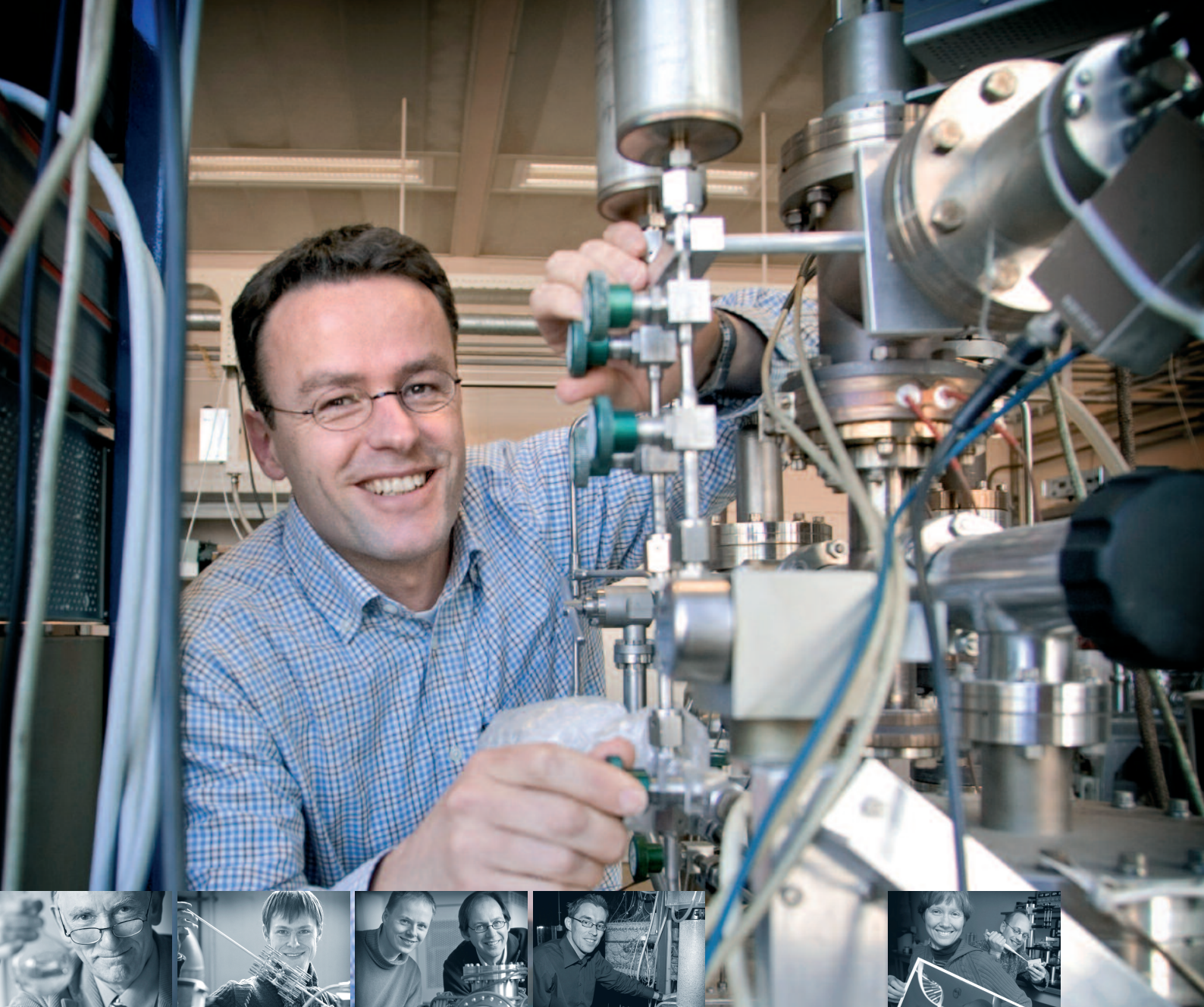
The air flow in each of the six hundred hollow needles can be individually controlled.

