welcome

Join our adventure

In this magazine, NanoNextNL gives an impression of its activities, partners, and way of working. NanoNextNL is a consortium of over one hundred companies, universities, knowledge institutes and university medical centres, aimed at innovating with micro and nanotechnology. Micro and nanotechnology are the manipulation, creation and understanding of new materials, fabrication techniques, processing and much more, all with one connecting theme: very small dimensions.

NanoNextNL started in 2010, and issues this magazine as its first public report.

To be able to monitor its performance, the consortium has translated its ambitions into numbers. Some of them are listed on this page. In this magazine, we demonstrate some of the stories behind the numbers: what the results are NanoNextNL is aiming for, and how we are going to achieve it.

We hope you will enjoy reading about our patents, partners, projects, publications and above all our people, all working in the exciting and utterly unpredictable field of micro and nanotechnology.

Colophon

nano<u>textnl</u>

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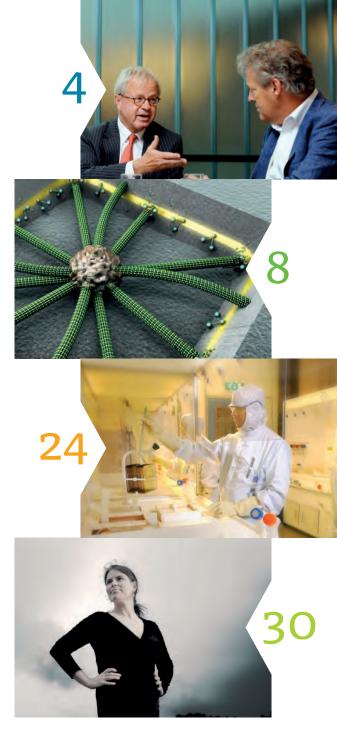
Ambition in numbers

	Aim (2016)	
Number of roadmaps composed for selected programs, defined jointly by industrial and academic participants	3	
Number of public awareness activities	99	
Number of peer-reviewed papers and conference contributions	1200	
Number of new start-ups or spin-off companies	15	
Number of workshops / conferences with industrial and academic participation to share results	270	
Number of patent filings	115	
Number of joint workshops / conferences with researchers from RATA and other themes	15	
Number of newly established collaborations between generic and application themes: joint patent applications joint publications	10 50	
Number of trained highly qualified knowledge workers	300	



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An island nation of bridges and boats





How did nanotechnology end up in the High Tech top sector?

AL: "The striking thing about nanotechnology is that on one hand, it's an independent field, with its own questions and techniques, but on the other hand it runs right through everything. Nanotechnology isn't just important for all the themes in the High Tech top sector – such as solar energy, light, health care and semiconductors – but also for the other top sectors, such as Agri&Food, Energy, Life Sciences and Water. But its centre of gravity does lie in the High Tech top sector."

DB: "It's good that we're anchored in a single top sector. That gives us a strong identity and ensures that we can powerfully attack common problems. From that home base, we're going to make sure that people in other top sectors become familiar with nanotechnology. When we call for research proposals, we invite everyone. It's definitely not the idea that High Tech will monopolise the field."

Does nanotechnology differ from those other research areas?

AL: "I notice that nanotechnologists really let themselves be inspired by what's happening in science; that connection is very strong. That makes the field challenging, and you need that to progress in leaps and bounds. In ICT, another High Tech theme, we still need to fight that battle."

DB: "Nanotechnology is a bit of a brazen field.

It attracts adventurous people with courage, because it's very dynamic."

Being present everywhere, in every research area and also in science, industry and the world of SMEs: that sounds like a significant organisational challenge.

DB: "It has been a long, tedious process, but fortunately we started thinking about it years ago. That was when we founded NanoNed, the predecessor to NanoNextNL. We were adamant that we weren't going to set up some huge organisational structure, with a

"We wanted to be more of a platform where people from research and industry could meet each other"

management team and our own office. We wanted to be more of a platform where people from research and industry could meet each other."

AL: "Yes, it's definitely given you a leg up that you had already set up a programme. Now you're jumping onto a speeding train, while

other areas still need to map out the trends." DB: "The 28 research programmes form the core of NanoNextNL. They're led by scientists, who maintain contact with groups at universities, companies and research institutes throughout the Netherlands. They provide the scientific connection. Next, ten overarching themes have been defined around the research programmes. Those are led by people from industry, who understand what's important in their field. They make sure the different programmes within a theme are aligned. We, as the board, ensure that all the themes come together into a single total programme for Dutch nanotechnology."

An ingenious structure.

DB: "Isn't it, though? By putting the programme directors, the theme coordinators and the board in contact with each other, NanoNextNL has woven together everyone in the Netherlands who's active in nanotechnology – and done it with very little overhead."

Is nanotechnology going to give the Dutch economy the boost for growth which we so badly need?

DB: "Absolutely. Our intention is to ramp up prosperity not only in the Netherlands, but also in the rest of the world, and in so doing, to give many families happier lives."



NanoNextNL is a broad consortium of over a hundred companies and institutes which form an open, dynamic and sustainable ecosystem to stimulate Dutch research into micro and nanotechnology. The programme is a result of the Netherlands Nano Initiative, launched in 2008, and is a selective continuation of MicroNed and NanoNed, the former research programmes on micro and nanotechnology. In NanoNextNL €125 million from companies and knowledge institutes and a €125 million investment from the Dutch government are brought together. All the projects within NanoNextNL fall into one of 28 research programmes, which are in turn divided across 10 themes. Nanotechnology is part of the Dutch Topsector High Tech Systems & Materials, and has an important connection within the topsectors Chemical, Energy, Water, Life sciences and Agri&Food.

More information:

www.nanonextnl.nl

That sounds ambitious. What concrete results can we expect from nanotechnology?

AL: "Take a company like ASML, a manufacturer of machinery for the semiconductor industry. Nanotechnology is crucial there. The

innovations come from smaller companies: university spin-offs, or young entrepreneurs starting out with a good idea. They play a crucial role in the ecosystem. That's why we deliberately seek them out."

DB: "In NanoNextNL, we not only work

"We intend for NanoNextNL to generate 50 to 70 spin-offs in the next five years, founded by some of the 300 young researchers we're training"

tinier the lines on a chip, the better iPads will soon look. In the race against foreign competitors, everything hinges on nanotechnology. Or consider the agrofood industry. With nanotechnology, we may be able to develop packaging which keeps products fresh longer. That also provides an enormous competitive advantage."

DB: "Suppose we discover that graphene is the material you need to develop a quantum computer. That means not only an enormous business boost for ASML, but also that we can increase our computing power so dramatically that problems currently beyond us become solvable."

SMEs are well represented in NanoNextNL. Is there a philosophy behind that?

AL: "It's true for the entire High Tech top sector. Our segment is so dynamic, you need to have a versatility you can hardly expect from large companies. And you see that many

with small companies, we also give rise to new companies. We intend for NanoNextNL to generate 50 to 70 spin-offs in the next five years, founded by some of the 300 young researchers we're training."

Many of those doctoral students come from other countries. Is there a danger that knowledge will seep away?

DB: "Roughly half our doctoral students do indeed come from other countries. That's the reverse of a brain drain: during their doctoral research, they're here and they contribute to the Netherlands' prominent position in the knowledge economy. After they graduate, many young researchers stay here. But even if they return to, say, India or China, the relationship remains. For example, my students do internships in other countries with people who were once my doctoral students. Or former students take jobs with the foreign branch of a Dutch company."

How does NanoNextNL address the risks and societal dilemmas associated with nanotechnology?

DB: "In every research programme which involves social aspects, we reserve 15 percent of the budget for technology assessment and risk analysis. That's a lot; I don't know anywhere else in the world where it's so high. We will work with institutes which specialise in technology assessment, of which we fortunately have a few very good ones in our country. The RIVM will take the initiative. We have them investigate things in independent projects, but we also ensure that technology assessment is part of the educational programme for young researchers. We need researchers in this programme who can think outside the box. Who can work with industry, but are also open to questions and doubts coming from the community."

What exactly are those questions?

