Volume 2 - July 2013

nanotextnl

nanonextnl magazine

Red nanosilver

Cell membrane platform

International ambitions

New cancer treatments

Plasmon light waves caught in the act, how cells develop in a tissue engineered heart valve, a powder that solidifies a swimming pool

nanonextnl

innovating with micro and nanotechnology

NanoNextNL at a glance

NanoNextNL is composed of 28 programmes which are part of 10 main themes. For up-to-date information, please visit our website www.nanonextnl.nl

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nanonextnl
innovating with micro and nanotechnology

welcome

Welcome back!

We are proud to present the second edition of our NanoNextNL magazine: NanotextNL. This edition, in our opinion, proves that the programme has picked up steam and has left the initial startup phase. You will find interesting stories on research topics which impact many different aspects of our daily life. All parties involved in NanoNextNL are keeping up their advanced work: the first innovations are already starting to have an impact.

This magazine shows a wide variety of interesting things happening in the labs and offices in the Netherlands. The story of Michel Versluis (page 22), for example, illustrates a project in which a whole chain of partners, from researchers to industry to users, is involved. This NanoNextNL project is aiming for medical applications in the near future, but the knowledge and network it creates might lead to much more. Also the story of Krassimir Velikov (page 14) is a good example of how the knowledge and know-how of interactions at the nano-scale lead to inventions which can be applied in industry.

At the management level, NanoNextNL is working on its own midterm evaluation: What is our current progress and what activities can we initiate to ensure the success of the micro and nanotechnology community in the future? An important aspect we are currently working on is establishing links with international organisations and platforms, for example through contacts with MANCEF (see page 4) and NIMS (page 28).

We hope this magazine leaves you with a good impression of our activities. We are looking forward to your reactions and to more stories of enthusiastic innovators in future magazines!

Dave Blank
Chair of the Executive Board

contents

Colophon

nanotextnl

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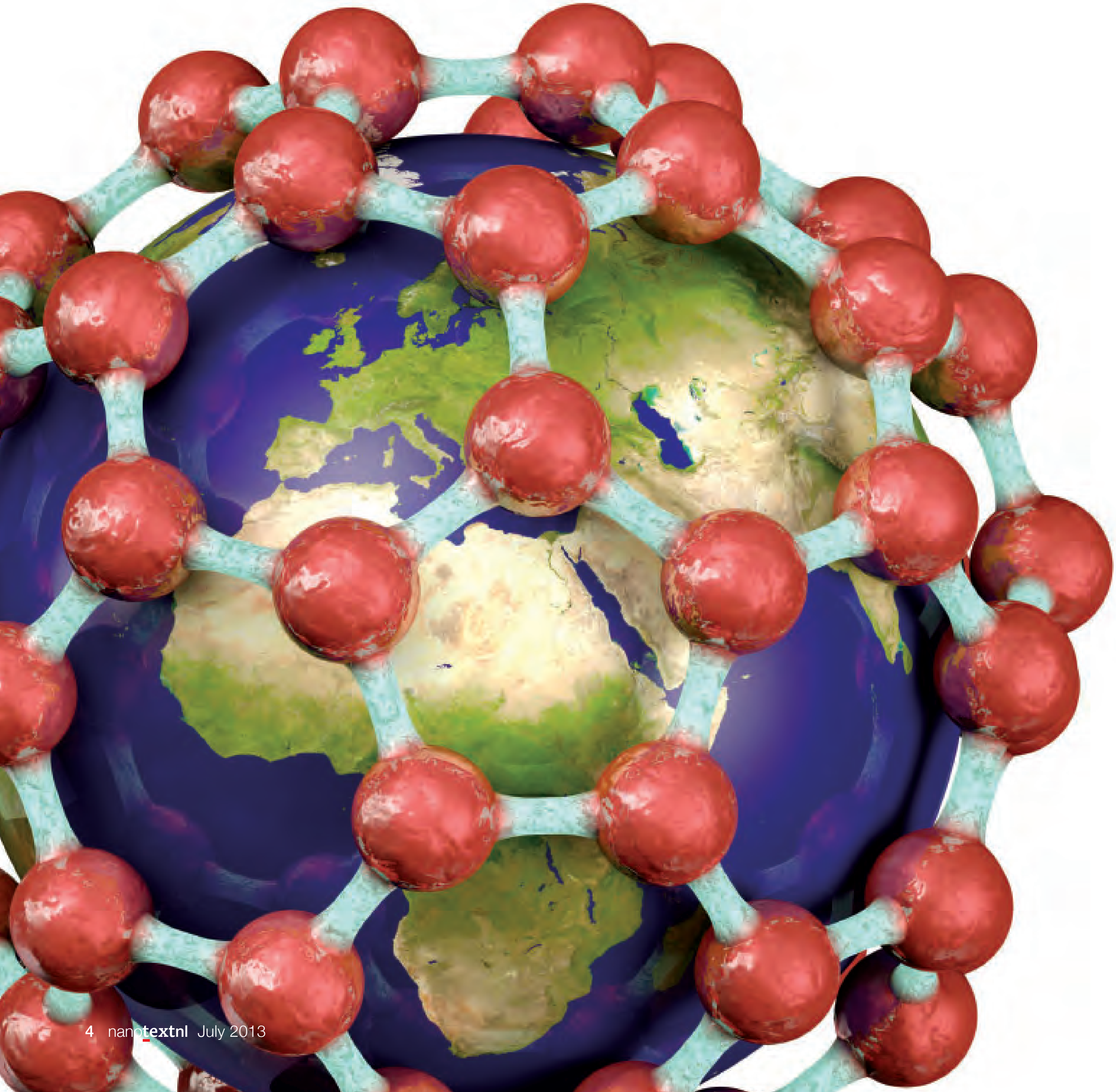
Uniting



small players

Text Sonja Knols / Photos iStockphoto, ASML and Boudewijn Payens

The NanoNextNL programme is running smoothly. "The time has now come to widen our horizon beyond the borders and start building bridges towards the future," says Executive Board member Frank de Jong. "Excellent timing. Other national clusters in this field are also starting to interact on a transnational scale," observes Volker Saile, president of the Micro and Nanotechnology Commercialization Education Foundation (MANCEF).

Before we start talking about the international ambitions of NanoNextNL, Frank de Jong first wants to set the record straight. "Most people don't know that NanoNextNL is more than a consortium executing a research programme. It is also a foundation that aims to ensure funding for micro and nanotechnology research and development, linked to economic activities. NanoNextNL has coupled business to the national network of universities built by MicroNed and NanoNed. Now the question arises: what comes after NanoNextNL? What happens with the field when this programme is over? And what happens with the excellent infrastructure we've built within NanoLabNL when that budget is exhausted?"

One first important step towards future activities has already been taken. "Within the theme 'High Tech Systems and Materials' of the Dutch public private partnership top sector policy a roadmap team was formed which has the responsibility of determining the future directions the Netherlands might take to advance nanotechnology. NanoNextNL, as the major player in this field, has taken the lead in this process," de Jong explains.

This wasn't the first national roadmap for the field, he emphasises. "Of course we have made roadmaps before. In fact, one of the most famous, the Netherlands Nano Initiative, formed the basis of the NanoNextNL programme. This newest roadmap is however slightly different: it has been made within the framework of the Dutch top sector policy, which is first and foremost a company policy, not a research agenda. Industrial and societal needs play a far more important role than they did in earlier roadmaps."

"What comes after NanoNextNL? What happens with the field when this programme is over?"

Heading for Europe

With this roadmap in hand, the first stop is Europe. "The Horizon 2020 programme should provide ample opportunities for the Dutch nanotechnology community to thrive and expand," says de Jong. "Universities and companies all employ international activities. Why not take that step towards Europe collectively, and take a stand as the Netherlands nano-community as a whole?"

Currently, the board of NanoNextNL is investigating the possibilities. "What kind of instruments are available, and where do we fit in best? Should we aim for a separate European Institute of Innovation and

Technology (EIT) or a Joint Technology Initiative (JTI), or should we try to align our current activities in the different Horizon 2020 Key Enabling Technology research lines?"

What role does NanoNextNL want to play in this European arena? "We aspire to be the Dutch focal point for nanotechnology at an international level. However, this does not mean individual companies, universities or even individual researchers should not try and apply for funds themselves," he stresses. "But I can imagine NanoNextNL can serve as a Dutch contact point for European calls. We can act as a matchmaker between universities and companies, or advise people on where to find what expertise. Naturally we will work closely together with Agency NL in this respect, since they have ample experience with European programmes."

"For now, our first major challenge is to make a choice. NanoNextNL is a very broad programme. Should we keep on investing in all of these subjects, or should we choose the most promising, the most challenging or the ones with the highest expected returns?" Whichever road the board takes, roadmaps will be key in the process, De Jong says. He therefore wants to urge all researchers to contribute to these roadmaps. "We use our theme coordinators to identify key elements, but all input from the field is valued highly. Most people underestimate the impact of such a roadmap. Our government, and also the EU and other funds use roadmaps as guides for future investments. In other words: if your research is not a part of such a roadmap, it will be harder to find funds for it."

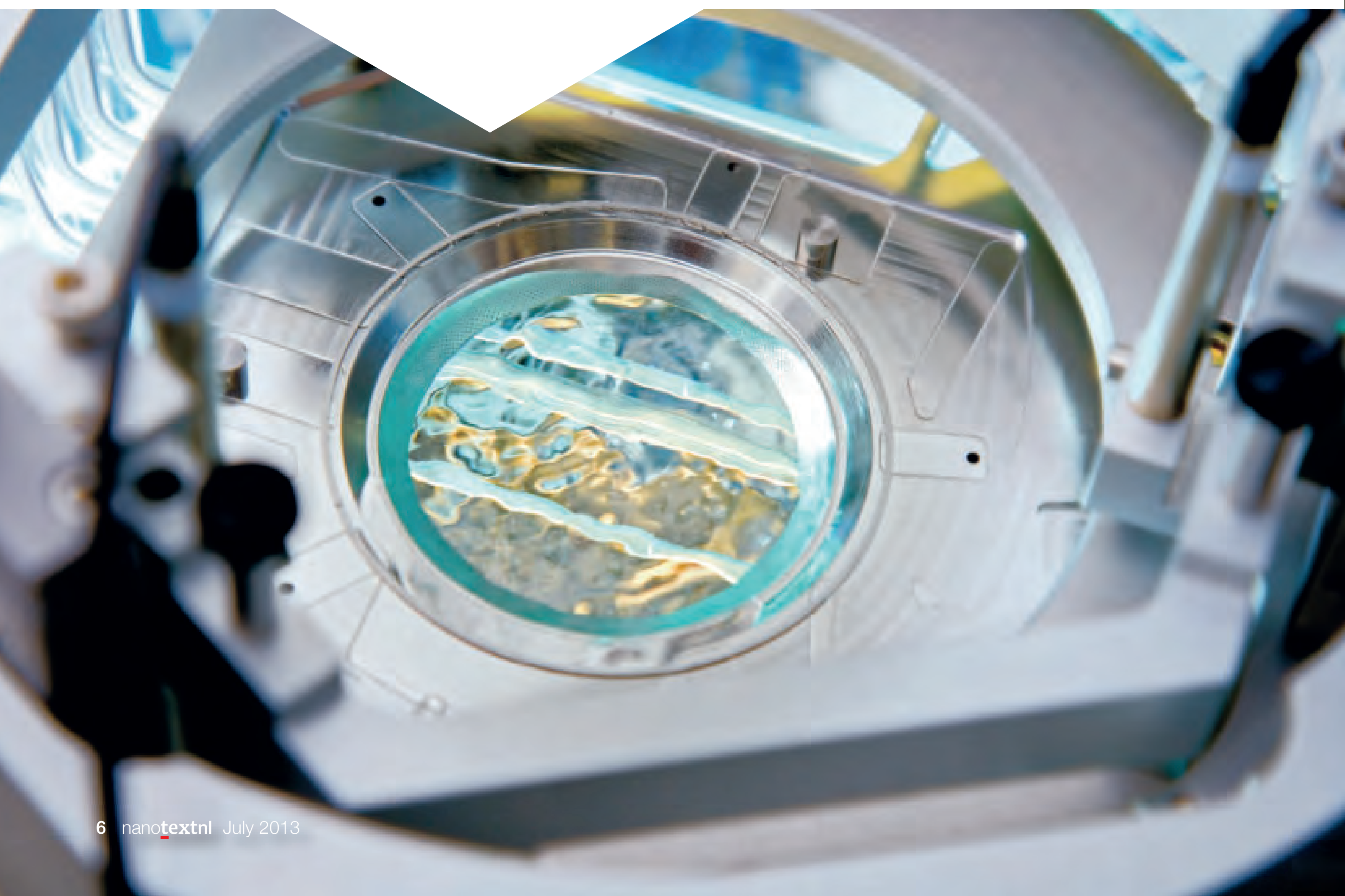
Showcasing results

Finding funds for research is one thing, but ultimately companies will have to be able to make money from the outcomes. One of the opportunities for Dutch researchers and start-up companies to showcase their expertise is the COMS (Commercialisation Of Micro-nano Systems) conference in August 2013 in the Netherlands. "COMS provides an enormous opportunity to present an international public with an overview of Dutch activities," says Volker Saile, president of the organising association MANCEF.