Luckily, Harteveld had a second measuring technique at his disposal. To measure bubble size, speed, and number, he used glass fiber probes suspended vertically in the column. 'When you direct light through a glass fiber, and its tip is in contact with water, the light is lost in the water because the two materials have similar reflection coefficients. The light simply disperses. When the tip makes contact with air, on the other hand, light is reflected straight back through the probe and can be measured at the other end of the glass fiber.' The pattern of reflected light provides information on the presence of bubbles. Probes with multiple tips of different lengths can even disclose their exact speed and direction.

The combined information allowed Harteveld to adjust the current models. 'It appears that stability at larger gas fractions is only possible when the bubble size is small. Larger bubbles cause large-scale turbulence, also at lower gas fractions.' The underlying principle, he explains, is the bubbles' hydrodynamic behaviour. The bubbles experience a horizontal lift force. Its direction depends on the bubbles' size and shape – larger bubbles are flatter. Larger bubbles tend to be drawn to the centre of the column, where they cluster, cause a lower fluid density, and cause large vortices. 'The larger the bubbles, the sooner a flow becomes turbulent,' says Harteveld. 'It is therefore necessary to integrate the effect of the lift force into the computer models. This is something that has always been overlooked. The interesting thing is that someone else discovered this at around the same time, only through a theoretical approach. This only makes our experimental findings stronger.'

A bubble flow with a gas fraction of fifty-five percent can still be non-turbulent.





Dr. Fokko Mulder - Department of Radiation, Radionuclides & Reactors

Nanoparticles for hydrogen storage

Hydrogen might well be the fuel of the future. However, effective storage of this gas remains a problem. Scientists in Delft are now working on new ways to store hydrogen inside the crystalline structure of light weight metals. Using neutron scattering, they study the actual storage processes at nanoscale.

Hydrogen is hot. With fossil fuel scarcity expected to become inhibitive in the near future, scientists are searching for alternative fuels, and hydrogen is a promising candidate. As its combustion yields nothing but water, it is perceived as a 'green' fuel. Moreover, its production is relatively easy. Current methods use either a reaction between methane and water or electrolysis of water. However, both reactions require much energy: the first in the form of natural gas at high temperature, and the latter in the form of electricity. 'This is what people often forget,' says Dr. Fokko Mulder at the Department of Radiation, Radionuclides & Reactors (R3) of the Faculty of Applied Sciences. 'Hydrogen itself may be a clean fuel, but its current production methods require energy from fossil fuels. This leads to the emission of carbon dioxide and pollutants.'

The main problem with hydrogen for mobile applications remains its safe, economical and practical storage. 'Some trials with hydrogen-fuelled cars are already being conducted,' says Mulder. 'They mostly use tanks that store pure hydrogen gas under pressure. However, pressurisation costs considerable amounts of energy, and the walls of the

tanks need to be thick and robust, which makes them very heavy.' Another method uses liquid hydrogen, which needs to be stored at 250 degrees Celsius below zero. Cooling the gas costs energy, and these tanks need to be very well insulated. 'In short, these methods cost more energy than one would like,' argues Mulder.

Nanopowder

Over the past decades, scientists have experimented with different storage methods. One option is to store hydrogen inside the crystalline structure of metals. 'Well-known examples are palladium and iron-titanium,' says Mulder. 'Their ability to bind and release hydrogen is excellent, but they are expensive and excessively heavy.' Some 500 to 700 kilograms of metal are needed to store six kilograms of hydrogen – the amount needed for a car to drive 500 km, an absolute minimum for market purposes. 'This is why we are now exploring the possibilities of metals that are lighter, and still have the right characteristics for hydrogen storage.'

One of these lighter, yet suitable metals is magnesium. It binds hydrogen with high density. 'Conventional methods use magnesium particles that have a diameter of several micrometers,' Mulder explains. 'These particles are actually too large. Hydrogen will not penetrate to their centre, so their storage capacity is limited and the reaction proceeds slowly.' The Delft scientists studied a smart yet simple solution: using a technique called high energy ball milling, they grind magnesium to produce particles that are ten to twenty-five times smaller. 'These nanostructured particles are so small that hydrogen can penetrate them entirely, which means that all of their magnesium mass is effectively used for storage.'