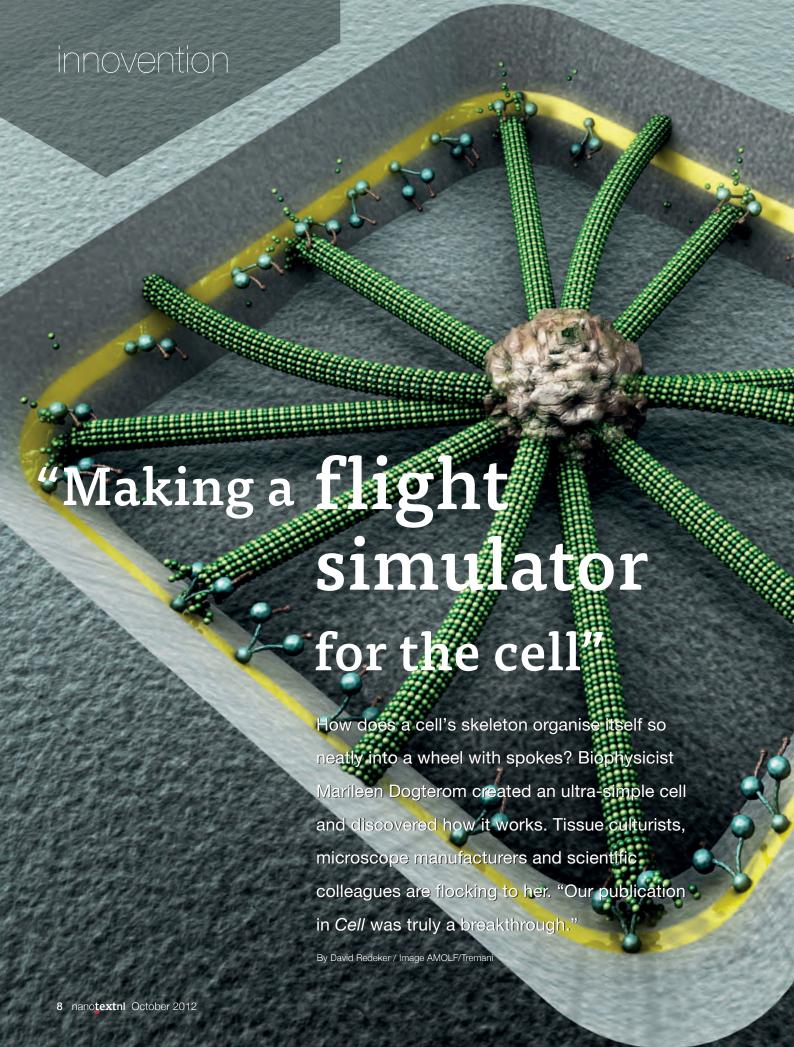
DB: "In technology assessment, you're concerned with the societal effects of a technological development. Suppose, for example, that you can detect cancer at a very early stage using a new technology. So early that the tumour isn't large enough to be resected. What do you do? Do you carry out useless operations, do you let people walk around knowing they have cancer for two years, or do you keep the technology off the market?"

And what about the risks?

DB: "Only a very small fraction of the products which are developed using nanotechnology involve risks. Then we're talking about nanoparticles which enter the human body or the environment, and we don't yet know whether they can cause damage if they accumulate there. Paradoxically enough, we also need nanotechnology in order to investigate at the cellular level whether damage has occurred."

NanoNextNL seems to be in good shape. What's the most important challenge you're facing now?

DB: "Preventing our strength from becoming our weakness. Nanotechnology is relevant for so many different subjects that there is a risk we'll drift apart. But I want people who develop a membrane to purify water to stay in contact with people who can use the same membrane in an artificial kidney. It's not so bad if islands arise, as long as there are also bridges, and ferry connections."



The dream

iologists already had an idea how the cytoskeleton organises itself so precisely, but we've demonstrated it. We built the minimal system and used it to simulate complex processes in a model. Our research reveals the basic mechanism. A cell can probably vary on this theme. My dream is to recreate a living cell in the lab. But I'll already be very happy once we can reproduce a number of important mechanisms. What we've done with the cytoskeleton is one example of that. We've reconstituted the cytoskeleton in a microfabricated chamber. We were able to show that dynein motor proteins ensure

"My dream is to recreate a living cell in the lab"

that the cytoskeleton is stretched into a kind of wheel with spokes. That resulted in a good publication in Cell. Now that we know this, we're better able to explain how cell division works and how cells move. For the research published in Cell, we used an essentially flat, square grid 15 by 15 micrometres in size - a two-dimensional system. We're currently trying to create a spherical cell, because that more closely resembles a cell's natural shape. We want to create vesicles enclosed by a lipid bilayer. And inside them, of course, the building blocks for the cytoskeleton and the motor proteins. We're making good progress, but the vesicles still vary widely

in size. We're trying to fabricate the vesicles using 'microfluidics on a chip', and this has recently started to

work. You can compare microfluidics on a chip with an inkjet printer. Only instead of equally sized little drops of ink, we want vesicles with a lipid bilayer on the outside and a cytoskeleton on the inside."

The partners

"We collaborate with several research groups. First of all, of course, the groups here at AMOLF. We have in-house experts who can measure the forces that cells exert on their environments. And we have scientists who are very good at making vesicles. We're working with them to try and create standardised vesicles. We're also working with researchers at the Max Planck Institute for the Physics of Complex Systems (MPI-PKS) in Dresden, Germany. They're very good in calculations and modelling. The article in Cell has helped us make new contacts as well. Or, actually, I should say the work described in the Cell article, because we had already presented our work at conferences, and that's what brought in the new contacts. For example, thanks to our research we are now working with a Max Planck Institute in Dortmund, Germany. They want to apply the same principle of the simplest possible cell in order to decipher the operation of the kinetochore. Kinetochores ensure that chromosomes which are in a condensed state during cell division are pulled apart so the DNA can be properly divided over two new daughter cells. The German group is currently hard at work purifying their proteins, and once they're finished with that, they'll come to us. A year ago we didn't even know each other. That's how quickly things can go."

The practical side

"I'm the programme director for the NanoNextNL programme 'Nanomolecular machines in cellular force-transduction'. But I think 'director' is a very big word. I'd rather call myself 'coordinator'. I make sure the research groups come together and that people talk with each other one-on-one. Most of all, I try to connect scientists and the industrial community. Because scientists will

find each other, but there's still a lot of ground to be gained in the contact between researchers and industrial partners.

NanoNextNL brings science and the industrial community together. By searching for common ground, both in and beyond the various parts of NanoNextNL, you make progress. That delivers added value. We challenge the current generation of microscopes and measurement equipment. Equipment manufacturers such as FEI, Nikon and NT-MDT are eager to work with us, so they can see what science's needs are, and what still needs improvement."

The future

"QTIS/e is participating in our NanoNextNL programme. That's a spin-off from the Eindhoven University of Technology. They're trying to culture tissue for hart valves, among other things. When you culture tissue, the cells in that tissue often deform. That's caused by the molecular motors and the cytoskeleton. In a culture, they don't get the signal that the cell has reached its ideal shape. As it happens, we're investigating precisely those molecular

"I try to connect scientists and the industrial community"

motors and the forces the cytoskeleton generates. I hope we'll discover new insights in the next few years, and that QTIS/e will be able to improve its tissue culturing as a result. Other scientists, such as Craig Venter, are also trying to create an artificial cell. But their approach is very different. They insert DNA into an artificial environment and try to turn it into something living. Our goal is to recreate a process so you can use it for practice, so you can understand it better. I sometimes tell my students that I want to make a flight simulator for the cell. Where you can turn the knobs and, in so doing, decipher the principles underlying cellular mechanisms."

events

The first year at a glance

NanoNextNL kicked off in June 2011. These pages display a selection of events, awards and grants which coloured the first year of the consortium.

And so it began

On 9 June 2011 NanoNextNL held its kick-off meeting in Utrecht. At the meeting, NanoNextNL celebrated the start of the program, the unique collaboration between industry and knowledge institutes and the opportunity to tackle societal needs with microtechnology and nanotechnology. The meeting was attended by partners and stakeholders. The chair of NanoNextNL, Dave Blank, emphasised the importance of the programme and was looking forward to the coming years.



MicroNanoConference 2011

The seventh edition of the Netherlands MicroNanoConference was held at Tuesday 15 and Wednesday 16 November 2011 at Hotel and Congrescentrum the Reehorst in Ede. Some 450 participants from industry, academia and governmental organisations attended the event. The Netherlands MicroNanoConference is organised by MinacNed Association for Microsystems and Nanotechnology and the NanoNextNL programme and is the major Dutch conference on micro and nanoscience and technology. The conference offers representatives from academia, industry and government the opportunity to meet and discuss the latest developments in these rapidly evolving fields. In 2012, the conference will be held at the same venue, at 10 and 11 December 2012. For more information, see www.micronanoconference.nl.

Secondary school kids provide solutions to industrial problems

teams of junior pupils of secondary schools entered the the grounds of the University of Twente with a prototype under their arms on Wednesday 23 May 2012. The teams were ready to battle each other during the Eureka Day 2012. The Eureka Day is the climax of the Eureka Cup, a national design competition with a technologically and scientific character. For this edition, the teams had been thinking about solutions to issues related to nanotechnology. Issues which professionals from Philips, ASML, Océ, SolMateS and MESA + had been pondering about for a while. At the end of the day, the team with the best solution and the best process of coming to this solution, was rewarded with a prize. In addition, there was a prize to be won for teamwork. NanoNextNL supported this event financially, to make high school pupils aware of the challenges of nanotechnology.