The conference is one of the main activities of MANCEF, Saile explains. "MANCEF dates

"There are not so many countries in Europe which are so deeply involved in nanotechnology as the Netherlands; a country that hosts fabulous institutions and an excellent infrastructure"

The Dutch company ASML invents and develops complex technology for high-tech lithography machines for the semiconductor industry.



NanoLabNL is the Dutch national infrastructure for nanotechnology research, located at 4 locations (Delft, Eindhoven, Groningen and Twente).

from the early nineties, when the microsystems technology started to take off. A small group of entrepreneurs and academics from the US and Europe discussed the future prospects of the technology and decided to organise specific conferences on the commercialisation possibilities. It became clear that you need an independent organisation to do that. That resulted in MANCEF: an international non-profit foundation, which besides the yearly COMS conferences also organises the drafting of international roadmaps on enabling technologies."

Asked about the impact of the Dutch nano-community on a European scale, Saile admits to be somewhat envious: "There are not so many countries in Europe which are so deeply involved in nanotechnology as the Netherlands; a country that hosts fabulous institutions and an excellent infrastructure. Consider for example the MESA+ facilities, and the presence of global high-tech companies like ASML and Philips. There are not many countries with comparable facilities and such a high density of high-tech SME's in this field."

Omnipresent

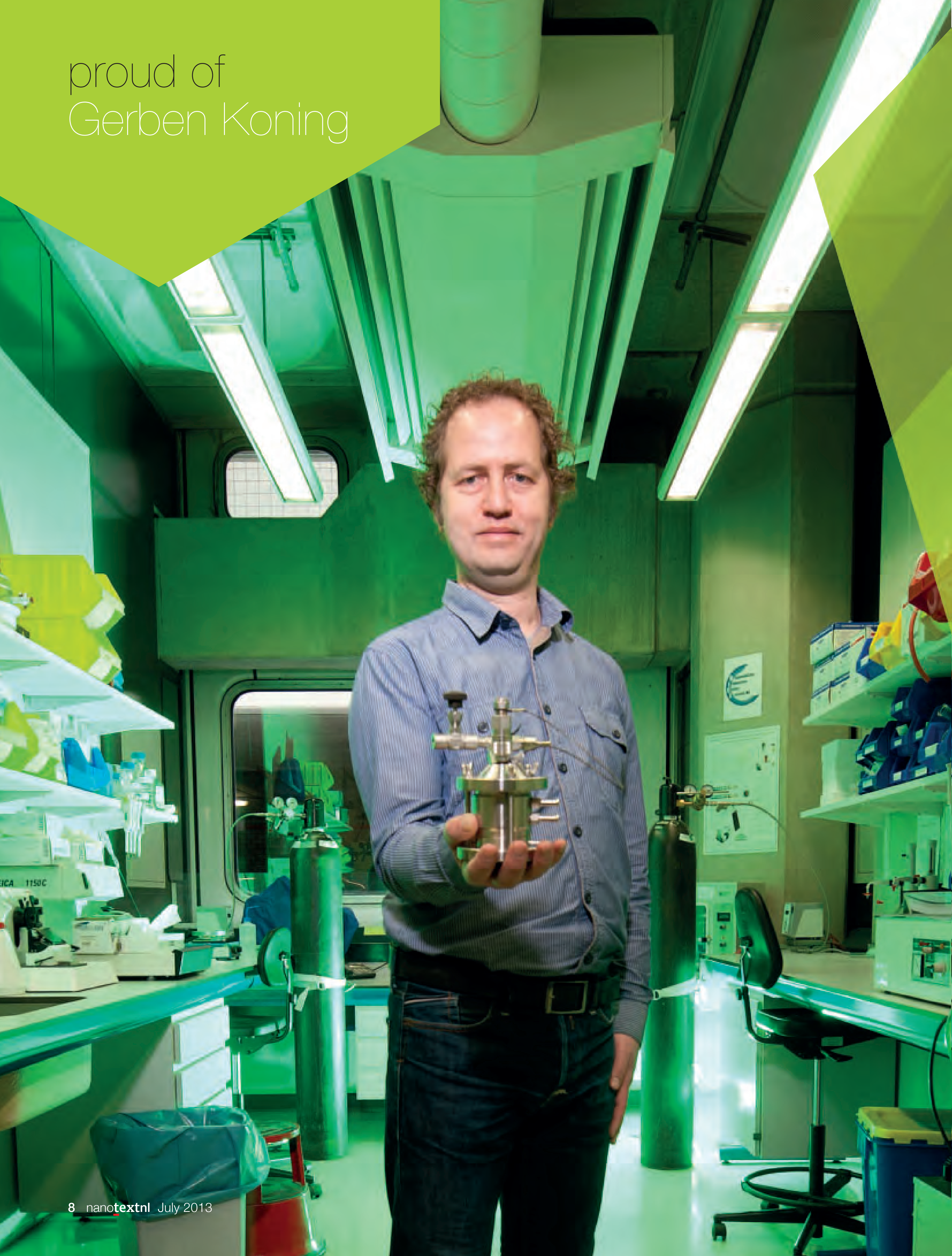
To promote nanotechnology effectively within Horizon 2020, it is key to cluster all the national know-how and partnerships such as NanoNextNL into larger, more internationally-orientated networks, Saile says. "We share the same interests, and face the same problems. Horizon 2020 is about pushing the future economics for this continent. And as the micro and nanotechnology community, we are weak in promoting the opportunities. When you ask someone about microchips, with gleaming eyes he will start to talk about his smartphone or his tablet. But microsystems are much less visible. The fact that they form the core of almost everything, from car applications to coffee machines and health care systems, makes it harder to pinpoint a single killer application. We should unite our efforts to show that enabling technologies are vital for our economy."

Ultimately, the international micro and nanotechnology community should strive towards a collective effort to advance the field and promote new applications, both men agree. Saile summarises his viewpoint aptly: "Small is beautiful, but not as visible as large constellations."

ambition

Number of awarded EU projects: **4** (Aim 2016: 15)
Number of roadmaps: **1** (Aim 2016: 3)

proud of Gerben Koning



Right on target

Gerben Koning studied in Utrecht and obtained his doctorate in Groningen, carried out research in Canada, Utrecht and Delft, before taking up his current, permanent position at Erasmus MC. He and his group, *Innovative Targeting*, are conducting research within NanoNextNL's Nanomedicine programme. His intention is to ensure that cancer medicines are delivered to exactly the right location in the body.

Text David Redeker / Photo Fjodor Buis

"When I was 24 my two-year younger brother died of cancer. That was one of the reasons why I wanted to continue in biomedical research. At present a major challenge in my work is the translation of research findings to clinical application. Once you have proven that a treatment works on laboratory animals, you must move on to take the last difficult step: the step to the clinic.

The theme that has run through my research during the past fifteen years is drug delivery, ensuring that medicines are delivered to exactly the right place in the body. I mainly use liposomes to do this. Liposomes are vesicles formed by lipids of approximately one hundred nanometres in size that can serve as a transportation vehicle inside the body. We modify these liposomes; put a drug inside them and, for instance, ensure that the drug is released at exactly the right time, i.e. when the liposomes have reached a tumour, and therefore deliver the chemotherapy only there.

This aim leaves us with several challenges. How, for example, do you make sure that the liposomes know when they have reached a tumour and must deliver their drug to that spot? Among other things we modify the liposomes in such a way that they will only open above a certain temperature. If we heat the tumour from outside by using microwaves, the liposomes will open there.

The second challenge is that you want to be able to visualise non-invasively whether the liposomes actually do arrive at the right place and release their contents there. And also whether the tumour does eventually shrink. This is the reason why we work closely with imaging specialists to be able to watch the entire process.

Last of all, we require a facility for making the chemotherapy-loaded liposomes we need in large quantity and in a controlled environment. For our current work with cell cultures and laboratory animals we make them ourselves. However, if we take the step towards application in human cancer patients, we will need to have a production facility, preferably in the Netherlands, that meets the approved production requirements. I also notice the same need in the start-up Ceronco Biosciences. This is a company that develops liposomes with specific lipids that make tumour cells more accessible for the encapsulated chemotherapy. A patent filed by myself and Netherlands Cancer Institute researchers is at the basis of this. Ceronco has the need for a production facility to manufacture this new nanomedicine for them to be used for clinical applications. The availability of such a facility in the Netherlands would be optimal to bring the different regulatory frameworks in line ensuring a sound and speedy development of clinical grade nanomedicines.

I was very pleased to be able to start my own group within the Laboratory of Experimental Surgical Oncology in Rotterdam in 2007. In the years before that I had numerous ideas and made many plans. I'm now able to work out those ideas and plans in greater detail.

> "Though we are able to conceive complicated drug delivery technology, if it is of no use to the clinic our work would be in vain"

Another advantage is that we are situated next to the clinic. This makes it possible for us to discuss with the physicians and hear first-hand what they need, what they are waiting for to effectively treat patients. Though we are able to conceive complicated drug delivery technology, if it is of no use to the clinic our work would be in vain.

It's one of the fantastic aspects of NanoNextNL that you collaborate with other disciplines. We get together to discuss with other research groups, start-ups and large companies. One of my PhD students recently said during such a meeting that we had difficulty producing our particles. He immediately received several useful suggestions. We trust each other and help one another. That's wonderful, isn't it?"

serendipity

Miraculous gel

Text Anouck Vrouwe / Image Caltiva

It was more or less by chance that a chemistry group in Nijmegen discovered a super-absorbent gel, the mechanical properties of which resemble those of strong protein structures in cells. The first three patents for this bio gel have already been filed.

"Across the world there are laboratories that work with gels only. We didn't, we knew nothing at all about gels." But things can change. Half the laboratory of chemist Paul Kouwer and his colleague Alan Rowan is currently working on a gel – more or less by chance. Supergel, as they themselves call it.

It's a classic story: a scientist is searching for one specific thing and comes quite unexpectedly across something else. "Your experiment then takes a different turning than you had anticipated. In that case you have two options. If it doesn't make the grade you can simply throw it in the waste bin. Or you still find it interesting and want to find out more," says Kouwer. "And if I can just be critical on this subject; nowadays there is far too little time in the scientific world to do the latter. There is little room for something that isn't really in your line."

Let's return to the story of the discovery. Mattieu Koepf, then a postgraduate at Nijmegen, fortunately discarded the idea of binning it. He had produced a polymer that frustrated him because it didn't dissolve well in water – that's until he left it to cool down for a while in the refrigerator. When Koepf took the dish out of the refrigerator he saw that the polymer had dissolved. When it started to warm up again it began to return to a firm gel.