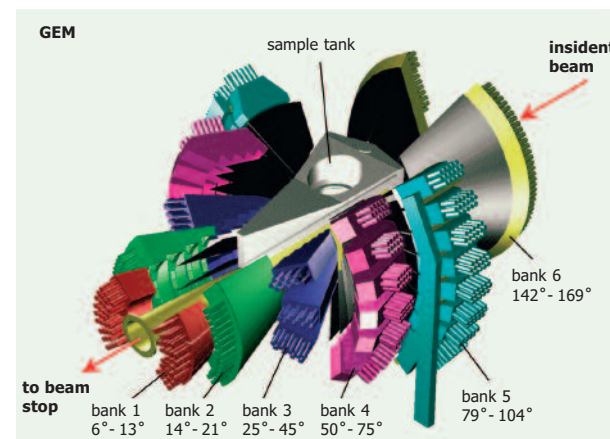
Nanostructured magnesium shows another distinctive advantage compared to the larger magnesium particles. In nanoparticles, the outer layer of magnesium atoms does not immediately achieve its maximum hydrogen content of two hydrogen atoms per magnesium atom. 'At first, this ratio remains between one and two,' says Mulder. 'We don't know why this is the case only in nanoparticles, but we do know it's an advantage. The 'empty' spots in the atom grid allow for a quicker inward diffusion of hydrogen and homogeneous hydrogen filling of the particle. Fully hydrogen-saturated magnesium, on the other hand, is like an impenetrable shield.'

Unique graphs

Another inventive step is the use of catalysts that enhance the absorption properties of nanostructured magnesium even further. Mulder and his colleagues at R3 studied the catalysts vanadium and niobium. These split the hydrogen molecules into separate atoms and allow their effective transport towards the magnesium particle, thus speeding up the sorption time by a factor ten and lowering the necessary temperature by fifty degrees Celsius.

'The interesting thing is that we found an entirely new compound in our reactor, which seemed to appear in the course of the reaction,' Mulder elaborates. 'This was an unknown type of perovskite: a compound consisting of magnesium, niobium and oxygen.' In addition to being an excellent catalyst, this new perovskite appeared to prevent the nanoparticles from clustering. Particle clustering and growth is a phenomenon that usually takes place in the course of several rounds of absorption and desorption of hydrogen, and that gradually slows down the reaction.

In order to study the composition of their materials during each of the stages of hydrogen sorption, the Delft scientists employ a measuring technique called neutron scattering. 'In contrast with electrons, used in electron microscopy, and X-rays, used in X-ray diffraction, neutrons penetrate through the pressurised sample environment and through the material itself,' says Mulder. 'This allows us to study the inside of materials. In addition, it allows us to locate the hydrogen atoms with a high degree of accuracy.'



A beam of neutrons enters the General Materials Diffractometer (GEM) on one side. The sample scatters the neutrons in all directions. Seven thousand detectors register their direction and wavelength.

Each material scatters neutrons in a distinctive way. Analysis of the scattered neutrons thus yields insights into the exact atomic composition of the material studied. 'Each material gives us a unique graph that shows peaks in intensity of scattered neutrons,' Mulder explains. 'The position of the peaks corresponds with the distances between the planes of the atom grid, while their height gives information about the elements that scattered the neutrons.' These graphs are like a barcode: when comparing their data with calculated graphs of known compounds, scientists are able to identify the compounds present in their sample.