Blank wins highest Dutch technological award

Technology Foundation STW has awarded the chair of NanoNextNL Dave Blank the title of Simon Stevin Meester 2011. On 6 October 2011, Blank and co-winner Oscar Kuipers each received half a million euros to be spent on research of their choice. Blank will use the money to explore new ideas and develop technology in the area of nanosensors. Blank is delighted with the prize: "The Simon Stevin Meester prize is one of the best awards you can be given, as it's a performancerelated prize."

awards grants

Polman wins ENI Renewable **Energy Prize 2012**

The prestigious ENI Renewable and Non-conventional Energy Prize 2012 has been awarded jointly to AMOLF director and NanoNextNL board member Albert Polman and Harry Atwater of the California Institute of Technology for their research on high-efficiency solar cells based on nanophotonic design. The Jury recognized their Candidature as 'outstanding and fully deserving the



First ERC Proof of Concept grants

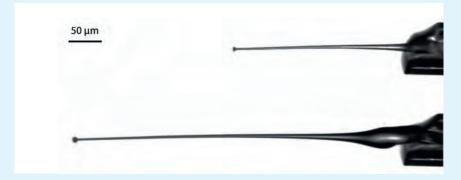
NanoNextNL researchers Detlef Lohse, Raymond Michel Schiffelers and Albert van den Berg are among the first European researchers who were granted the new European Research Council (ERC) Proof of Concept grant.

These 'top up' grants, worth up to €150,000 each, are designed to help in the valorisation of ERC-funded research. In total, 30 top researchers, already holding ERC grants, were given this additional support to bridge the gap between their research and the earliest stage of a marketable innovation. The funding can cover activities related to for instance intellectual property rights, technical validation, market research or investigation of commercial and business opportunities.

Lohse (NanoNextNL programmes 3B and 10B) received the grant for his research on Needle-free injection with supersonic microjets. Schiffelers (NanoNextNL programme 3D) received the grant for his concept study to commercialise a micro vesicle drug delivery system and Van den Berg (programme director of 3B) for his research on the FICS chip (Fast Impedance-based Cell Sensing).

Needle-free injection with supersonic microjets

Images of a supersonic microjet generated in a 50 micron capillary tube. The capillary is visible on the right side; the jet tip is shown on the left. The jet travels from right to left with a speed of 490 metres per second. Time between images is 500 nanoseconds.





One of NanoNextNL's priorities is to ensure that knowledge finds its way into applications through spin-off companies, for example. BAIT Pharmaceuticals is just such a spin-off.

Or, as company founder Marc Robillard prefers to call it, a spin-out. The story of a start-up.

By David Redeker / Photos Bram Saeys

arc Robillard, the CEO of BAIT Pharmaceuticals, explains what his company does in one sentence: "We make biomolecules to image cancer and to irradiate it." BAIT stands for Bioorthogonal Agents for Imaging and Therapy. The company uses its molecular bait to capture tumours. BAIT is a working title, a holdover from the time the company was still a Philips project. It all began in 2004. Philips was manufacturing imaging scanners and the associated software, but not the contrast agents to acquire good images. Competitors Siemens and GE were, so Philips built a lab to develop antibodies and synthetic molecules which help make cancer visible. Because antibodies can be used not only to image cancer, but also to irradiate it, Philips immediately investigated potential therapeutic applications. "And then you enter the pharmaceutical industry's territory," says Robillard, "which in the case of BAIT was outside Philips' core business. In the meantime, I'd become deeply involved with the subject, and I wanted to keep pursuing it. So I decided to spin it out."

A two-stage rocket

BAIT uses an ingenious trick to irradiate cancer cells. Robillard compares it to a two-stage rocket. First, you inject an antibody. That antibody searches for the tumour and plants a flag, so to speak. After a few days, a second, smaller molecule is injected. Within thirty minutes, it finds the flag marking the tumour. You can attach a radioisotope which shows up well in the scanner to the second molecule. That allows a doctor to see the tumour very clearly. But you can also use a therapeutic radioisotope instead of an imaging isotope. And then you're no longer just observing the tumour; you're irradiating it.

Why does it take two steps? Can't it be done in one? "Current radiation therapies do indeed work in a single step," Robillard says. "But the radioactive antibodies which don't bind with the tumour stay in the blood for a long time and end up in the

liver. Before you know it, you've destroyed the bone marrow or the liver. Our two-stage rocket provides much more effective radiation. Our radioactive molecule binds only to the flag on the tumour and the portion that doesn't bind is rapidly removed to the urine. That process goes much more quickly with our second molecule, because it's so small. The two-stage rocket is so effective that we can administer a dosage ten times higher than with current methods without serious side effects or radiation build-up. The disadvantage, of course, is that with our method, you have to go to the hospital two or sometimes even three times for an injection."

Broad support

Robillard left Philips around Christmas 2011. "I still get a lot of support from Philips. They're an important stakeholder. I was able to rent my own office back, and they let me use the labs." Another source of support is Robillard's father, an emeritus professor of chemistry. "He's retired, but he works with me behind the scenes. I do a lot of talking with him about the company. My father has started three companies, so he has the experience."

And then, of course, there's NanoNextNL. Robillard's company is participating in programme 3C, Molecular Imaging. "Thanks to NanoNextNL, I have a whole consortium at my disposal. And I don't even have to pay them. That's what makes NanoNextNL so great for starters like me. I'm working with the research groups led by Luc Brunsveld and

"Thanks to NanoNextNL. I have a whole consortium at my disposal. And I don't even have to pay them. That's what makes NanoNextNL so great for starters like me"

Klaas Nicolaij in Eindhoven. Brunsveld knows everything about nanoparticles. Nicolaij is a master at imaging techniques. And then there's SyMO-Chem, a company specialised



problem Robillard's large antibodies have: they circulate in the body for a long time, they accumulate in the liver and they aren't easy to image. "The biggest difference between us is that I work with biomolecules and try to alter them, while the nano folks construct a molecule from scratch."

Towards take over

At present, Robillard is looking for a pharmaceutical company which wants to invest in research on his therapy. "We already have good contacts with universities and hospitals," says Robillard. "Now I want to find a pharmaceutical company which will first invest in us, then, if BAIT is successful, can take us over."

BAIT now holds eight patents, has been conducting preclinical trials for several years and wants to carry out its first human trials within three years. What are Robillard's hopes for the future? Where does he expect to be in five years? "I hope that in five years, we've matured into a true biotech company. From a one-man beginning to an established start-up. And that NanoNextNL helps us get there."



One of NanoNextNL's guiding principles is that scientists should work together. Herre van der Zant at Delft University of Technology and Sywert H. Brongersma at the Holst Centre in Eindhoven are a perfect example. The two researchers are collaborating on an energy-efficient electronic nose.

One researcher works in Delft, the other in Eindhoven. How did you find each

SB: "Bert Koopmans brought us together. He was setting up a nano cluster about three years ago, and he told me there was a group in Delft investigating MEMS, microelectromechanical systems."

VDZ: "Koopmans saw that we had roughly the same research interests. So we invited Brongersma to sit on a doctoral committee, and after that we visited the Holst Centre a

few times to see their equipment and listen to their ideas."

SB: "Yes, and now, just three years later, we're already applying for a patent together."

Can you two briefly explain what you're trying to accomplish?

SB: "We're building an electronic nose. We fabricate a series of nanoscopic silicon nitride beams which are fixed at both ends, and print a polymer on each one. The beams can be made to resonate electrically using a piezoelectric material. Each polymer adsorbs volatile molecules from the air, which alters the beam's resonant frequency. We place eight to ten beams next to one another, each coated with a different polymer which adsorbs the molecules in a different ratio. Each beam reacts to its environment in a slightly different way. Using a complex algoritm for the changes in vibration, we can calculate which volatile molecules are present in the air. And we can do it continuously." VDZ: "And all that on a single chip. You don't need any large equipment."

And what can we use this nose for?

SB: "Electronic noses are suitable for all kinds of applications. Examples include measuring air pollution, detecting lung cancer using breath gas analysis, or identifying wine based on its aroma. For our nose it all depends on

the polymers you print onto the beams. The nose itself measures 3 by 4 millimetres, as tiny as the letter 'o'. If you install it in a mobile phone, you've got a computer to perform the calculations right there with you."

But there are other electronic noses, aren't there? What makes yours special?