In other words, the Nijmegen chemists were not working on gels – but they had made one. And what a gel it is. 'Nijmegen supergel solidifies when warmed up', was the heading of an article in *de Volkskrant*. 'Powder that solidifies a swimming pool', was a header in *NRC Handelsblad*. And the British magazine *Wired*: 'New supergel has strange biological properties'. Each stressing a different property, but they are all correct.

Differing from a jelly that sets in the refrigerator, this gel solidifies if you warm it up and returns to liquid if you cool it down. "It was that property that the media gave most attention to," says Kouwer. He himself finds that the least interesting part. There are more substances that have the same property. He finds the super-absorbent properties and the seemingly biological characteristics of the gel far more exciting.

One gram per bucket

You only need one gram of polymer to transform a bucket of water into gel – or two kilos for a garden swimming pool – according to the NRC's calculations. Kouwer: "We continued to dilute it but it still remained gel. It then appeared that we were far below the value of the best absorbent gels known."

Kouwer says that this meant that the research group was faced with having to make a choice. "Either publishing in a hurry that we had discovered a supergel without knowing how it works, or postponing publication in order to study the properties ourselves. It's taken us two years, but I'm pleased that we made the decision to do the latter. It has now been published in *Nature*, otherwise it would have been in some much less significant journal."

"After investigating it more thoroughly we found that the material showed a striking similarity to the biological proteins that bring about firmness in the cell. Thanks to polymer side-groups the strands knit together at higher temperatures. This is why helical structures are formed – like the strands of a rope. Quite surprisingly, that results in a great deal of firmness," explains Kouwer. "In biology that's quite normal, firm chain-like materials in an aqueous environment. But this is the first synthetic material that has similar properties.

> "We feel that we have something really special in our hands"

And like its biological counterparts, this material suddenly becomes much stronger if you exert pressure on it – that too is quite remarkable."

Kouwer and Rowan's gel group is now looking into potential applications together with Noviotech, Radboud University's commercial partner. Radboud University Medical Centre also plays a role in this respect. The researchers gave thought to making a plaster out of the material – you apply the material in its liquid form and it firms up automatically from the body's heat. To remove the plaster you only need to cool it down. The gel could also serve as a base for cell cultivation – "which could lead to all sorts of biomedical applications". The material patent for the gel has already been obtained, and the first two application patents are being processed – including the one for the plaster. "We feel that we have something really special in our hands now. A synthetic gel with properties that are similar to what happens in nature; you can do fantastic things with that," says Kouwer.

ambition

Number of peer-reviewed publications:
82
(Aim 2016: 1200)

Text David Redeker / Image Erik Vriezekolk

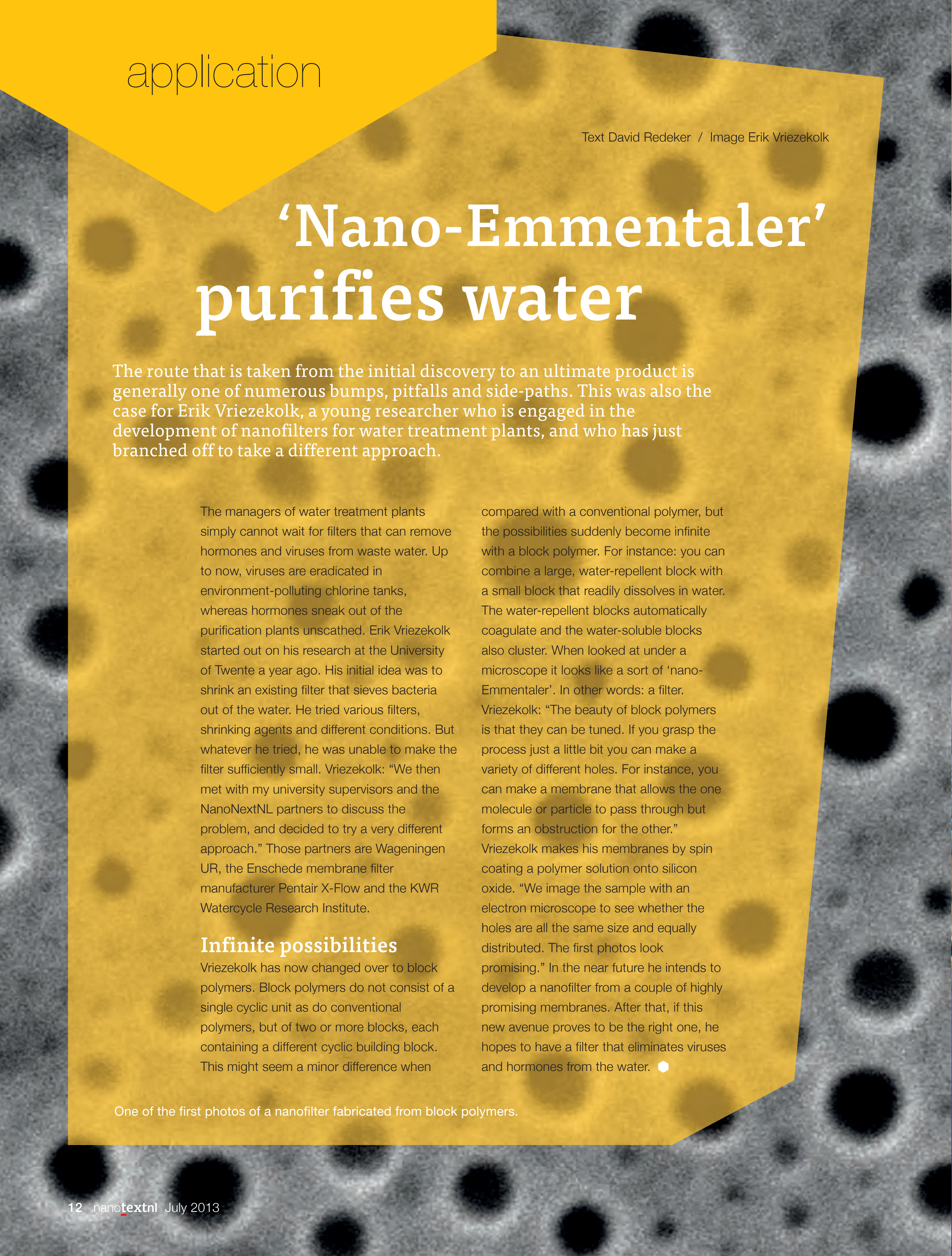
'Nano-Emmentaler' purifies water

The route that is taken from the initial discovery to an ultimate product is generally one of numerous bumps, pitfalls and side-paths. This was also the case for Erik Vriezekolk, a young researcher who is engaged in the development of nanofilters for water treatment plants, and who has just branched off to take a different approach.

The managers of water treatment plants simply cannot wait for filters that can remove hormones and viruses from waste water. Up to now, viruses are eradicated in environment-polluting chlorine tanks, whereas hormones sneak out of the purification plants unscathed. Erik Vriezekolk started out on his research at the University of Twente a year ago. His initial idea was to shrink an existing filter that sieves bacteria out of the water. He tried various filters, shrinking agents and different conditions. But whatever he tried, he was unable to make the filter sufficiently small. Vriezekolk: "We then met with my university supervisors and the NanoNextNL partners to discuss the problem, and decided to try a very different approach." Those partners are Wageningen UR, the Enschede membrane filter manufacturer Pentair X-Flow and the KWR Watercycle Research Institute.

Infinite possibilities

Vriezekolk has now changed over to block polymers. Block polymers do not consist of a single cyclic unit as do conventional polymers, but of two or more blocks, each containing a different cyclic building block. This might seem a minor difference when compared with a conventional polymer, but the possibilities suddenly become infinite with a block polymer. For instance: you can combine a large, water-repellent block with a small block that readily dissolves in water. The water-repellent blocks automatically coagulate and the water-soluble blocks also cluster. When looked at under a microscope it looks like a sort of 'nano-Emmentaler'. In other words: a filter. Vriezekolk: "The beauty of block polymers is that they can be tuned. If you grasp the process just a little bit you can make a variety of different holes. For instance, you can make a membrane that allows the one molecule or particle to pass through but forms an obstruction for the other." Vriezekolk makes his membranes by spin coating a polymer solution onto silicon oxide. "We image the sample with an electron microscope to see whether the holes are all the same size and equally distributed. The first photos look promising." In the near future he intends to develop a nanofilter from a couple of highly promising membranes. After that, if this new avenue proves to be the right one, he hopes to have a filter that eliminates viruses and hormones from the water.

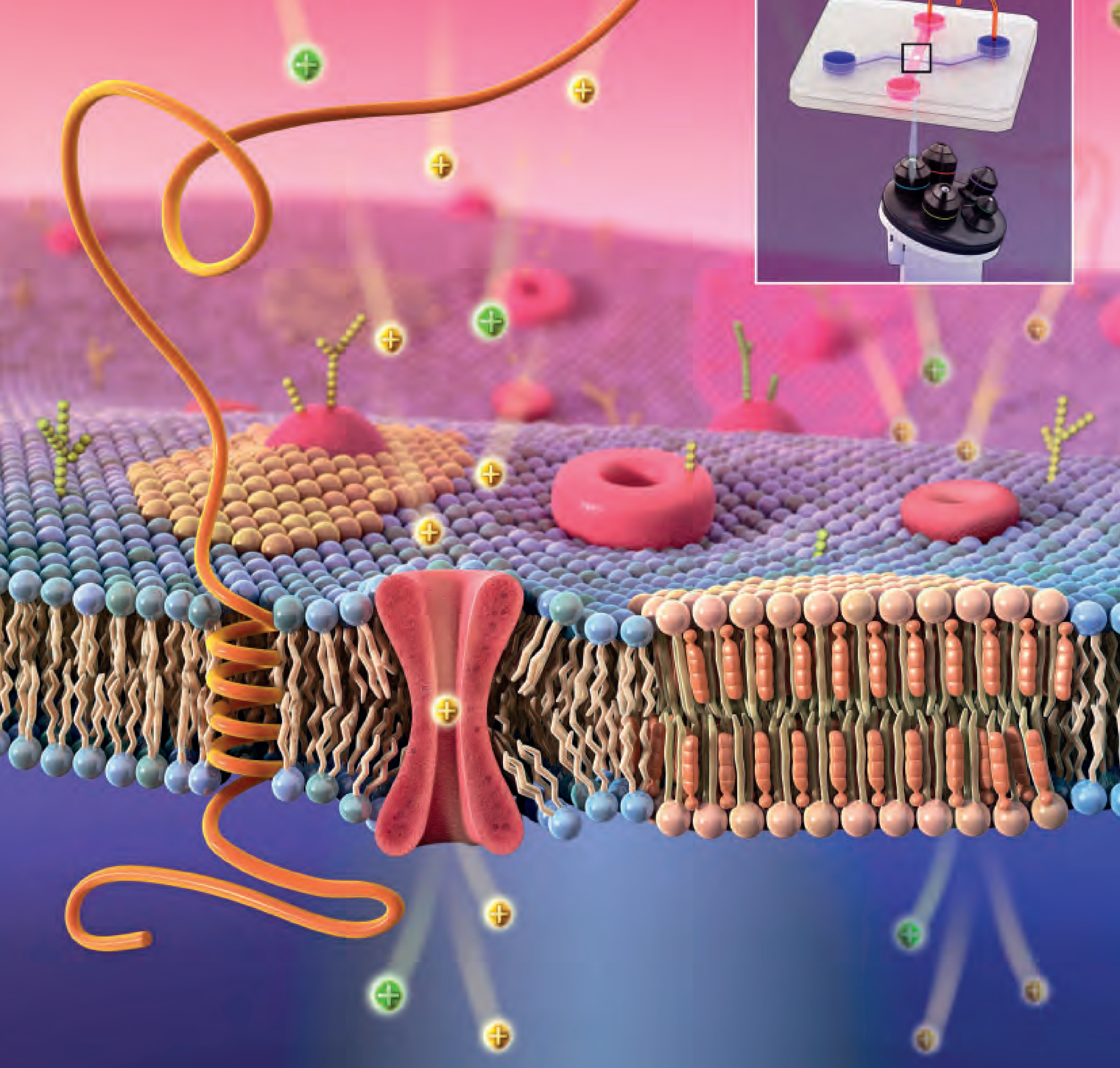


One of the first photos of a nanofilter fabricated from block polymers.

in sight

Séverine Le Gac and her team at the University of Twente have developed a microfluidic platform for experimentation on cell membranes and membrane proteins. The platform is suitable for electrical and optical measurements, including confocal microscopy. An artist impression of their NanoNextNL research made it to the cover of the magazine *Small, Volume 9, Issue 7*. The image shows a lipid bilayer membrane in a microfluidic chip including proteins such as ion channels.