Sustainable energy grant

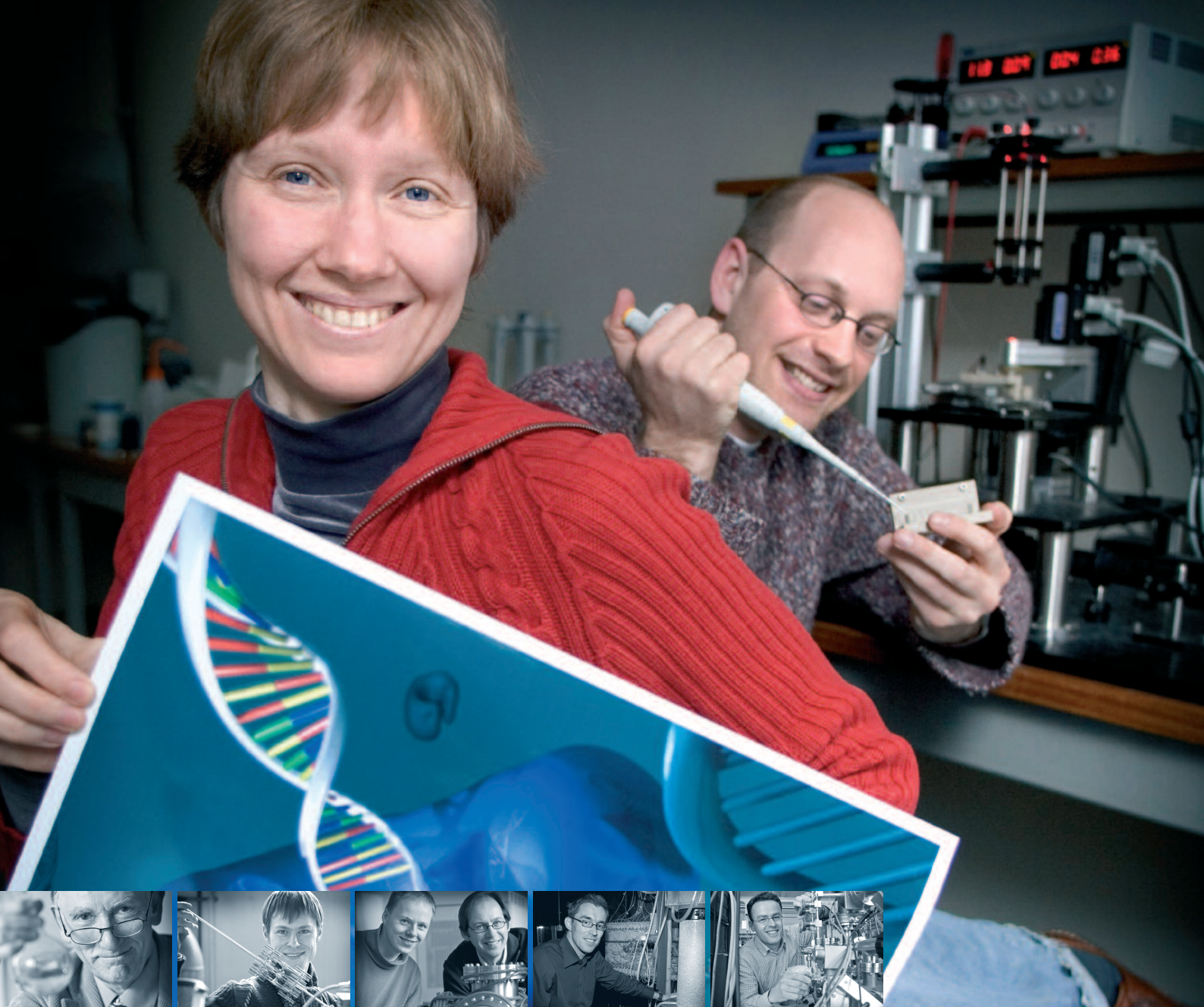
Despite the promising results, Mulder remains realistic. 'We're not there yet,' he laughs. 'The bottleneck is the fact that the reaction between magnesium and hydrogen yields energy that is released in the form of heat. In order to maintain the ideal circumstances for absorption, the reactor needs to be cooled continuously. Similarly, a considerable amount of heat is required to release the hydrogen again in order to allow its use.' It would be ideal if this process could be driven by the heat that a hydrogen-powered fuel cell releases as a by-product. Such a heat-recycling fuel cell, however, requires an innovative design and is not yet a reality.

Generally, though, Mulder is optimistic about future applications. 'The storage capacity of nanostructured and catalysed magnesium is around seven mass percent,' he says, 'which is amply sufficient in practice. This is more efficient than any other material that binds hydrogen reversibly.' Some practicalities remain to be resolved, including the fact that cars will need to be equipped with a new type of fuel tank. 'Most likely, when going to a gas station, you'll need to replace the entire tank,' says Mulder. 'Refilling the tank will take some time, and it will need to be done under controlled circumstances.'