SB: "Our nose is extremely small and energy efficient. For example, it doesn't use laser light sources as other MEMS noses do, and it works at room temperature so it doesn't have to be heated. In addition, the development of the micromechanical system in the clean room only has to take place once to use it for any application. The choice of polymers and the way they are applied enables different applications and can be done inexpensively."

Back to your collaboration. What makes you two such a good fit?

VDZ: "Sywert and his group ask the right questions. They know what the industry

SB: "Herre's group is very good at studying and understanding the characteristics of our micromechanical systems."

VDZ: "Our partnership is truly symbiotic. We both have the feeling we need each other, that we'll accomplish more together. That's the perfect foundation for a fruitful collaboration."



Solar panels make poor use of the sunlight they receive; a large percentage of the energy is instantly lost. Silicon nanocrystals could put a stop to that. Tom Gregorkiewicz made the pages of *Nature Photonics* with his research into how the crystals work.

By Anouck Vrouwe / Photo Debbie Mous

photovoltaic cell is like a coffee machine that requires exact change. Whether you toss in one euro or two, you get a single cup of coffee and no money back. Or, in the case of the solar cell: whether you hit it with an ordinary red or an energetic blue photon, at most one electron is released. The change - unused energy - is lost to heat. A silicon solar cell converts at best one-third of the energy in sunlight into electricity.

"A solar cell's yield would increase dramatically if you could use the residual energy from energetic particles to knock loose a second, and maybe even a third, electron," explains Tom Gregorkiewicz, professor of Optoelectronic Materials at the University of Amsterdam. "In theory, even to levels above fifty percent."

Scientists have been speculating on ways to do just that for the past decade. Nanocrystals made of silicon seem to be the solution. These tiny particles have different properties than the bulk silicon

commonly used in conventional solar cells. Thanks to quantum effects, an energetic blue photon could knock loose more than one electron in silicon nanocrystals.

One becomes two

"A lot of research has been done into this effect," Gregorkiewicz says. "Some of it is ours. But the process is so fast that all the evidence previously found was indirect. Now we've demonstrated that a single incoming, energetic photon can indeed knock two electrons loose." Gregorkiewicz and his team were able to do this using a femtosecond laser, which was quick enough to capture the moment the nanocrystals released two electrons. Their work earned them a publication in Nature Photonics.

"Our research is fairly fundamental," Gregorkiewicz admits. "But I always keep the potential applications in mind. Thanks to the NanoNextNL programme, I've come into contact with people who - unlike us actually build solar cells. That will help me when I have to decide which direction the research should take."

Gregorkiewicz expects the use of solar cells to increase explosively in the coming years. "Not because of all the uproar over the greenhouse effect. It's much simpler than that. With photovoltaics, you can generate energy locally, and you aren't dependent for fuel on those few countries which happen to have oil." He expects that the silicon nanocrystals from his research will be added to solar cells within the next few

"Thanks to the NanoNextNL programme, I've come into contact with people who - unlike us actually build solar cells"

years, perhaps in an antireflective top coating. "We aren't able to do that yet, because the nanocrystals are manufactured at high temperatures. We're currently trying to come up with other methods of manufacture. But I don't expect that to be a deal-breaker."

how things work

Real-time optical analysis of microreactor performance

Optic chip knows best icroreactors are becoming increasingly more important in research and production in the fine chemicals and pharmaceutical industry. Within NanoNextNL, Lionix BV - in association with academic and industrial partners - is engaged in developing an optofluidic chip that can carry out a real-time analysis of chemical reactions in a microreactor on the basis of light absorption. The ultimate goal is to 6 incorporate the optofluidic chip in the microreactor so that chemical reactions can be adjusted real-time. Microreactor pump The microreactor used comprises a small glass plate into which microchannels are etched (diameter: 300 µm) and a second plate that covers these channels. Two pumps feed a 1 reactant 1 (or reactants 2) and a catalytic agent 3 into the reactor. Both fluid flows are blended in a static mixer 4. The product of the reaction 5 leaves the 2 cm microreactor through an outlet channel. Labtrix unit 6 The microreactor is secured inside 1.4 mm height 5 cm a container. An electrical Peltier element located below the container ensures that the

D E

temperature.

Benchmark reactio

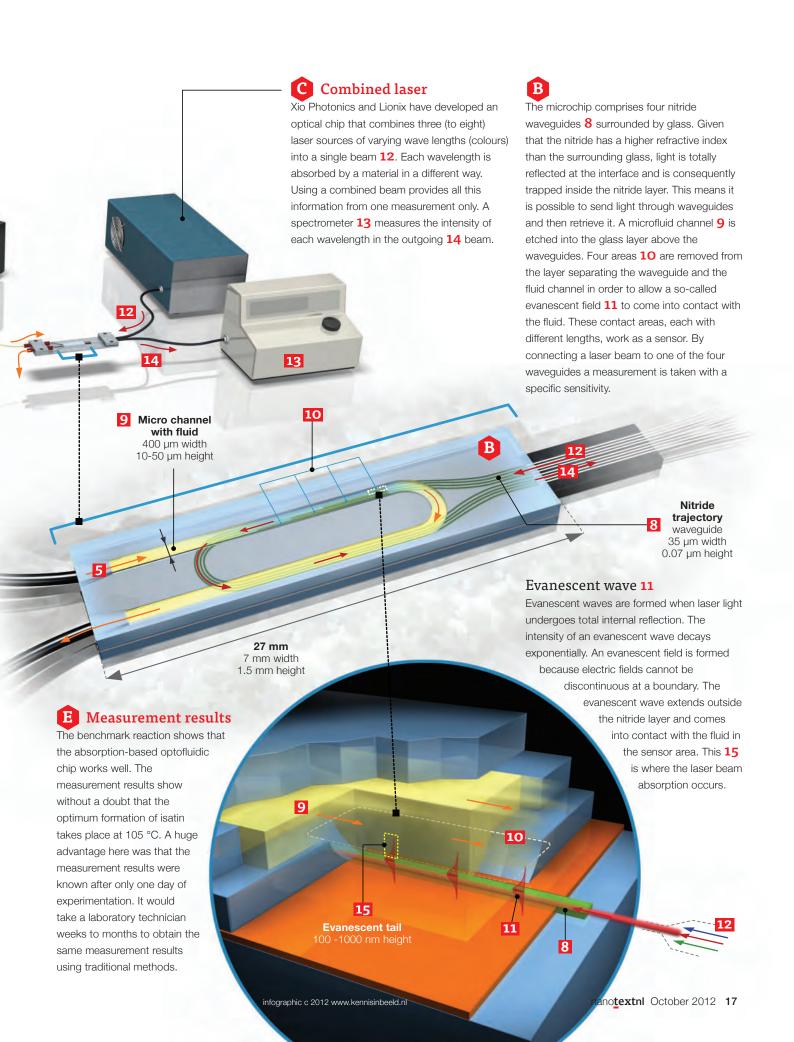
temperature (range: 15 °C to 190 °C). A special thermocontroller **7** accurately regulates the

microreactor remains at the desired

Using sulphuric acid as the catalyst, Isonitrosoacetanilide is converted into Isatin inside the microreactor to test the working of the optofluidic chip. The optimum temperature for this reaction is 105 °C. By gradually increasing the temperature inside the microreactor from 30 °C to 105 °C, the Isatin level of concentration will become considerably higher. The laser beam 15 combines three wavelengths (blue 488, green 532 and red 638 nm). Isatin (not the reactant or the catalyst) has a high absorption coefficient at 488 nm and 532 nm, and thus the concentration of Isatin can be monitored perfectly with the optofluidic chip.

Absorbtion spectrometry

When light shines through a material, then that material absorbs part of the beam. The degree of absorption depends on the type of light (wavelength) and type and concentration of the absorbent material. Given that every material has its own absorption spectrum, an unknown material (and the concentration thereof) can be identified on the basis of its absorption performance. Measuring the absorption spectrum and the associated intensity of the laser beam that leaves the microchip provides real-time information about the reaction product.





By Nienke Beintema / Photo Shutterstock

Nanotechnology promises many marvels, but to realise them we must also consider the potential risks. If we don't, some nano-innovations may be delayed on their way to market – or may not make it there at all. That makes risk analysis the leitmotiv running through every NanoNextNL theme.

o an Internet search on the term nanoparticles: it'll scare you to death. "Nanoparticles in sunscreen cause cancer." "Nanoparticles in antimicrobial socks harm the aquatic ecosystem." "Carbon nanotubes are more dangerous than asbestos." While scientists wax lyrical on the opportunities nanotechnology offers, the average citizen grows increasingly anxious, and the first 'anti' campaigns have already burst forth.