Image Nymus3D



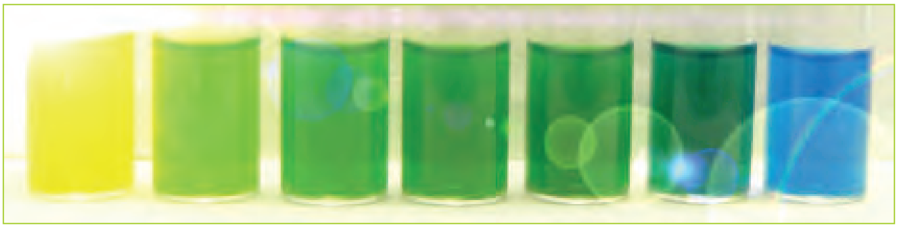
Green is a desirable colour in the food industry: it carries the promise of freshness. However, it is also a notorious colour: it is difficult to make and it easily fades. Ashok Patel and Krassimir Velikov at Unilever have filed a patent for a novel solution: colourant-carrying colloidal particles.

Shades of green

Text Nienke Beintema / Images Eastbourne B&B and Unilever

"Our invention is based on a completely novel approach," says Krassimir Velikov proudly. "We are able to produce any shade of green, and make sure that the colour is maintained at various pH values, especially at acidic pH where the natural green colourant chlorophyll is not stable." This feat, the Unilever scientist explains, is one of the long-standing challenges in the food industry. Whereas green is one of the most desirable colours, given its association with 'fresh' and 'natural', it is also one of the most challenging to preserve. Natural green pigments such as chlorophyll – which customers strongly prefer to synthetic colouring – have a tendency to lose their brightness when exposed to heat, light or a low pH.

"This challenge has plagued food scientists for many years," says Velikov. "We are the first to have found a way to combine water-soluble and water-insoluble colourants in a single product, in a way that is safe, robust and highly pH-stable." The trick, he explains, is to attach both the yellow and blue colourants to so-called colloidal particles: very small particles that remain stably suspended in liquids. Unilever uses nanoscale colloidal particles consisting of corn protein. They range in size from around 175 to 300 nanometre. The scientists can 'load' these particles with either curcumin, which is a water insoluble natural yellow colourant, or indigo carmine, a synthetic, yet nature-identical blue colourant. 'Loading' means that the colourants are incorporated in the protein matrix. By changing the ratio between the two colourants, the scientists can produce every imaginable shade of green.
"The protein suppresses the recrystallisation of insoluble pigments allowing maximal interaction with light," Velikov explains, "and it also protects the pigments against external influences. In short, we combine two colourants with different solubility profiles in a natural, digestible, fully biocompatible carrier. There you have it!"



By changing the ratio between yellow and blue colourants, every imaginable shade of green can be produced.

Interactions

The idea may be simple, as Velikov emphasises, but the practical application requires advanced nanoscience. Making the right nanoscale particles – with the right composition and structure – and controlling their interactions with the colourants requires a carefully designed production process. Unilever has recently filed a patent that covers this technology, as well as the composition of the colloidal particles and products that comprise them. The patent demonstrates how the combination of strong molecular interactions between selected proteins combined in nanoscale delivery systems allows design of new food-grade functional colorants. This challenge is at the heart of the NanoNextNL programme 'Molecular Structure of Food' where the overarching objective is to understand existing functional edible micro- and nanostructures and design new alternatives. "The particles can be made compatible with all kinds of food products," Velikov highlights, "ranging from drinks to semi-solid and solid foods. I think that especially the beverages market will benefit. Many beverages have a low pH, which affects colourants that are applied in a traditional way." Even when the colloidal particles are suspended in a beverage, he stresses, will the fluid remain clear and stable.
The main challenge lies in controlling the molecular interactions between the particles, the pigments and the food product they are added to. "It is all about having sophisticated and better control of what is happening inside these materials," says Velikov. "They are not just susceptible to pH, but also to light for instance. And both colourants attach to the particles in different ways. Making exactly the right shade of green is actually quite difficult to do."

Velikov enjoys the challenge of getting all the process parameters right. "It's like putting together the pieces of a complicated puzzle," he says. "It involves a lot of fundamental science, but it also has a very practical component. Whatever we come up with in the lab could be reflected in what a future product will look like. And this is incredibly important when it comes to consumer preferences and safety." Corn protein, he empha-sises, is a natural, digestible and fully biodegradable material. The colourants are food-grade. "One of them, curcumin, even has additional advantages as an antioxidant, which others claim to be beneficial in terms of health."
The technology is currently still in the patenting phase, which usually takes at least several years. Velikov finds it impossible to say when consumers will be able to buy foods coloured with these colloidal particles. "But I am confident that this technology will find applications in food and beyond," he concludes.

"Whatever we come up with in the lab could be reflected in what a future product will look like"

ambition

Number of patent filings jointly filed between industry and academia: **3**
(Aim 2016: 25)

A cell embedded in a matrix of fibrin fibers.

Cells and surroundings: an organic system

How a cell exactly develops depends on its surroundings; an effect that works both ways – and an important aspect for tissue engineers. Biophysicists are therefore studying the reasons why on the nanoscale.

Text Nienke Beintema / Images AMOLF, Xeltis

The human body has the amazing ability to repair damaged tissue itself. How a wound heals is a perfect example of this. Yet the body is capable of far more than just that, certainly when given a helping hand. *Tissue engineering* is a rising discipline devoted to this subject. For instance, tissue engineers are able to replace damaged bone with porous ceramics that subsequently fuse with the body's own bone cells.

"Our company takes that principle one step further," says Martijn Cox of biotech company Xeltis. This young company, which recently merged with Eindhoven spin-off Qtis/e, produces sections of blood vessel and even complete cardiac valves from biopolymers. Once they have been placed inside the body the biopolymers disintegrate and are gradually replaced by the body's own cells. "At the end of the process you have a normal cardiac valve," says Cox, "with several specialised types of cell and exactly the right haemodynamic characteristics."

As yet little is known about how this particular process exactly takes place. For example, how do the new cells know what shape they collectively need to adopt, and what tasks they have to perform? To answer that question, Xeltis engineers need a great deal of fundamental knowledge: about the development and structure of cells and about how they interact, both with each other and with their environment. Part of this knowledge they generate themselves, but they also appeal to the academic world. "The nanostructure of our polymer, for instance, influences which type of cell migrates to it," explains Cox, "and how those cells react to the polymer, which proteins they will make and how strong the whole structure is. If you wish to improve the end result you must first have an understanding of the underlying processes. It is for this reason that we work together with research institute AMOLF via NanoNextNL.