And then there is still the challenge of producing hydrogen in a sustainable way. Mulder is convinced that this will eventually be possible through the use of solar or wind energy. 'These types of energy will produce the electricity needed for electrolysis of water,' he notes, 'or sunlight will be used directly for photocatalytic splitting of water. Colleagues here in Delft are working on this. We just have to wait for the appropriate technologies to emerge, but this will surely only be a matter of time. After all, we have to. Our current source of energy is limited.'

In the meantime, Mulder and his colleagues have their own scientific challenges to tackle. One is screening other kinds of light metal hydrides and other kinds of catalysts in order to find combinations that perform even better. A second is designing an energy-efficient fuel cell that produces the heat needed for releasing the hydrogen from the storage material. For this research, the Department R3 recently received grants through the Delft Institute of Sustainable Energy (DISE), an umbrella institution that aims to focus cooperation between the University's faculties. In addition, this work will be sponsored by the new partnership between the Netherlands' three technological universities, through one of its Centres of Excellence. 'There is still much to be done,' Mulder concludes, 'but I am positive that such grants will enable us to make significant progress.'





Dr. Nynke Dekker (left) and Drs. Daniel Koster (right) - Kavli Institute of Nanoscience

Manipulating a single molecule

Nanoscientists at Delft University of Technology have succeeded in measuring, handling and even manipulating single DNA molecules. Their experiments have shed light on how DNA interacts with certain proteins.

DNA, our genetic material, is a crucial compound in any living cell. This molecular blueprint influences what a cell – and thus an organism – looks like and how it functions. James Watson and Francis Crick unravelled the structure of DNA in 1953, showing that each molecule is in fact a double helix. It consists of two complementary strands that are chemically bonded and intertwined like a winding staircase. This discovery won them a Nobel Prize.

‘Still, many interesting questions remain about the physical properties of DNA and its interactions with proteins,’ says Dr. Nynke Dekker, molecular biophysicist at the Faculty of Applied Sciences’ department of Nanoscience, ‘particularly during replication and transcription.’ Transcription is the process by which the blueprint is ‘read’ – it is the first step in the production of proteins as encoded by the DNA molecule. ‘Until recently, DNA studies were restricted to measuring the combined properties of many molecules together. Looking at the dynamics of single molecules was never an option: they’re simply too small. However, over the past ten years the field of single-molecule biophysics has developed to the point that this is now routine.’

Dekker and her PhD student Drs. Daniel Koster have

succeeded in applying these technical advances to manipulate, and even twist, single DNA molecules. Their research, carried out with the group of Dr. Stewart Shuman of the Sloan-Kettering Institute in New York, US, has yielded new insights into how DNA interacts with topoisomerase IB (TopIB), a protein that plays an important role in replication and transcription. It is also one of the molecules targeted by certain cancer drugs. By blocking the functionality of TopIB, these drugs inhibit DNA replication, thus inducing the death of the cell. ‘Conventional cancer medicines are not very discriminative,’ says Dekker. ‘They also kill healthy body cells. By looking at the exact role of TopIB, we hope to contribute to the development of medicines that are more specific, targeting only the tumor cells.’

Rotating a tiny bead

DNA, as Dekker points out, is just like a piece of rope. If you twist it a couple of times while holding one end steady, it will bend and coil. The more you twist it, the more entangled the rope will be. ‘This is exactly what happens to a DNA mole-

cule during replication and transcription,' she says. 'Both processes require the separation of the helix's two strands. This unwinding results in torsional tension within the molecule, which in turn induces the formation of coils.' These coils hamper the cell's molecular machinery. The role of TopIB is to remove the excess coils. It achieves this by cutting one of the DNA strands. This allows the strand to rotate freely around the other strand, which releases the torsion in the DNA molecule. TopIB then sticks the two ends of the strand back together, thus repairing the double helix.

'Molecular biology experiments have demonstrated the removal of coils by TopIB,' says Dekker, 'but we were the first to examine the interaction between a single DNA molecule and a single TopIB enzyme, allowing us to accurately monitor the reaction in real time.' Using a technique initially developed in France, the Delft biophysicists attach a tiny magnetic bead to one end of a DNA molecule while anchoring the other end to a glass plate. The magnetic bead, which has a diameter of one micrometer, or one millionth of a meter, can be rotated by using a magnet. Dekker: 'This allows us to purposely entangle the DNA molecule, like the chord of an old-fashioned telephone. We then add TopIB to untangle the coils.' The entire process can be followed through an optical microscope. The DNA molecule itself, being only 0.002 micrometer wide and perhaps five thousand times as long, is invisible through the microscope, but the magnetic bead is not. Its position relative to the glass plate can be accurately measured. 'The more the DNA molecule is entangled, the shorter it is,' Dekker points out. 'By measuring the position of the bead, we can measure the degree of entanglement. We can literally see that when we add TopIB and it starts to remove coils, the shortened DNA molecule increases in length.'