"There's only one way to combat doom-andgloom stories - and, of course, avoid accidents," says Han van de Sandt, "and that's to thoroughly investigate the risks beforehand and draw your conclusions from the data. And then communicate your

conclusions clearly." Van de Sandt is a research manager in the risk analysis department at TNO and director of NanoNextNL's 'Human Health Risks' programme.

The mission

Van de Sandt's programme is part of the theme 'Risk Analysis and Technology Assessment' (RATA), one of the ten NanoNextNL themes. RATA isn't meant to be a self-contained theme, Van de Sandt emphasises, but one interwoven through all the other themes. "Nanotechnology is driven by the search for new functional developments," he says. "That's very important, and we should definitely

continue doing that. But while we're doing that, we must also always investigate the risks." And it's important to start doing that at the drawing table, he emphasises. "At that point you can still adjust the process in several ways. You can select option A instead of option B or C, thereby significantly increasing your product's safety and chance of success. That's ultimately in everyone's best interest."

It's no easy task to implement RATA. Take sunscreen, for example. How do you determine whether the titanium dioxide particles in it are bad for our health? You have to study a multitude of factors: the toxicological properties of the nanoparticles being used, the degree to which the user is actually exposed to them, and the relationship between those two factors and

human health. It may turn out that the nanoparticles in sunscreen are, indeed, harmful - but only if you drink litres of it. The RATA researchers in NanoNextNL investigate how best to design processes like this for different applications. "And that's pretty tough," Van de Sandt says. "You can't always discuss the content in detail as a result of patents or intellectual property issues. Fortunately, that's starting to change now. The important thing is that the developers of nanobased innovations achieve a kind of RATA mindset themselves. That they truly become interested in thinking about risks and about how they might choose alternative routes. Largely out of enlightened self-interest: their products' successful market introduction."

A given

Edith Gelens knows all about that. She's the R&D manager at Nano Fibre Matrices (Nano-FM) in Groningen, the Netherlands. The company uses nanofibres to create gel-like materials within which mammalian cells can optimally grow. These matrices are currently being used primarily for scientific research into mammalian cells. In the future, however, the company plans to investigate whether they can also be used to culture human tissues, for use in regenerative medicine, for example. "At the nanoscale, the fibres consist of building blocks that fit precisely together," Gelens explains. "We're developing a technology through which the building blocks assemble themselves in water into a three-dimensional structure, like a plate of spaghetti. Cells can easily attach themselves to the assembled fibres and they thrive in that environment. Apparently our matrix closely resembles the natural matrix in which mammalian cells grow."

Nano-FM is working with new, synthetic particles that have new properties. "So they might also carry new risks," Gelens says, "and we need to investigate those. If we don't, our product may receive negative media attention." Gelens herself is convinced the nanoparticles her company uses are not harmful to our health. "If only because cells feel so at home in the matrix," she says. "We also know that our nanofibres are fully biodegradable, and they break down into

"Thinking about potential risks isn't an immediate part of your plan, and it isn't where your expertise lies"

individual molecules on their own." The fibres employ a cyclohexyl structure, she explains. Proving that structure isn't toxic at the molecular level appears to be the greatest challenge so far. "We're working on that now. In any case, the molecules don't seem to be toxic when swallowed or when they get under the skin."

For Gelens, risk analysis is a given. "Of course you want to study a product down to the smallest detail to determine whether it's completely safe," she asserts, "especially if it may later be used in the human body." To learn more about risk analysis methods, Gelens attended the 'Safe Design of Nanomaterials' workshop organised by TNO and NanoNextNL in early May 2012. "Participants there came from completely different corners," Gelens remembers. "TNO, the government, companies, research institutes. We discussed different strategies to identify and minimise risks. I enjoyed looking at that from different points of view. Did I learn anything new? Yes, primarily in terms of methodology, on how to estimate risks. But also new facts about nanoparticles. How quickly they can penetrate a cell, for example, and how difficult it is for them to leave it again."

Reinventing the wheel

Gelens agrees with Van de Sandt that it's hard for companies to implement RATA. "Your core business is manufacturing a product," she says. "Thinking about potential risks isn't an immediate part of your plan, and it isn't where your expertise lies. Yet it's a matter of life and death literally, for the people you serve, but also for your company."

RATA has to come from the companies themselves, Van de Sandt believes. Measures to enforce it, such as imposing penalties on companies which don't pay it sufficient attention, are not sufficiently effective, he feels. "Obviously, companies are legally responsible for the safety of their employees and products, but the point within NanoNextNL is to stimulate interest in RATA. That's why we organise meetings through NanoNextNL; we visit companies and we actively invite others to visit us. We also want to hold training sessions for doctoral students and their advisors." Gelens also has more faith in a positive approach. Her company doesn't yet have official RATA protocols in place; Nano-FM has only recently launched and numbers just six employees at present. "I think it's important that companies use standardised

"The important thing is that the developers of nano-based innovations achieve a kind of RATA mindset themselves"

RATA protocols," she says. "Perhaps the government can play a stimulating role there. For example, there's already a lot of data on the potential toxicity of specific substances, but the data isn't freely available because companies want to protect their intellectual property. You'd like for companies to be required to report it if they discover that a particular substance is toxic. Then we don't all have to reinvent the wheel." NanoNextNL is also trying to further the legal and policy aspects of RATA, Van de Sandt says. "Not only government policy," he clarifies, "but also corporate policy. Because that's where it has to happen." In that regard, much has already improved, he says. "In general people are open to it. Actual execution varies in practice, of course, but people definitely want to do it. RATA is much more than just an idea on paper."



Lowlanders don't think so!

t our booth on the island, we asked Lowlanders to share their opinions on nanotechnology. Using statements written on t-shirts, we prompted people to consciously consider nanotechnology before we sent them to check out other parts of the Nanoplaza. For example, we wanted to know whether Lowlands attendees have even heard of nanotech to begin with, and whether they think it's scary. But we also wanted to find out whether Lowlanders know how a lab on a chip works and think nanotech is 'green'. Visitors could drop candy wrappers into tubes marked 'agree' and 'disagree'. Lowlands visitors snapped up the tasty lozenges like hot cakes.

Nano: what's that?

Most visitors were able to tell us that nanotechnology is 'tiny things'. The first day, 54.8 percent of Lowlanders could explain what nanotech is to us - at least a little. Strikingly, after the day-two Lowlands University lecture by Albert van den Berg on nanotechnology, many more visitors suddenly knew what nanotech is: on the second and third days, a respective 67.9 and 61.3 percent of visitors could define it for us.

Nanotechnology scary?

Most visitors (82.1 percent) didn't think nanotech is scary. Common responses were "Nanotechnology scary? What do you mean?" and "Nanotechnology is progress, isn't it? Why would we be scared of that?" In addition, 65.2 percent of visitors viewed nanotech as

By Roxanne van Giesen

The yearly three-day pop festival Lowlands for the third time contained a floating sustainability platform, Llowlab. As always, science and innovation were front and center. During the festival, Llowlab welcomed some 20,000 visitors. This year, visitors were treated to nanotech jewellery from the University of Groningen, shmeat from the University of Maastricht, and a sustainable hot tub from the Delft University of Technology. NanoNextNL was there, too!

'green' and 85.7 percent felt it's good for us. Though many visitors believed the technology itself is not yet very sustainable, they also thought nanotech makes highly sustainable things possible, such as more efficient solar cells and better batteries, and that it's useful for helping developing countries achieve objectives such as better water purification.

Hospital on a chip

Lab on a chip: another one of those strange terms. Fortunately, the University of Twente gave a live demonstration of this lab on a chip - because most people had never heard of such a thing (67.3 percent) and thought it meant some kind of implant, with all kinds of frightening implications. A short while later, visitors biked up a sweat and saw how fluids in the highly magnified lab on a chip spread to one side. That cleared everything up. All in all, Lowlands attendees were delighted (after the demo) with the opportunities such a chip

makes possible, and they're waiting with bated breath to see what the future will bring. Wouldn't it be great if you could perform all kinds of medical tests yourself at home? A whopping 70.7 percent of visitors said they would be interested in using a lab on a chip. But, as a few critical visitors pointed out, "It's probably best not to leave everything to a chip" and "Do we really want to be able to test for all kinds of diseases at home?"

'Na-no' or 'Na-ves'?

It looks like nanotechnology is ready to meet the future! Though the risks of nanotech are not yet known, the technology enables a slew of new applications. Lowlanders recognised this, and they're very positive about nanotech and its potential applications. Lowlands attendees are also very forward-thinking, and they view nanotechnology as the prime example of technological progress. Make that a big na-yes!

odd man out

Nanotechnology - that's all about materials,
electronics, physics and chemistry, isn't it? So why are a dairy giant,
a water supply company and a seed breeder partners
in the NanoNextNL

consortium?