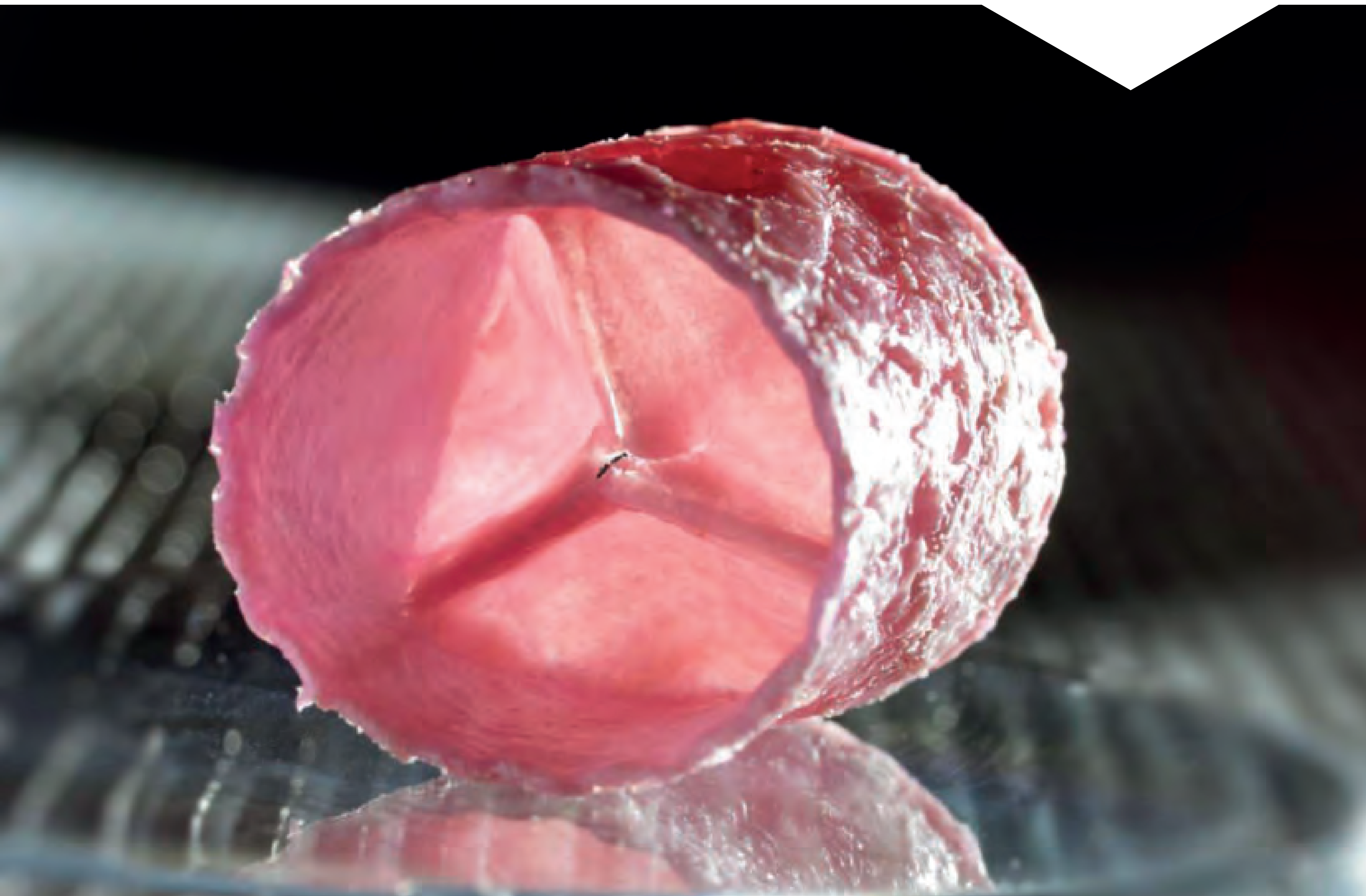
Biophysics

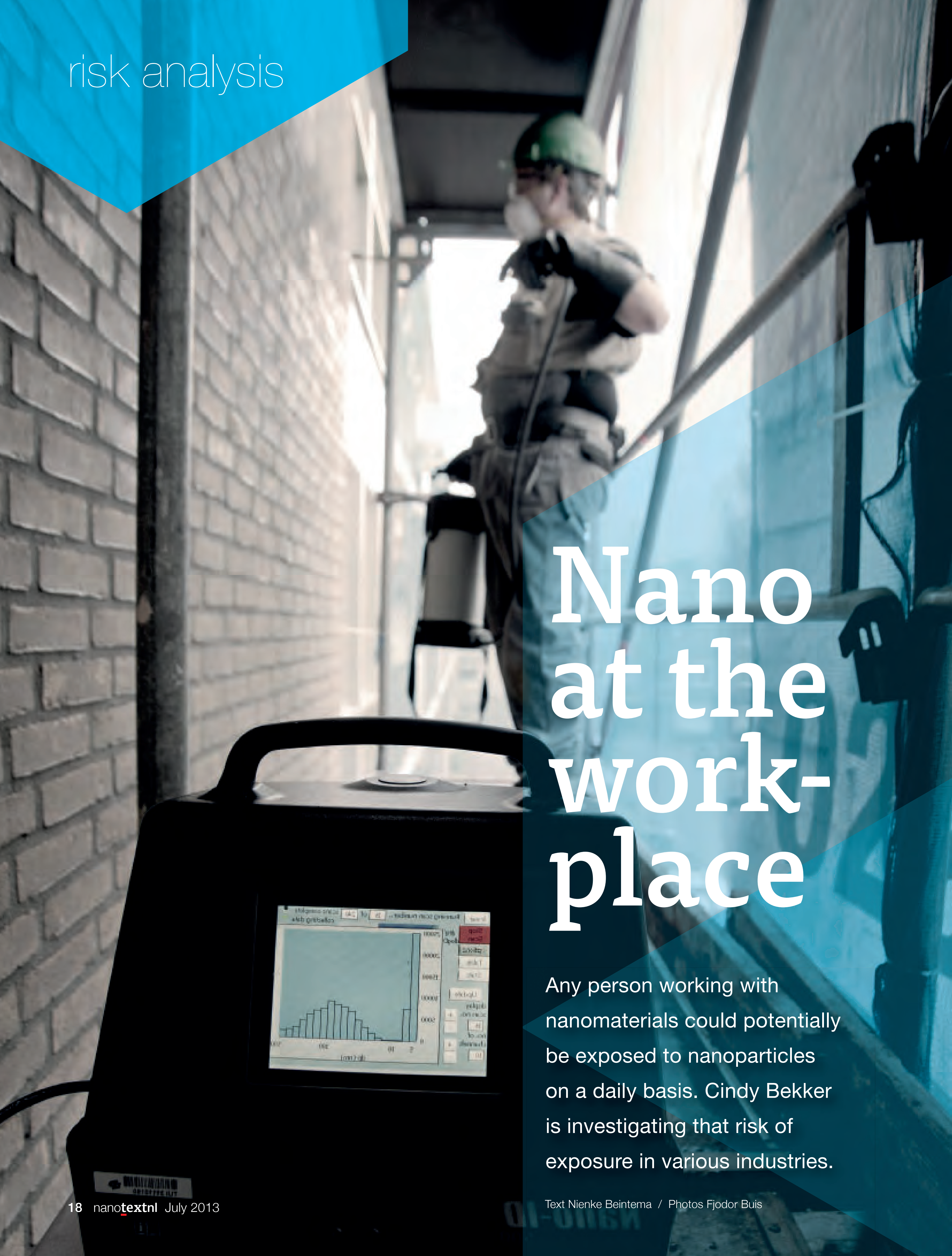
"We are investigating the interaction of cells with the body's own matrix," says Gijsje Koenderink of AMOLF. The cells in the body are built into a static or dynamic matrix of for example collagen, a substance that gives firmness to the tissue concerned. "Several years ago it was demonstrated that the matrix firmness influences how cells develop," says Koenderink. "Cells tug on the matrix as it were to find out how firm it is. Depending on the firmness they can develop themselves in different ways. The same type of stem cell can develop into a nerve cell in a soft matrix and into a bone-type cell in a firm matrix. That's how extreme the effect is."

> "The same type of stem cell can develop into a nerve cell in a soft matrix and into a bone-type cell in a firm matrix"

Koenderink and her colleagues are investigating how cells exert such powers on their surroundings. Thanks to advanced microscopes they now know for instance that cells use their cytoskeleton to generate powers through so-called molecular motors. Complexes of protein form a connection through the cell membrane, between the cytoskeleton and the collagen matrix fibres. "We discovered that this effect works both ways," says Koenderink. "Cells not only react to the matrix firmness but also influence the process themselves. The harder they pull, the firmer the matrix becomes. These feedback processes have potentially major consequences on the structure of a cardiac valve. You don't want it to become too firm so that bone-like cells start to grow."
The AMOLF research is fundamentally biophysical, stresses Koenderink. "Colleagues are working to find an answer to the biological significance of these processes. It can take years before we find that out. Plus the fact that from the beginning it has never been exactly clear what Xeltis can do with this information."
A statement endorsed by Martijn Cox of Xeltis. But he isn't worried by that: no matter what, both parties benefit from the collaboration. Both provide a stimulus for each other's work and thus make it more relevant. "We now have a prototype that behaves the way it should on the basis of current knowledge," says Cox. And like all biomedical innovations it will still take some time before it can be used in a clinical setting. But maybe in the meanwhile improvements can be made on the basis of newly generated knowledge. Cox: "Maybe the research will lead to specific aspects that we can improve, or we could discover that you can apply this principle to other parts of the body. On the other hand, maybe the conclusion is that improvements are unnecessary. I'm really curious."

Previous version of the cardiac valves Xerxis grows from tissue engineered materials.





Nano at the work-place

Any person working with nanomaterials could potentially be exposed to nanoparticles on a daily basis. Cindy Bekker is investigating that risk of exposure in various industries.

Text Nienke Beintema / Photos Fjodor Buis

Nanoparticles are frequently in the news. The distinctive size related properties of nanoparticles help to improve the properties of many materials. Therefore the particles are incorporated in a wide range of products such as cosmetics.

Yet there are potential risks attached to nanoparticles: because of their nanospecific properties some particles could be toxic or even carcinogenic. “Reason enough to be vigilant, especially when people work with them on a regular basis,” says Cindy Bekker. She is investigating exposure to nanoparticles at the workplace in a joint TNO and Utrecht University project that was set up within NanoNextNL. “Nanomaterials are used in many industrial sectors,” she says. “In the paint and coatings industry for instance. Nanoparticles can become airborne when powders are used to manufacture such products. Moreover, coatings are often applied by means of a spray. All such processes give rise to exposure and consequently workers are potentially at risk.”

Inhalation zone

In her project, Bekker is mapping the whole life cycle of nanoparticles for relevant industries, starting from the production of the material itself to its application by workers. To do this she first of all draws up a list of the companies in the Netherlands that work with nanoparticles. “For some obscure reason that’s not yet known,” she explains. “Developments are going at a rapid pace and the potential risk of nanoparticles has only been on the agenda of policy makers and researchers for a few years now.” Bekker first asks companies whether they are interested in participating in her project. Initially she limits herself to companies working with synthesised nanoparticles which are added to a product for a specific reason. Bekker then takes precise on-site measurements. “But measuring the number of particles in the air alone is not enough,” she says. “We still don’t know which metric – the number, size, surface area or mass of the particles or possibly their shape – provides the most relevant indication of the potential health risk. It is for this reason that we take a measurement of all aspects.” Bekker uses various direct reading instruments to measure the number of particles and the distribution of particle size in the worker’s breathing zone. In addition, she collects the particles on a filter and subsequently studies their characteristics under an electron microscope to find out what the particles look like and whether they are coagulated.

Reference values

The problem, according to Bekker, is that the risks are still unknown. There is simply not enough known about the effect of most nanoparticles on the human body. While a great deal of toxicology research is being carried out on animal models, the outcomes of that research are often contradictory.

Spray coating might release nanoparticles into the air.

Cindy Bekker (left) is measuring the exposure to nanoparticles during the spray coating of a building facade.

"That's why no health-based occupational exposure limits for nanomaterials have been determined as yet," explains Bekker. "The Social and Economic Council of the Netherlands has however advised to use the non-health-based precautionary reference values as pragmatic guidance values in 2012. We test the exposure measured at the workplace against these reference values." She is therefore unable to draw a conclusion as to the health risk for workers. Bekker is however able to give advice: how can companies limit that exposure? "For instance,

"We still don't know which metric – the number of particles, the size of those particles or possibly their shape – causes the potential risk"

it can be done by using personal protective equipment, such as respiratory protection equipment, ventilation or by carrying out the work in a fume cupboard. You can of course also limit the emission of nanoparticles, e.g. by using an alternate spray technique." Bekker is not only identifying all potential exposure scenarios. She is also working on improving measuring strategies and inhalation exposure models. "Harmonizing our measurement strategy will enable us to exchange data and learn from one another," she says. "We also speak with toxicologists on a regular basis: what do we want to measure precisely, what are we able to measure now, and for what area should we still develop alternative measuring methods? Yes, I'm optimistic about the future. We've already gained a great deal of progress and will certainly continue our work in this field."

Do's and don'ts in nanolabs

As the Safety, Health, Welfare and the Environment chairman of the ChemE Department of Delft University of Technology, Freek Kapteijn, professor of Catalysis Engineering, initiated a practical guidebook on how to work safely with nanomaterials in laboratories. This booklet soon became popular and is currently being developed further for wider distribution. "Chemical technologists often work with small particles such as silicon powder, quantum dots and a variety of catalysts," says Kapteijn. "Some five years ago we realised that there were no explicit rules for handling such things safely." A flowsheet for nanosafety (Quick Check) was subsequently drawn up: a sort of short checklist setting out the points you should keep in mind when working with various materials. The Nanosafety Guidelines, which contain background information, are included with the flowsheet. The most recent version was published in 2010. Meanwhile, more has been done in this field both nationally and internationally. A project team that includes Delft University of Technology, TNO, the Dutch Institute for Fundamental Energy Research (DIFFER), Foundation for Fundamental Research on Matter (FOM), and Leiden University, is currently elaborating the manual. Are people happy with it? "Yes, it's very useful. All new employees have to take a digital nanosafety test, and you must have read the manual to do so successfully." The guidelines are available on www.nanonextnl.nl/safety

Text Anouck Vrouwe / Image FutureChemistry

Reactive gases under control

Reactive gases are difficult to dose and tricky in terms of safety: chemists in companies and at universities consequently often try to avoid using them.
The Nijmegen company FutureChemistry is developing a gas module which helps chemists to work accurately with small amounts of these gases.

Pieter Nieuwland, research director of Radboud University Nijmegen spin-off FutureChemistry, explains what makes working with reactive gases so problematic: “A huge gas cylinder is located somewhere in the laboratory, but chemists only need to use the tiniest amount of gas for their reactions. How do you get it inside your flask safely and how do you get the dose right?”