How on earth does Dekker succeed in attaching such a tiny bead to one DNA molecule? 'We actually work with a large amount of beads,' she laughs, 'and a small number of DNA molecules, and mix them in a solution. The beads, as

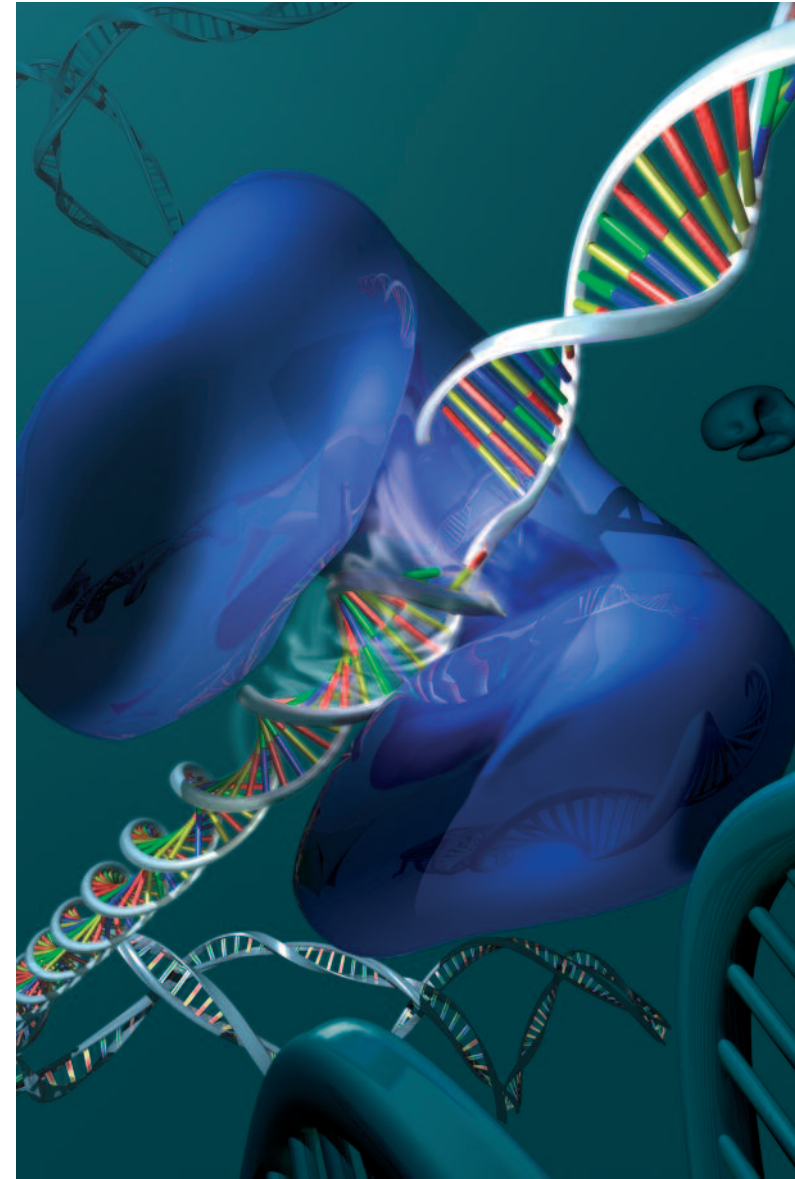
well as the glass plate, are coated with a protein layer containing certain receptors that easily bind with specific markers at the end of our DNA molecules. This is a trick that is widely used in the field.' Looking through a microscope, the scientists are able to single out beads that show the desired behaviour: behaviour that can only be explained by a single DNA molecule being attached both to a magnetic bead and to the glass plate.