Dairy

Ger Willems, director of Scientific Affairs and Intellectual Property at FrieslandCampina:

"The combination of dairy with nanotech doesn't seem obvious? That depends on how you define nanotechnology. At FrieslandCampina, we're interested in very different things than the high-tech materials and electronics guys. Every organic system, including man, is filled with tiny particles: molecules and larger aggregates. It's largely these tiny particles which determine the properties of foodstuffs. Miniature globules of fat and casein determine the structure and behaviour of dairy products, for example. If you want to improve those properties, then you're doing 'nano'. And that makes nanotechnology as old as mankind. Through NanoNextNL we invest in research into these product properties, at Wageningen University and Research Centre and at NIZO food research, to name two examples. This research complements the in-house work we do. We hope to acquire insight which we can use to improve the properties of our products. Communication is very important. If we aren't careful with our message, the public will quickly think, 'No nano in my food!' That's another reason we're involved in NanoNextNL: to participate in that discussion, and to make it clear that food has been 'nano' since time immemorial."

Water supply

Ron Jong, Process Technology specialist at water supply company Vitens:

"Our goal is to produce quality drinking water which meets every requirement. An important part of that is that we want to know exactly what's in our water - down to of consumer products and other applications can end up in the environment. We anticipate that our customers will be asking us about that in the near future, but we don't yet have a good answer for them. Our analytical methods aren't yet sufficiently NanoNextNL, we and a variety of partners are investing in the development of better analytical techniques. We ultimately hope to be able to analyse groundwater and drinking addition, we're taking advantage of new developments in the field of water another link with 'nano'. But the main question remains, how can you detect those particles in drinking water?"

Seed

Jan-Willem de Kraker, biochemical researcher at Enza Zaden:

"Our company focuses on breeding vegetable varieties, including tomatoes. An important factor in that is the tomato's taste. We have a hundred tomato varieties under development, and it would be difficult to have them all test-tasted by people. That's why it would be ideal if we had a device which could do it. For example, you could put the proteins which form the taste receptors on our tongues onto a chip. That's the nano aspect of this story. If one of these receptors is triggered by a certain flavour, it sends a signal to the measuring device. Of course, taste comprises a huge number of different factors, but this is a way you can at any rate test samples for properties we know contribute to a pleasant taste. There is no such device at present, but researchers at Plant Research International in Wageningen, the Netherlands have made significant progress toward one. Through NanoNextNL, we're participating in their process: we deliver the plant material and brainstorm with them on the research direction and outcomes."

Water seeking new technology

Producing clean water using less energy and fewer chemicals: nanotechnology should make it possible. Water experts and nanotechnologists are working together to develop new water separation technology. "The flight path is different, but we're interested in the same topics."

By Anouck Vrouwe / Photo Ivar Pel

ert Hamelers at Wetsus can name several things which are on his wish list. "A filter for ammonia. It takes a lot of energy to produce ammonia, but we throw away the ammonia in wastewater. That's a shame. A good method for extracting lithium from seawater. Reliable sensors to detect pathogenic bacteria in drinking water."

We're consuming larger and larger amounts of water: not only drinking water, but above all water for industry, agriculture and energy production. It's taking more and more technology to purify all that water. In the laboratory at the Wetsus centre for sustainable water technology in Leeuwarden, the Netherlands, water companies and research institutes are joining forces to improve water purification methods. Hamelers is the programme's director.

A two-hour drive away, at the University of Twente, Rob Lammertink has a list of his own

- filled primarily with questions. "How do you remove nanosilver from wastewater? And medicine residues? Could you use the separation mechanisms cell membranes use?" His research group, Soft Matter, Fluidics and Interfaces, is studying the ways nanotechnology can be used to separate substances. For example, Lammertink is investigating catalytic water purification, in which water is directed along a surface where nanoparticles break down the contaminants. "We're studying what happens on that surface, which substances work best." Applications loom on the horizon: "The greater objective is to get around the use of chemicals in water purification - the fewer substances you need to purify the water, the better."

Complementary approaches

One man's expertise is primarily in the water industry, the other's in nanotechnology. One is used to large volumes, cubic meters hundreds of them - while the other works at the nanoscale. Yet Hamelers and Lammertink have found each other in the NanoNextNL programme 'Nanotechnology in Water Applications'. Each man brings his own knowledge and expertise to the table. They invite each other to conferences and workshops and make use of each other's facilities. "At Wetsus, they know everything about the process side of water purification," says Lammertink. "You can take measurements under processing conditions in their lab." Hamelers adds: "Our doctoral students make use of the university's clean rooms and measurement equipment. We come in with scientific questions from the water industry, they from nanotechnology. The flight path is different, but we're interested in the same topics." Such as biomimetic membranes, a subject which makes both men's hearts beat faster. "To be frank, we currently use fairly simple separation methods. We have filters which allow water to pass through, but not salts. And filters which let water and salts



Bert Hamelers (Wetsus, left) and Rob Lammertink (University of Twente, right) work together on new water separation technologies.

through, but stop microorganisms. But what we're not very good at yet is extracting one specific substance from water," Hamelers explains. "Such as the ammonia I mentioned earlier." Something Mother Nature is good at, Lammertink adds, and he wants to learn her trick. "Cell membranes have passages which are only open to a single substance. The question is whether you can translate those components to a synthetic system."

Research direction

The contact with Wetsus helps Lammertink take decisions about the direction for his own research. "It ensures that I keep an eye on applicability. You hear what's important in the field. That helps you determine your priorities. In my research, I'm always looking for a mix of fundamental questions and societal relevance." Especially for technology scaleup, knowledge from the field is crucial. "First and foremost, a good idea produces beautiful science," Lammertink says. "But after that,

the question is always whether it's applicable in the real world. Will your nanomaterial stop working after a couple of weeks, will it clog up, will algae grow on it? To answer those questions, you have to test it under working conditions. Wetsus can do that."

"Our contact ensures that I keep an eye on applicability"

Both Hamelers and Lammertink hope that a number of their ideas will have evolved into new applications by the end of the NanoNextNL programme. Hamelers expects them primarily in the field of sensors. "It would be great for us if sensors which recognise microorganisms have been developed. For example, there's a bacterium which is no problem whatsoever in drinking

water, but it must not be present in the water used to extract oil because it can clog the oil wells. A sensor which could detect that bacterium would be very useful. Or a sensor which responds to pathogenic bacteria in drinking water." Lammertink hopes there will be direct applications for his research into catalytic purification by then. "Consider, for example, equipment for countries where drinking water isn't always reliable. In those places, they subject the water to a last cleanup at the point of use, in the people's homes. It would be nice if you could do that with catalytic surfaces. Then you don't have to add any substances to the water."

Nanotechnology as export product

Nanotechnology is an important export product for the Netherlands, and government, entrepreneurs and society should work together on bringing the field to the next level. That way, nanotechnology can become our manufacturing industry for the future. Says Ronny van 't Oever, CTO of Micronit Microfuidics, one of the many SME partners in NanoNextNL.

By Sonja Knols / Photo Micronit Microfuildics

icronit Microfluidics is a fastgrowing SME specialised in the production and development of glass-based lab on a chip products such as microchips for protein analysis, DNA research and the development of new medicines. In the 13 years since its foundation, the company has grown to become a leading supplier of microfluidic and lab on a chip devices in life sciences and chemistry. The company is involved in the research projects of NanoNextNL within theme 10, 'Sensors and actuators'. With the participating partners it is developing scalable functionalised microstructured reactors.

CTO Ronny Van 't Oever explains why his company is involved in the programme. "Micronit maintains close contact with the academic world. That's no coincidence since we started as a spin-out from the MESA+ institute of University of Twente, and we still deliver microfluidics chips to research groups. Our collaboration with academic partners gives rise to new research questions which we try to tackle in joint project proposals, such as the one in the NanoNextNL programme." Before NanoNextNL started, Van 't Oevers' company also took part in its predecessors MicroNed and NanoNed.

Nevertheless, research is not Micronit's core business, the Managing Director stresses. "We make our money by mass producing lab on a chip applications for others. For example, we provide a company like Medimate with chips which they use for their point of care lithium measurements for mentally ill patients. Our participation in research projects is aimed at investigating new possibilities. This way we are able to provide our customers with the latest technological solutions for the integration of nano-based sensor techniques into complete devices."

International work field

Besides taking part in the research programme, Van 't Oever is also included in the organisational structure of NanoNextNL. As a member of the Supervisory Board of NanoNextNL he represents the small and medium-sized enterprises involved in the programme. As chairman of the board of MinacNed, an association consisting of research institutes, equipment manufacturers, suppliers and users of technological components, he knows the needs of this group from within. "NanoNextNL is a unique programme in the sense that so many SMEs are involved. But they don't all have the time to actively contribute to the programme management. I represent them. I feel it my duty to make sure the programme is executed in a workable, efficient and application-oriented way, and that the overhead will be kept as low as possible."