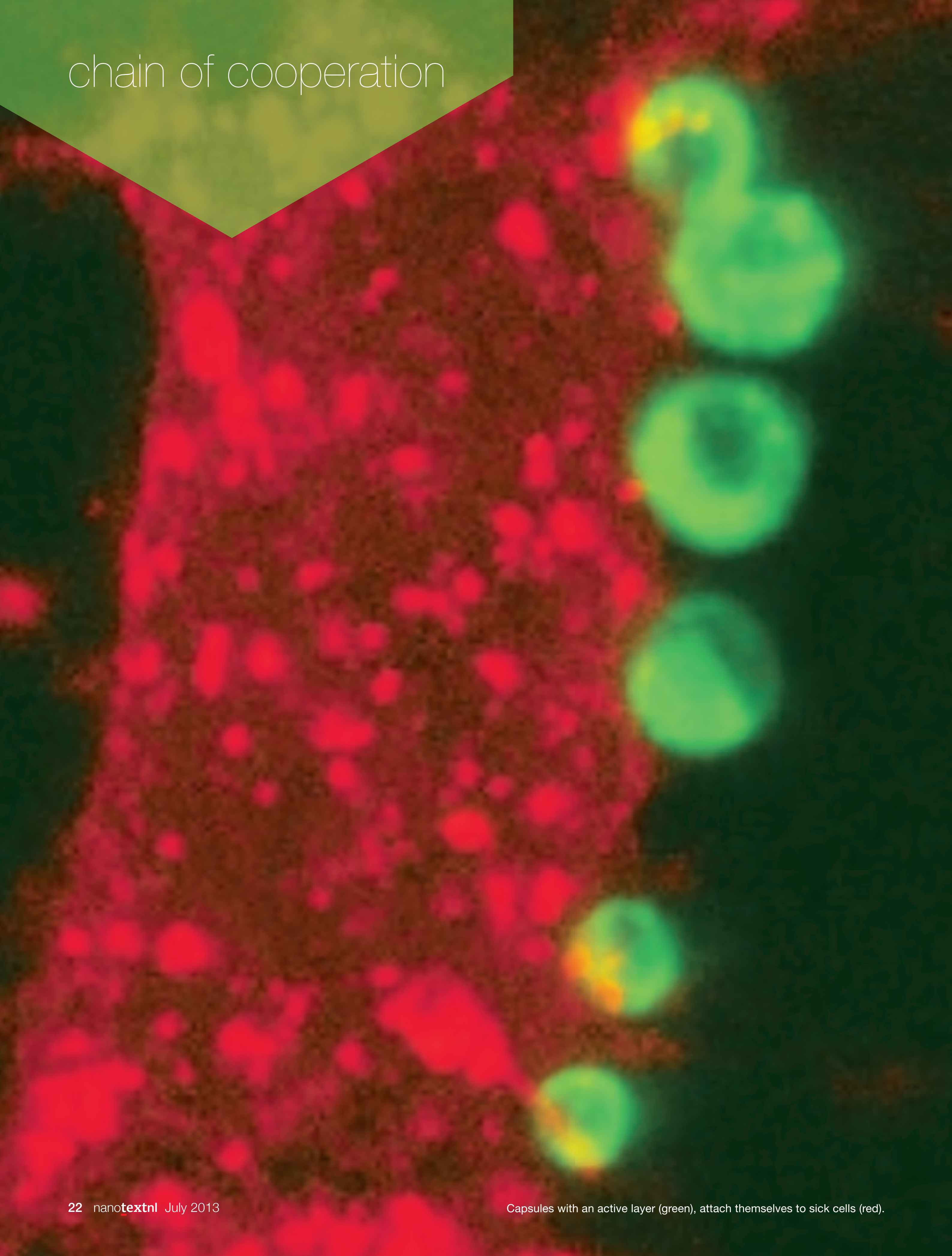
> “We cleverly combined our own and current technology in this gas module”

FutureChemistry is now marketing a gas module for working with reactive gases. The small amount of gas needed for the reaction is first dissolved in a liquid. The liquid and gas are then transferred to a micro reactor. This is where the reaction takes place. The reaction product is then collected and analysed. Moreover, by using a spectrometer the amount of gas subsequently remaining in the liquid can be monitored precisely.

The emergence of micro reactors has made it much easier for chemists to work with liquids. “We wanted to do the same for working with gases too,” says Nieuwland. “We cleverly combined our own and current technology in this gas module.” What makes the module so special, says Nieuwland, is the dosing accuracy, leading to more and better control of the reactions. A new type of gas-permeable membrane which is resistant against solvents allows, among other things, gas to be added to liquid in small doses.

This gas module is for the time being available as a prototype. Modules have already been installed at a number of FutureChemistry’s customers. The current module is suitable for small-scale synthesis of substances. But work is also in progress on a larger type, albeit not at FutureChemistry itself. “Flowid, our affiliated company in Eindhoven, is investigating whether the gas module principle can be up-scaled for large-scale production, which is the ultimate aim of our NanoNextNL project,” says Nieuwland. “In addition, research at the University of Twente, and at Micronit Microfluidics BV, investigates whether it is possible to apply for example higher pressures. This would widen the scope of this technology even further.”

chain of cooperation



Capsules with an active layer (green), attach themselves to sick cells (red).

Text Anouck Vrouwe / Illustrations Michel Versluis

Vibrant nanocapsules

"It's me again," says Gert Veldhuis when entering Michel Versluis' office. Both men are from two entirely different worlds: Veldhuis manages a company, Versluis a research department. Yet they both have a fascination for nanocapsules for medical applications. Hence, the two are engaged in joint research.

"Look, this is an application that's already on the market." The small, glass vial he holds up reveals nothing special to the naked eye. All there is to see is some white powder at the bottom of the vial. And yet it is not just any powder; this is a giant bag of marbles on the nano scale. "This vial contains five billion air-filled capsules with a diameter of three to five micrometres," says physicist Michel Versluis of the University of Twente's Physics of Fluids research group. By using the included fluid and injection needle, the solution can be injected into the bloodstream. This allows hospital medical staff to monitor the blood flow in organs, e.g. after a myocardial infarction to see where the blockage is. The capsules are of the same size as a red blood cell but differ from the cells in that they react strongly to ultrasound thanks to the air inside the capsule. Whereas blood remains virtually invisible on an ultrasound image, the hollow capsules light up clearly.

Versluis intends to develop these capsules further. He wants to make 'vibrant nanocapsules'; capsules that do not simply roam around the body but gather at those sites where something is amiss: in a tumour, at an inflammation site or on a layer of plaque formation in a blood vessel.

"We do this by covering the outer side of the capsules with what we call an active layer. For example, with antibodies. These antibodies attach themselves to the sick cells and the capsules become attached at that point. You can then detect them by ultrasound." This is one example of molecular imaging, a technique the University of Twente is conducting a great deal of research into.

Chain of four

Versluis is not alone in his research into nanocapsules. In a NanoNextNL project both he and Veldhuis are in the middle of a chain of four. That chain starts with microsieve manufacturer Lionix. Nanomi, the company owned by Gert Veldhuis, makes the nanocapsules with the aid of Lionix's sieves. Versluis, together with a PhD student, characterises the capsules, monitoring their behaviour. His laboratory houses a special microscope that can make super-fast images. This produces a movie showing how a capsule reacts to ultrasound or laser light.

"Everything goes back and forth between us several times," adds Veldhuis. "Michel suggests giving the capsules a different dye so that they will react even better to the laser light. But we find that this makes them become brittle when we add the proposed

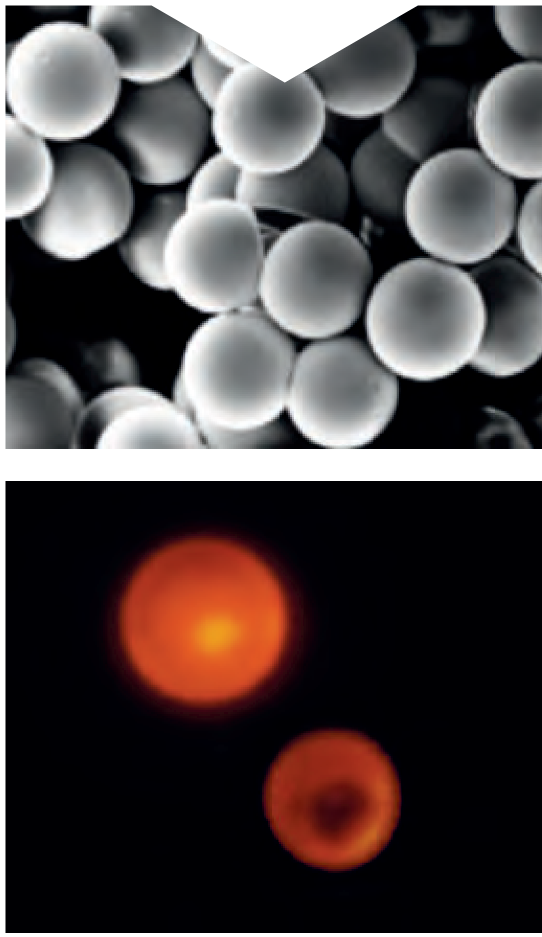
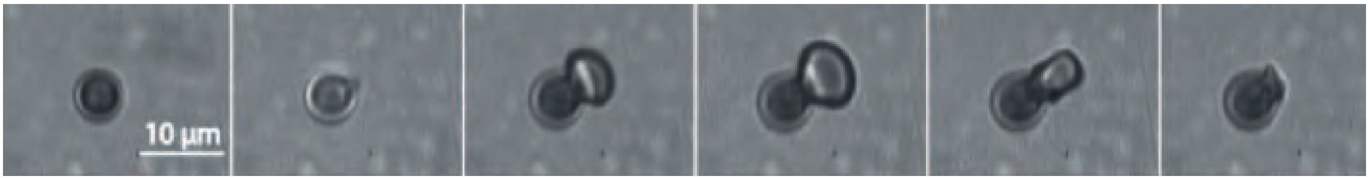


Image of capsules taken with SEM (upper image) and with fluorescence techniques (bottom image).



When activated by a laser beam, the capsules release the medicine in a controlled way.

dye formulation. We then start looking for an alternative. And that's the way it goes, taking turns, gradually taking us a step further." Once the two men are satisfied, the capsules are sent to Rotterdam where a PhD student of the Erasmus Medical Centre, the fourth partner in the NanoNextNL project, examines them to see whether they really do what they are intended to do in living tissue.

Besides adding an active layer, Veldhuis and Versluis have another important goal: to make the capsules ten times smaller than they are at present, while all have the same size. "That's especially essential for the detection of tumours. The blood vessels surrounding tumours tend to leak. This means that the smaller capsules can seep out of the blood vessel and penetrate deeply into the tumour. If our capsules are ten times smaller than they are now we expect that this will succeed," says Versluis. "We must ensure that they are all exactly the right size. The capsules resonate to the frequency of the ultrasound and consequently the monodisperse capsules present the strongest signal."

Finer sieves

The current capsules average 5 micrometres, in other words they must be brought down to 0.5 micrometres. And that's not simply a question of ordering finer sieves from Lionix. Veldhuis: "Lionix is on the verge of what's possible with the current production method. The company is therefore experimenting with new methods." He explains that the sieves can be compared to an ultra-fine shower head that produces droplets. "If you let those droplets dry you are left with the capsules," says Veldhuis. "Now that may sound simple, but it certainly isn't. The composition is extremely precise. If you mix the substances in the wrong proportions then you can end up with capsules with a hole in them. Either that or the capsules are not hollow. If the capsules become smaller, the formula for the capsules has to be changed."

Veldhuis explains why Nanomi is participating in this NanoNextNL project. "That's simple: because by joining forces we progress further than if we all work on our own. We are engaged in industrial research. In practice, that's often a nice term for 'trial and error' until you have actually developed something that works. You can't go much further, that costs too much time and money. We can go much deeper with the people at the university. They want to grasp the whole process in detail and be able to manipulate it. They benefit from our practical know-how and we learn a lot from their thorough research."

> "They benefit from our practical know-how and we learn a lot from their thorough research"

Veldhuis hopes that in a couple of years an application will be on the horizon that he can use to attract bigger investors. "At present they feel it's too early to invest in us, so the first steps in that process will need to be taken by Nanomi." But even if that application isn't found immediately, Veldhuis feels that the collaboration is certainly worthwhile: "Of course I hope that we achieve our goal: that we develop an application we can take to the market. But if we don't accomplish that goal it doesn't mean that the collaboration has been a failure. We are learning a great deal, and the things we discover now we will be able to use for something else."

The two have made sound arrangements regarding publications. The university may publish but should the article include information about Nanomi, then it will need to be discussed.