Molecular embrace

The experiments showed that TopIB untangles the DNA molecule in steps of different size, which are separated by short time intervals. After an average of fifty rotations, the loose strand is reattached. When the applied torsion is low, this results in an average of fifty coils being removed during one cut-and-paste round carried out by TopIB. 'We discovered that the number of coils being removed in each step depends on the amount of torsion in the DNA molecule,' says Dekker. 'The more torsion, the more coils will be removed before the loose strand is reattached.'

In addition, the biophysicists could confirm that TopIB is actually tightly wrapped around the DNA molecule during the entire procedure. They observed that the rotation of the free strand causes friction between the DNA and the TopIB, which significantly slows the rate of DNA rotation. This effect had been predicted on the basis of TopIB's crystal structure, but had not yet been experimentally observed. 'The interesting thing is that these purely physical phenomena do indeed determine processes at the molecular level,' notes Dekker. 'But, to the best of my knowledge, the influence of intermolecular friction on a DNA-protein interaction had never been demonstrated so clearly.' This finding was awarded with a prominent position in *Nature* (2005). The group's visual representation of a TopIB molecule embracing a DNA helix even featured on the magazine's cover.

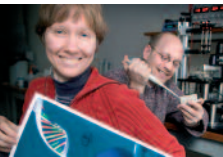
TopIB is wrapped around the DNA helix during the untangling process. This visual representation featured on the cover of *Nature* (2005).



Enthused by these findings, Dekker, Koster and MSc student Elisa Bot are currently expanding their experiments, in collaboration with the group of Prof.Dr. Mary-Ann Bjornsti of St. Jude Children's Research Hospital in Memphis, US. They aim to measure the functionality of TopIB in the presence of certain cancer drugs. 'There are particular cancer drugs that attach themselves to the DNA molecule at the exact place where TopIB cuts one of the strands,' Dekker highlights. 'This prevents the loose ends from being glued back together. TopIB cannot carry out its job properly, and the cell eventually dies. It will be very interesting to see if our single-molecule experiments can contribute to understanding this mechanism.'

The eventual goal is the development of drugs that more effectively target cancer cells, but this, as Dekker stresses, lies far beyond Delft's expertise. 'Our task is to unravel the biophysical processes at the molecular level,' she says. 'The road to pharmaceutical applications is long. After all, what we do is as in vitro as it gets. We measure the interactions between one DNA molecule and one protein under controlled laboratory circumstances. How this translates to interactions in a living body, with all its intricate transport mechanisms, remains to be seen.'

Still, the knowledge that her research serves an ultimate purpose is important to Dekker. 'My motivation is three-fold,' she concludes. 'We continuously develop new molecular techniques, we work on fundamental biophysical questions, and our results might eventually be useful. That makes this a very exciting field to be in.'



Facts & figures

2005

The Faculty of Applied Sciences is the largest Faculty within TU Delft. Research at the Faculty is fundamental and application-oriented in nature and spread over six Departments. The Faculty offers research-oriented education at both undergraduate (BSc) and postgraduate (MSc, PDEng, PhD) levels.

The domains of science the Faculty targets through its education and research are life and health science & technology, nanoscience & technology, chemical engineering, radiation science & technology and applied physics.

Professors	59
Tenured academic staff	137
Post-doctoral researchers and PhD students	442
Publications (per year)	1900
PhD dissertations (per year)	60
Patents (per year)	50
Students	1400
International students	200
Budget (millions)	80
- From external sources (%)	35

BSc programmes

- Life Science & Technology
- Molecular Science & Technology (starting Septembre 2006)
- Applied Physics

MSc programmes

- Life Science & Technology
- Chemical Engineering
- Biochemical Engineering
- Applied Physics
- Nanoscience
- Industrial Ecology (in preparation)
- Science Education & Communication (in preparation)
- Teacher Training Programmes
- Sustainable Energy Technology (requested)

Colophon

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Address

Faculty of Applied Sciences
Delft University of Technology
Lorentzweg 1
2628 CJ Delft
The Netherlands
T +31 (0)15 278 48 41
F +31 (0)15 278 26 55
www.tnw.tudelft.nl

Information

c.j.a.zeeuw@tnw.tudelft.nl