The SMEs involved have a specific profile, he says: "Nanotechnology is an important export product for the Netherlands. Therefore SMEs involved in this type of work are internationally oriented. They rely for a majority of their income on export of products and services. These companies are indeed tomorrows' Dutch manufacturing industry."



Why is it that so many SMEs want to participate in this programme? "To maintain relations with research institutes and other relevant companies. And of course to stimulate economic action. There is a lack of funding to bridge the gap between research and product development. NanoNextNL provides this financial support in the precompetitive phase. This way, the research results can be further developed to a point where they can attract serious customers. And that's where it becomes interesting for us."

One of the key factors to the international success of Dutch SMEs is the national NanoLabNL facility, Van 't Oever says. "These labs have very expensive, highly specialised equipment we can use to codevelop new products together with our clients. We pay a commercial rate for the use of the facilities, but that is still a lot less money than if we were to buy all of this equipment ourselves. Take for example very high resolution microscopes. When we are

etching micro channels we need to use a sophisticated microscope to see what we have made. It would be very expensive to buy one of the microscopes ourselves for the few hours we need it. This NanoLabNL model of working together and sharing facilities on a national level, is a very valuable asset for high-tech SMEs. Our customers also appreciate it. We often work with them on classified projects, and since we can use the equipment ourselves instead of asking the lab personnel to do our work for us, we don't need to inform people from outside the project."

The lab is somewhat like a beehive, he says. Since so many people from so many different industries and universities use the facilities there, it's easy to meet people and share knowledge and ideas. "The NanoLabNL works as a magnet for people and knowledge. It is an excellent base. Compare it with a farmer who owns a decent piece of land. Of course he still has to sow the seeds and take good care of his plants, but the quality of his crops will be good. NanoLabNL is the result of a

development that was started many years ago. Now it's time to harvest. Sharing such large, specialised and expensive state of the art facilities is an excellent way to help high-tech

"This NanoLabNL model of working together and sharing facilities on a national level, is a very valuable asset for hightech SMEs"

SMEs fill the gap between knowledge and market. Furthermore, programmes such as NanoNextNL can lead to new start-ups in this field. Since these high-tech SMEs immediately lead to export, they generate an excellent return on investment. I hope in the coming years the combination of infrastructure and NanoNextNL will lead to many more innovative products. Designed and made in Holland."

both sides By Anouck Vrouwe / Photos Ivar Pel

Daan Bijl: Smart tips

"There's a pickaxe in my office. I got it for a presentation to investors. The shape of the axe is a macroscale model for our product, the tip of an atomic force microscope (AFM). But it's also symbolic. They always say about the Gold Rush that it was mostly the sellers of picks and shovels who got rich. I've explained to investors that SmartTip makes the picks and shovels of the nanotech rush."

"AFM is a technology in which you scan a surface at the atomic level using an ultrasmall needle, a tip. The AFM was invented in the 1980s. The instrument has grown up over the past twenty-five years, but the measurement needle probe has barely changed in that time. That field is unfolding now. My company, SmartTip, focuses on the development of smart probes."

"Take the AFM tip with a very tiny channel, the FluidFM probe. That's a kind of micropipette with an opening three hundred nanometres in diameter. SmartTip can now manufacture several of them simultaneously using wafers. You can do all kinds of things with this tip. For example, you can use it like a fountain pen to deposit nanoparticles. Biologists are particularly happy with it. They can use it to penetrate the cell wall, which allows them to inject substances into the cell with no appreciable damage to the wall. Or they can deposit controlled viruses onto the cell wall with it. But the pipette can also be used as a pick-and-placer for the cell itself you apply suction to the cell, pick it up and put it down somewhere else."

"We do a lot of research into functionalising the tip. We make magnetic probes, and probes with an active chemical layer. We're currently investigating whether we can bind those active layers to the tip in a different way, chemically speaking, so they become more stable and more robust."

"The next step is to add biologically active layers. People often ask us if we can do that now. We're currently researching it with Wageningen University. Instead of a chemical layer, you attach proteins to the tip.

The question is whether it's feasible. Every biologist wants a different protein, so to make it commercially viable, you need to have a lot of different proteins in stock. Making the tips won't be easy, but packaging them will be even harder. How do you keep them from spoiling, especially if the customer won't be using them right away?"

"We're always walking the edge of what's possible - for example, in terms of microprocessing. But our users are also working on the cutting edge. New pickaxes open up new gold mines, both scientifically and commercially. That's the beauty of this work."

By touch

It was a quick Nobel Prize: in 1986, six years after they developed their Scanning Tunnelling Microscope (STM), IBMers Gerd Binning and Heinrich Rohrer won the granddaddy of all prizes for it. It was the first time surfaces could be imaged at the atomic level. An STM brings a needle - the probe - so close to the surface that electrons can tunnel from the surface to the probe's tip. The shorter the distance, the more electrons make the jump: the number of tunnelling electrons is thus a measure of the surface height. The STM now has several younger siblings, all of which fall under the name scanning probe microscopy. The most famous of these is the atomic force microscope (AFM). An AFM actually touches the surface it scans and measures the pressure exerted on the needle.

Joost Frenken:

Microscopes for the real world

"We'll soon be entering new territory. We've read all the textbooks, but we might as well throw them over our shoulders. We have to discover in the field which rules apply here."

"Most people are only familiar with the catalysts in their cars, but industry uses them for all kinds of things. These are substances that help chemical reactions get going, without being consumed themselves. They're often made of expensive metals such as gold, palladium and platinum. Catalysts are big business; the stakes are high. Including the environmental stakes. A good catalyst helps the chemical reaction run more efficiently, so that less energy is required and fewer harmful by-products are generated."

"Most catalysts work at temperatures of a few hundred degrees Celsius and pressures of a few atmospheres. But the lack of microscopes that could tolerate these conditions meant that scientists always carried out the fundamental research at room temperature and low pressure. Industry was interested, but they couldn't do much with the results in the real world – so the development of new catalysts remained largely trial and error."

"That's why we developed a scanning tunnelling microscope (STM) in our lab a few years ago which works at high temperatures and pressures. The tip with which the microscope scans the surface is contained in a tiny reactor tank. The temperature and pressure in that tank can go way up, without affecting the rest of the device. This research formed the basis for a commercial

microscope, which we sell through our own company, Leiden Probe Microscopy (LPM)."

"Unfortunately, the Scanning Tunnelling Microscope has a downside: it only works if the surface you're studying conducts electricity. We used to study model catalysts in the form of flat, metal surfaces; those conduct well. But in practice, catalysts are often tiny metal particles. These nanoparticles are scattered across a carrier material, which usually doesn't conduct electricity. That means the STM can no longer form an image. We need to go a step further to be able to study that land of bumps and bubbles."

"We're now developing a microscope that combines STM with a microscope technology which doesn't require a conductive surface: atomic force microscopy (AFM). Non-contact AFM, to be precise. You bring the oscillating needle so close to the surface that the attractive force between atoms alters the oscillating frequency. That change is what you measure. We're currently making the technology suitable for field conditions in industry. A difficult task, but it's possible.

New measurement technology leads to new science. Soon we'll be able to see what happens at the surface of the catalyst. That's new territory; only then will we know how it really works."





Testing taste

By David Redeker / Photo Shutterstock

Safe food for everyone. That's the ultimate dream underlying the United Nations' first millennium development goal. The NanoNextNL theme 'Food' contributes to

this objective. Maarten Jongsma heads the

programme exploring new ways to ensure food quality and safety. "But our technology-in-the-making doesn't have to be limited to food. The pharmaceutical industry can also use it to their advantage."

aarten Jongsma works for Plant Research International, a research institute at Wageningen University and Research Centre in the Netherlands. What's his specialty? "People smell and taste using receptors,"

> Jongsma explains. "These are located not only on your tongue and in your nose, but also in your brain. In the lab, we put those receptors on a chip. We can place 1600 receptors in a square centimetre. How we do that and what the chip does with them, I can't say just yet. We're in the middle of a patent application, you see, and that would be compromised if I go into too much detail. At any rate, we can expose the chip to foods and then read it out. That shows us the food's footprint, so to speak. I'm sorry to be so vague, I'd love to tell you more, but, you know, the patent."

What's the point of a chip with an artificial tongue, nose and brain? Is that something we really need? According to Jongsma, the possibilities are nearly endless. "The food industry can put the chip to very good use - for example, in the search for sugar substitutes or to see whether a food curbs appetite. The chip can help us predict how new foods will taste, and give us greater insight into the composition of the different active substances in existing foods."