But why does Versluis work with Nanomi if they are unable to make the small capsules he needs? Why doesn't he go somewhere else? "Yes, that's a good question – why indeed?" asks Versluis Veldhuis laughingly. "H'm, we had looked forward to getting one good formula from you at the start," he aptly responds. Both men laugh; after which Versluis, with a serious look on his face, says: "Simple, if Nanomi can't produce the capsules I want, then nobody can. Most of what we are doing is new. They have the know-how. So if we make advances by working together then it's in my interest too."

Airfilled capsules with diameters of three to five micrometres are used to monitor blood flow in organs.

Text David Redeker / Image Michael Faes

Fuel from the sun

Leiden University professor of Catalysis and Surface Chemistry, Marc Koper, wants to solve the energy problem with catalysts that use sunlight to fix carbon dioxide and convert it into fuel.

What do catalysts have to do with the energy problem?

“We use our catalysts to simulate photosynthesis. A plant uses light to convert water and carbon dioxide into sugar and oxygen. Our aim is to achieve something similar with our own catalysts. We make hydrogen, methane or formic acid. If you burn up these substances as fuel, you are left with water and carbon dioxide again. In other words: nothing is lost and there is no waste. The only thing you need is sunlight.”

What are we waiting for?

“We're waiting for the ideal catalysts. The problem is twofold. Catalysts are available for the water oxidation reaction, but they are expensive and unstable. And catalysts that help the reduction reaction become poisoned very quickly.”

How do you find a good catalyst?

“Well, one way is to just try various materials. But know-how and experience are also crucial. Let’s take a look at the catalyst that makes formic acid from carbon dioxide. There’s a multitude of catalysts that do exactly the opposite. We’re now trying to make such a well-known catalyst work the other way round, and the results are certainly promising. We’re also doing much research on copper catalysts, which are known to be good catalysts for CO_2 reduction. The idea is that if we understand all aspects of copper and model them in the computer, we will then be able to calculate other catalysts even before we have made them.”

What will the future bring? Huge factories or people making their own fuels at home?

“I think it will be both. While aircraft fuel and diesel-like fuels will be produced in large factories, you will be able to make other fuels upstairs in your own attic. Suppose, you have solar panels on your roof. In the future you will be able to store or convert the surplus energy generated in the daytime by those solar panels into hydrogen gas. That hydrogen can be used to tank your fuel-cell powered electric car, or it can be regenerated into electricity at night. At present this can only be done with batteries, but batteries do not have enough storage capacity. You can sell the surplus to the electricity grid, but if everybody starts to use solar panels this won’t work anymore. That’s already happening in Germany; it’s starting to creak everywhere. If people do start to produce their own stock of fuel in their homes, then you get a system that’s more immune to fluctuations. I’m all in favour of that.”

> “Nothing is lost and there is no waste”

Lights on,

Chemist Evelien van Schrojenstein Lantman of Utrecht University devised a trick to be able to follow photocatalytic reactions live. She brings the microscope into position and switches the reaction 'on' by laser light.

Text Anouck Vrouwe / Photo Fjodor Buis

"Light fascinates me. I don't know why, it could be because I have a thing about colours. Like these water-filled vials. All the vials contain nanosilver, but the colour varies from yellow to purple depending on the particles' size and shape. I used this sort of nanosilver for my experiments.

I work in a chemistry department that's specialised in catalysis. Catalysts are auxiliary substances that accelerate and simplify reactions. Because you can save a great deal of time and money by using a well performing catalyst material, this area of research is both immense and important to our society.
How catalysts work exactly is mostly unknown – you can take measurements before and after catalysis, but what happens during the process itself is often a mystery. That's partly because the catalysts used are frequently in the form of finely distributed nanoparticles. Such an ultra-fine powder gives you the largest possible reaction surface. But if you want to investigate how the reaction takes place it's not very practical. Many microscope technologies are not powerful enough to let you observe at that level of magnification. They do show structure but not the reaction. The objective of my doctoral research was to develop a measurement technique that can be used to take measurements at the molecular level during catalysis. And we were successful. It was rewarded with a well-received publication in *Nature Nanotechnology*. Plus the attention of the chemical industry.

In my experiments I study a so-called photocatalytic reaction, that's a catalytic reaction that takes place under the influence of light. Photocatalysis is important when making solar fuels; a sort of synthetic photosynthesis in which you make fuel, such as methanol, from CO_2 and water. That's not cost-effective at present, but my promotor, Bert Weckhuysen, hopes that our new measurement technique will help this research field to progress further. I've looked at a single category of photocatalytic reactions; a reaction which is only possible with green light. The great thing about this is that the reaction only starts when I turn on a green laser.

I carried out my measurements in Jena, Germany. A measurement system is located there that has the desirable properties of an Atomic Force Microscope (AFM) in combination with Raman spectroscopy. You shoot your laser light at a material and – the same as it does with those vials of nanosilver – an interaction takes place between the light and the surface. By analysing the scattered light with Raman spectroscopy you can see which material is present on the surface. It's even better if you place a thin layer of metal, in our case gold, beneath the material to be analysed. The AFM is a microscope that scans the surface with a sharp needle and shows the structure at nanometre scale. However, in this case the needle plays a double role. It's coated with nanosilver that amplifies the measurement signal like an antenna when we use a red laser. Simultaneously, the silver also acts as a catalyst, but only for a green laser.
So what does that give us? A microscope, a spectrometer plus a reaction that we can control: after all it only starts when I turn on the green laser light and bring the tip of the AFM to the surface. And because we can time it so well we are able to follow the reaction precisely. This produces magnificent images that allow you to watch the surface changing during the reaction. Arjan Mank of Philips' Analysis Department

reaction!

ambition
Number of PhD's & other highly qualified knowledge workers: **235**
(aim 2016: 300)

cooperated in interpreting the measurements – Philips also found it interesting to work with a new measurement technique. VibSpec, a spin-off of the university specialised in vibrational spectroscopy, was also involved in the follow-up research.

We have demonstrated that this new measurement technique works for this one reaction. It now has to be expanded. A new doctoral candidate is investigating whether the same principle also works for a different

> "A microscope, a spectrometer *plus* a reaction that we can control"

reaction. In hindsight, it appears that we have been lucky with the selected reaction. When I returned to Jena for the second time I had already achieved a whole series of fantastic results, while the people around me were plodding away and not making any advances at all. But that's the way it goes in chemistry – something should work in theory, but in practice it's often much more difficult to realise. I'm very curious whether the developed analytical approach also works well for other photocatalytic reactions. And the people in the industry are as well."

events,
seminars,
courses,
people

Professionalising nanotechnologists

Currently NanoNextNL offers two courses, which are open both to participants of NanoNextNL and those from outside the NanoNextNL community.

The NanoNextNL **IP awareness and valorisation course** kicked off on 29 and 30 October 2012. In this course, entrepreneurial researchers are introduced into the commercial aspects of research outcomes. Course leaders Jaap Renkema en Pieter Schendstok navigate the participants through a variety of topics surrounding this theme.

Participants get the opportunity to prepare a realistic business case. PhD researcher Jasper van Weerd prepared the best case in the first edition of the course: “We put into practice what we were taught during the course: a switch from technical to customer-oriented thinking. Don’t explain the technical aspects of your product, but take its perceived advantages for customers as the starting point. It is also important to emphasise that the product is safe and inexpensive for customers. Finally, it helps if you pitch your story in an easy-going manner.”

Besides this IP awareness course, NanoNextNL also offers a two-day course on **Risk Analysis and Technology Assessment**: how do research findings ultimately find their way into society? And how can researchers navigate obstacles along the way?

In this course, researchers learn about the art of risk and technology assessment, and how to apply it in their own (PhD) research. Programme leaders of the NanoNextNL RATA research programmes are present to provide feedback and advice on the spot. The first edition of this course was held at 4 & 5 July 2013.

Read more: www.nanonextnl.nl/courses

ambition

Number of researchers that have followed an IPR awareness course:
32
(aim 2016: 300)

MicroNanoconference

Looking back at the eight version of the annual MicroNanoconference, it can only be said that the 2012 edition on 10-11 December 2012 was a very successful one. Over 440 participants visited the showcases of the latest and best what micro and nanotechnology can offer. One of the highlights was the spectacular evening lecture by David Quéré, École Supérieure de Physique et de Chemie Industrielles de la Ville de Paris. David Quéré shared his latest results on nonwetting materials.

The MicroNanoconference 2013, organised in cooperation with MinacNed, will be held on 11 - 12 December 2013.

Read more: www.micronanoconference.nl

Collaboration with Japan

In January 2013 a NanoNextNL delegation visited the Japanese National Institute for Materials Science (NIMS) as part of a trip to the NanoTech Expo Tokyo 2013 in order to enable collaborations between the programme partners and Asia. NIMS welcomes collaborations with Dutch industrial and academic partners. NanoNextNL gladly offers to mediate between NIMS and interested Dutch parties.

A few months later, the Japanese National Institute of Advanced Industrial Science and Technology (AIST) visited NanoNextNL. This institute also welcomes new partnerships with Dutch parties.

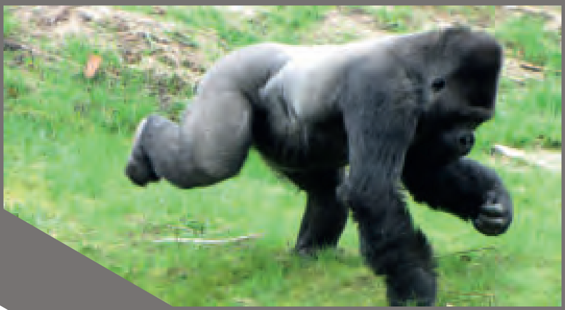
Follow the monkey

On 4 October 2012 the annual Intelligent Sensor Networks conference (ISN2012) took place in the Apenheul in Apeldoorn. The conference was organised by TNO-AMSN and NanoNextNL. The main question at hand: “How can society profit from the latest developments in sensor technology, intelligent network systems and their applications?”

Presentations from both the academic and the industrial world lead to inspiring discussions, in which it became clear that society already benefits from sensor developments, and that these developments are moving faster by the day. In the Sensing-session, organised by NanoNextNL, ample examples were given on how many applications are becoming reality now and in the near future. By precise control of chemical bonds to (nanoscopic) surfaces, sensors can be constructed which are both very sensitive and very specific. This combination leads to many applications, such as the direct detection of minute quantities of viruses in blood.

One of the highlights of the day was the opening of the TNO SensorLab@Apenheul on the Gorilla-island. With the extensive sensornetwork installed it is now possible to follow the gorilla’s on the island and to study their behaviour without disturbing their habitat.

The workshop Sensing Matters 2013, held at 25 April 2013, showed even more options for sensors in the future. From mechanical and chemical to optical sensing principles, applied in fields varying from weather forecasting to security and safety.



Safe Design of Nanomaterials

Fall 2012 NanoNextNL and TNO organised the interactive workshop Safe Design of Nanomaterials. The workshop generated 10 action points and related follow-up actions. Together with the presented overview and visions, the actions are bundled in the green paper *Safe Design of Nanomaterials - Paving the way for innovation*.

The first actions have already been taken: The RIVM (National Institute for Public Health and the Environment) has been asked to make a start with the Safe Design Platform. Furthermore, the first NanoNextNL RATA-meeting has been organised and was a success. The resulting green paper can be read at nanonextnl.nl/safebydesign

ambition

Workshops between programmes: **5**
(aim 2016: 60)

Nano on stage

Nanotechnology influences many application areas. As a natural result, researchers involved in NanoNextNL not only present their work to peers. From people interested in acoustics, to chemistry teachers, to the viewers of the Dutch tv-show ‘De Wereld Leert Door’: the past year NanoNextNL researchers could be found at all kinds of different occasions and locations.

ambition

Number of seminars and lectures for non-specialists: **16**
(aim 2016: 50)

New theme coordinators

During the past year, NanoNextNL has welcomed Hans Huiberts (Philips) as theme coordinator of theme 6, Beyond Moore, and Machteld de Kroon (TNO) as theme coordinator of theme 10, Sensors and actuators.