Chip to market

What are the next steps? And how does Jongsma's research align with other projects at NanoNextNL? "We're currently developing an application," Jongsma says. "After that, we need to focus on making it commercially viable. We can't do that within the institute. It would be a logical step to start a spin-off, a small company built around the application which can bring the chip to market. Pharmaceutical companies can also use our chip. For example, they could test urine, blood or saliva instead of food. So our research is an excellent fit with the NanoNextNL 'Nanomedicine' cluster, for example." Jongsma is the programme director for NanoNextNL's 'Food process monitoring and product quality assessment' programme. "I've just had a meeting with my programme team. Things are really starting to move. When we were ready to sign the contracts, a couple of companies backed out. We've now replaced

"Pharmaceutical companies can also use our chip. For example, they could test urine, blood or saliva instead of food"

those, and the new companies presented

themselves at the meeting. It's very promising, and it's on its way now."

Companies which have participated in the research programme since the beginning include microscope manufacturer Nikon and seed breeders Enza and Syngenta. Can you test seeds using the chip? Jongsma laughs. "No, no, no. But of course you can look at the products which grow from those seeds.

At tomatoes and peppers, for example. If you want to create a better-tasting tomato, you have to hire expensive panels of professional tasters. That's much less expensive with our chip, plus you can much more precisely determine exactly which substance in the tomato makes it taste so good." What about Nikon - what's their interest in Jongsma's research? "We can read out our chips using Nikon's special microscopes," says Jongsma. "As partners, we can create optimal food in an optimal environment. That's the essence of nanotech."

Taste explained

Back to the endless possibilities Jongsma foresees using his chip outfitted with taste, olfactory and other receptors. What does the future look like? "What I'd love to see is that, in five years, there's a small company putting our chip technology on the market," Jongsma says. "I participated in an entrepreneurs' contest in the life sciences some time ago, and that was very inspiring. We definitely need to keep pursuing this research. I call it 'decoding taste'. If you think in broader terms, you could also detect spoilage and identify contamination risks. And all of it faster and more cheaply than by current methods. Online, anywhere. Right now we need a whole lab to do it, but in the future, it'll fit onto a chip."

Jongsma could talk about it forever. "We're on the threshold of a huge nanorevolution. I'm fascinated by tiny creatures, by insects, by mosquitoes, for example. Amazing, all the things such a tiny little pest can do. It can do almost as much as an elephant. And that's actually what we're trying to do with nanotechnology: turn an elephant into a mosquito. Nano brings the lab to the consumer, the farmer, the seed breeder, the manufacturer. You name it."



Recognised talent

By Anouck Vrouwe / Photo Fjodor Buis

his spring, I was appointed a fellow by the American Physical Society (APS). It's a great honour; most members are older than I am, or have done really phenomenal things. More than for the award itself, I was proud to learn that I have been nominated by my former colleagues from Brookhaven National Lab, in America. I've been gone for ten years; they didn't have to do that. It's a sign of their appreciation for my research. At Brookhaven, my colleagues and I investigated why PZT (lead zirconium titanate) is so much better than other materials. PZT is the piezoelectric material everyone has worked with since the 1970s, but it's always been unclear why it was so good. My work showed that the answer is in its atomic structure. That research changed the field and the way we look at piezoelectricity.

Movement and energy

I study piezoelectric materials. These are materials which can convert mechanical energy (pressure or deformation) into electrical energy, and vice versa. You could use them to absorb

vibrations from cars or heavy machinery and use them to generate electricity. We're not talking giant amounts of power here, but our electronic devices are needing less and less. At the moment they can already power sensors, LED lighting and other small devices, as well as charge batteries.

A great deal must happen before they are used more broadly. When I talk to people in the energy harvesting industry, they all tell me the material itself is a stumbling block. In the first place, the power has to increase, from microto milliwatts, and preferably to watts. That's hard, but we'll see how far we can get. But that's not all. The P in PZT stands for plumbum, Latin for lead. That element is responsible for the structure, which makes the material so useful. But lead is also toxic. There are some really nice demonstration projects, such as a dance floor which generates energy, but they aren't taking off now, because of the

So we're searching for alternatives, with colleagues at the University of Twente and others. In an article in Nature Materials last year, we showed that you can create piezoelectric behaviour by forcing very thin (~100 atoms thick) layers of material to adapt to a

carefully chosen crystal substrate. The chemical composition becomes less important in this way and that can lead to alternative materials without toxic elements. Another general approach is, indeed, to shrink the piezoelectric material. Current applications use sizeable chunks. Within the NanoNextNL programme we're looking for ways to develop much smaller piezoelectric materials, such as thin layers and nanocrystals with dimension of just a few hundred atoms. If you could make the material so small and light, you only need a little bit. Then even if we continue using PZT, the use of lead is surmountable. Cobblestones that provide electricity for street

lights, shoes that charge mobile phones... right now these are just demonstration projects. But, believe me, in the next few years you'll be hearing more and more about harvesting energy with piezoelectric materials."

What do you hope to have achieved in five years?

"My chief goal is to help paving the way such that piezoelectric materials will soon be used everywhere. That may sound a little crazy, knowing they only generate about 0.5 milliwatts per cc right now, that is 100 times less than with solar cells. But piezoelectrics do not depend on the weather and can be hidden under the floor in highways, railways and bridges, so if they are light and non-toxic, we could pave very large surfaces with them. That's where I want to go. You can use piezoelectric materials to turn vibrations into electricity. You could harvest energy which is wasted now, such as vibrations from cars, trainsand machinery with very high efficiency (above 50%) compared to other ways of harvesting energy. First applications will be in the fields of movement and pressure sensors and in wireless and self-powering of lowconsumption electronics, such as LED lights. Five years is a short time, but if you look at where we were five years ago..."

NanoNextNL at a glance

All NanoNextNL projects fall within one of 28 programmes, which in turn fall within one of 10 themes. For up-to-date information, please visit our website www.nanonextnl.nl.

1. Risk analysis and Technology assessment (RATA)

1A Human health risks
Dr. ir. J. J. M. yan de San

Dr. ir. J.J.M. van de Sandt (TNO) Environmental risks

Dr. A. van Wezel (KWR)

1C Technology Assessment Prof. dr. ir. H. van Lente (UU)

2. Energy

2A Efficient generation of sustainable energy Prof. dr. W.C. Sinke (ECN)

2B Efficient energy utilization by secondary conversion of energy and seperation Prof. Dr. F. Kapteijn (TUD)

3. Nanomedicine

3A Nanoscale biomolecular interactions in disease

Prof. dr. V. Subramaniam (UT)

3B Nanofluidics for lab-on-a-chip Prof. dr. ir. A. van den Berg (UT)

3C Molecular imaging Prof. dr. K. Nicolaij (TU/e)

3D Drug delivery Prof. dr. G. Storm (UU)

3E Integrated Microsystems for Biosensing Prof. dr. H. Zuilhof (WUR)

4. Clean Water

4A Nanotechnology in water applications
Prof. dr. ir. R.G.H. Lammertink (UT)

5. Food

5A Food process monitoring and product quality assessment
Dr. ir. M.A. Jongsma (WUR-DLO)

5B Molecular structure of food

Dr. K.P. Velikov (Unilever)
5C Food products and processes

Prof. dr. ir. R.M. Boom (WUR)

5D Microdevices for structuring and isolation
Dr. ir. K. Schroen (WUR)

6. Beyond Moore

6A Advanced nanoelectronics devices

Prof. dr. B. Koopmans (TU/e)

6B Functional nanophotonics
Prof. dr. L. Kuipers (AMOLF)

6C Nano-bio interfaces & devices Prof. dr. S.G. Lemay (UT)

6D Active nanophotonic devices

Prof. dr. P.M. Koenraad (TU/e)

7. Nano materials

7A Supramolecular and bio-inspired materials

Prof. dr. A.E. Rowan (RU)

7B Multilayered and artificial materials

Dr. ing. A.J.H.M. Rijnders (UT)

8. Bio-nano

8A Nanomolecular machines in cellular

force-transduction

Prof. dr. A.M. Dogterom (AMOLF)

8B Bionano interactions for biosensing Prof. dr. ir. G.J.L. Wuite (VU)

9. Nano fabrication

9A Nano-inspection and characterization

Prof. dr. J.W.M. Frenken (UL)

9B Nano patterning

Prof. dr. ir. P. Kruit (TUD)

10. Sensors and actuators

OA Systems and packaging

Prof. dr. U. Staufer (TUD)

10B Micro nozzles

Dr. ir. H. Wijshoff (Océ)

10C Microdevices for chemical processing

Dr. ir. M. Blom (Micronit)