Text and illustrations: Eric Verdult

Microscope makes plasmon light visible by means of a smart mirror

Measuring light at nanoscale

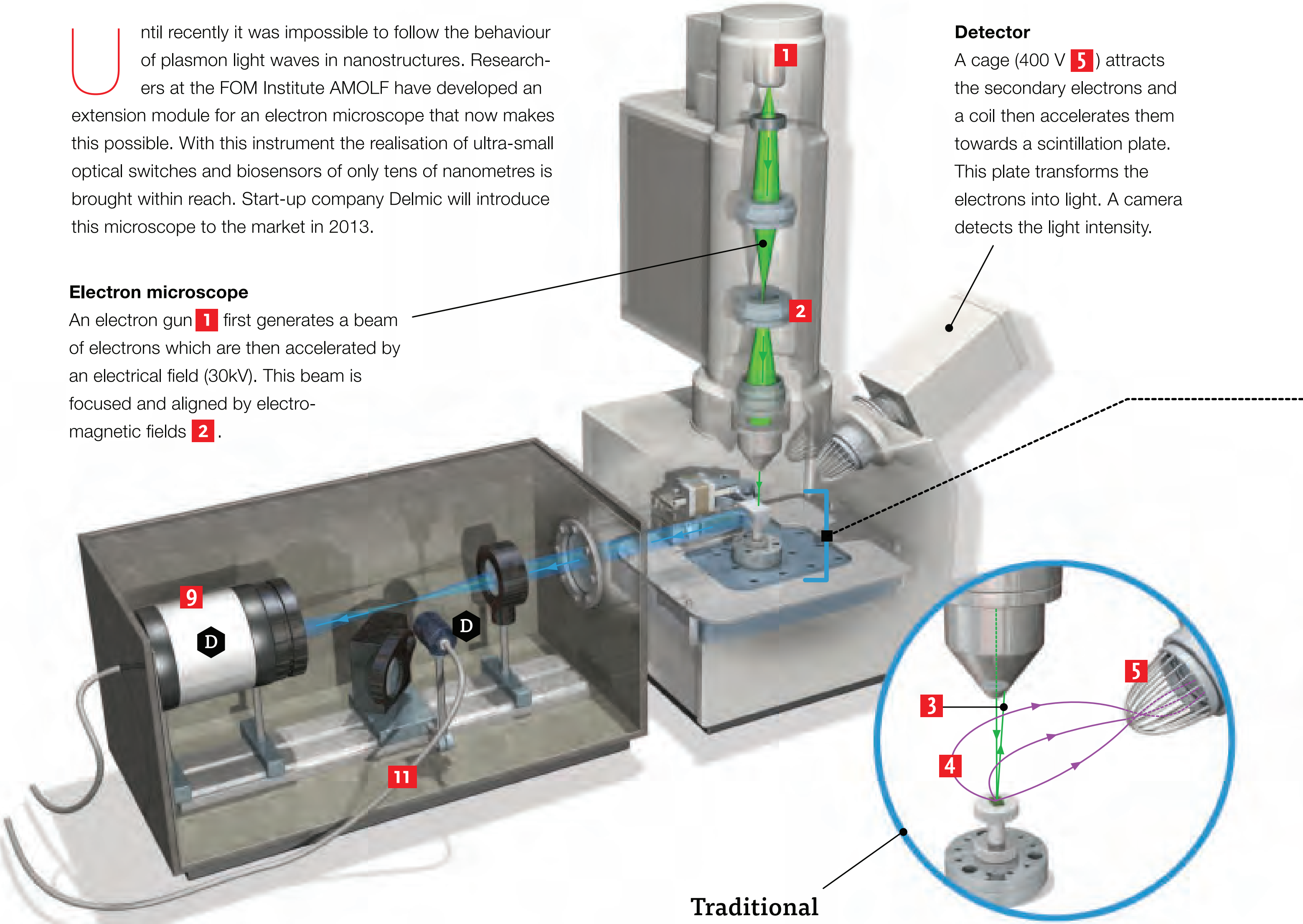
Until recently it was impossible to follow the behaviour of plasmon light waves in nanostructures. Researchers at the FOM Institute AMOLF have developed an extension module for an electron microscope that now makes this possible. With this instrument the realisation of ultra-small optical switches and biosensors of only tens of nanometres is brought within reach. Start-up company Delmic will introduce this microscope to the market in 2013.

Electron microscope

An electron gun 1 first generates a beam of electrons which are then accelerated by an electrical field (30kV). This beam is focused and aligned by electromagnetic fields 2.

Detector

A cage (400 V 5) attracts the secondary electrons and a coil then accelerates them towards a scintillation plate. This plate transforms the electrons into light. A camera detects the light intensity.



D Detector: light emission angle and colour

The light beam is directed onto a CCD camera 9 which measures the intensity of the light. AMOLF software calculates the angle at which the light is emitted (10 example of a measurement in a photonic crystal) on the basis of the CCD's hit point and the mirror's geometry. The measurement precision (at a resolution of 30 nm) is unique in the world. By switching a mirror into the light beam the light is led to a spectrometer 11 that determines the colour of the light.

Traditional electron microscope imaging

When an electron comes into contact with the sample it can be rebounded immediately ('backscattering' 3) or it can release an electron from the sample (secondary electron 4). The number of secondary electrons per unit of time is related to the angle of inclination of the sample surface and provides information about the surface geometry. The intensity of the backscattered electrons is related to the atomic number and provides insight into the composition of the sample.

A Plasmon waves

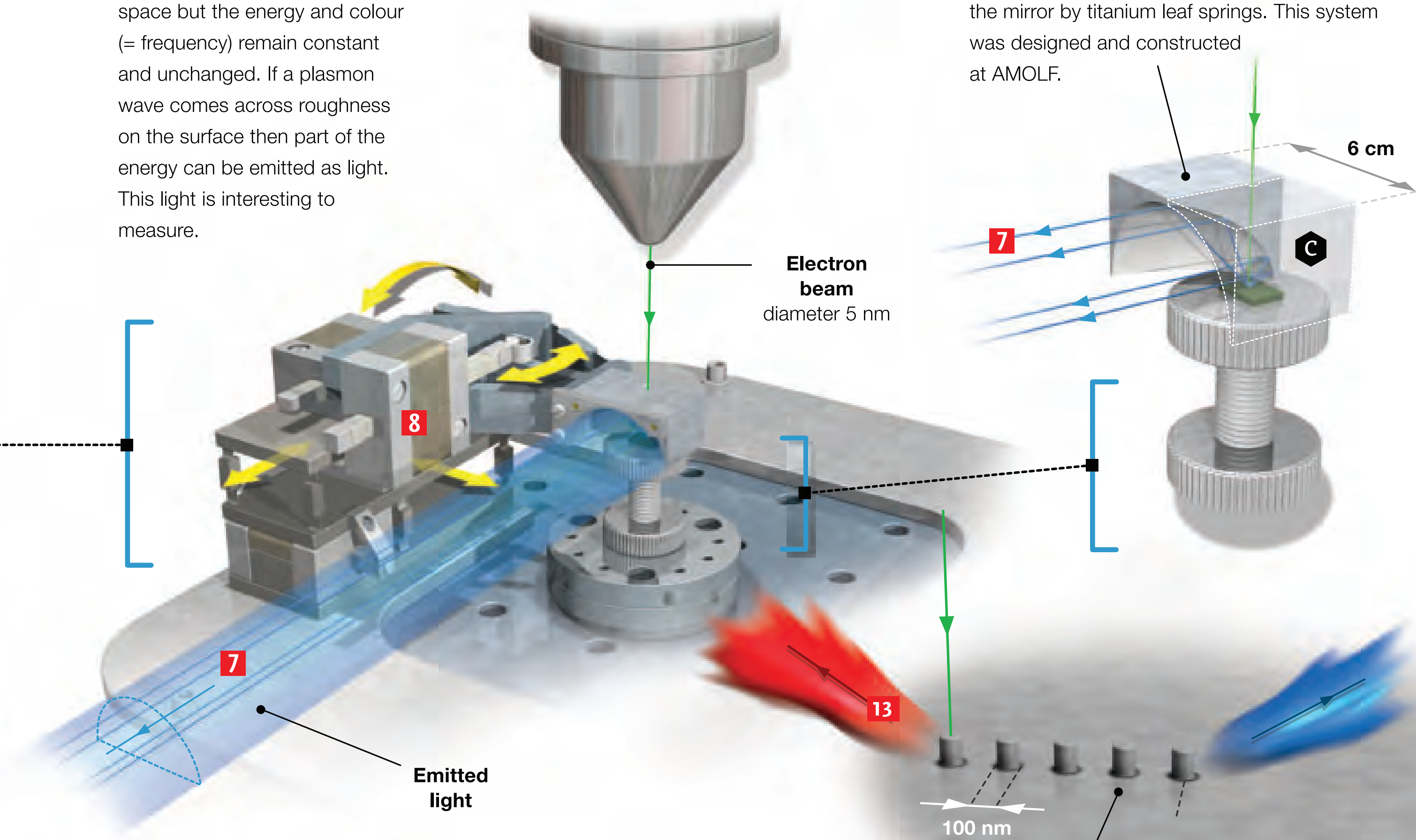
If an electron comes into contact with a sample a special kind of light is generated: surface plasmons 6 . These light waves are transmitted along the surfaces of metals. The wavelength of plasmons is smaller (e.g. two to a hundred times smaller) than that of light in free space but the energy and colour (= frequency) remain constant and unchanged. If a plasmon wave comes across roughness on the surface then part of the energy can be emitted as light. This light is interesting to measure.

B Optic nano behaviour

In order to study the optical properties of nanostructures their behaviour must be measurable. The problem here was that while an electron microscope does make nanostructures (smaller than 100 nm) visible, it does not make the generated light visible. Hence there was the need for a microscope that could measure light on a smaller scale than the wavelength of light itself.

C Parabolic mirror

A parabolic mirror catches the light and reflects it as a parallel beam 7 to the detector outside the microscope. The mirror has a 0.5 mm round hole in it to enable the electrons to pass. Prior to each experiment the mirror is aligned precisely, otherwise the beam will diverge and fall outside the range of the detector. Alignment is done by means of four piezoelectric motors 8 which are connected to the mirror by titanium leaf springs. This system was designed and constructed at AMOLF.

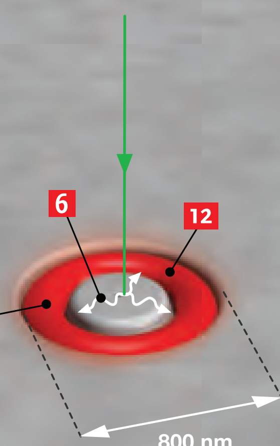


Nanomeasuring: Antenna

If electrons hit the left particle, the structure emits blue light on the right side and red light on the left. Vice versa is also possible. This depends on the interaction between the particles and their dimensions and relative distance.

Nanomeasuring: Ring

The electrons generate white light in the groove. The ring works like an organ pipe in which light resonates. Depending on the geometry of the ring, red light, for example, starts to circulate while other colours fade out.



Plasmon manipulation

Using nano fabrication techniques surfaces can be made that have special optical properties: e.g. they can either localise 12 or guide 13 light. This makes it possible to manipulate light (plasmons) on an extremely small scale. The small diameter of an electron beam is essential to generate plasmon light locally in the nano structure. This cannot be done with a standard light source (laser) because the beam diameter is larger than the nano structure.

NanoNextNL

NanoNextNL is a broad consortium of over a hundred Dutch companies and institutes which form an open, dynamic and sustainable ecosystem to stimulate Dutch research into micro and nanotechnology. In NanoNextNL investments from companies, knowledge institutes and the Dutch government are brought together.

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