NANOTECHNOLOGY TAKES OFF

Small particles, big potential

An electronic tongue, sieves that can detect pathogenic bacteria within an hour, and molecules that can help with tracking down and killing tumours. Wageningen UR is going full steam ahead with nanotechnology – but not without weighing up the potential human and environmental risks.

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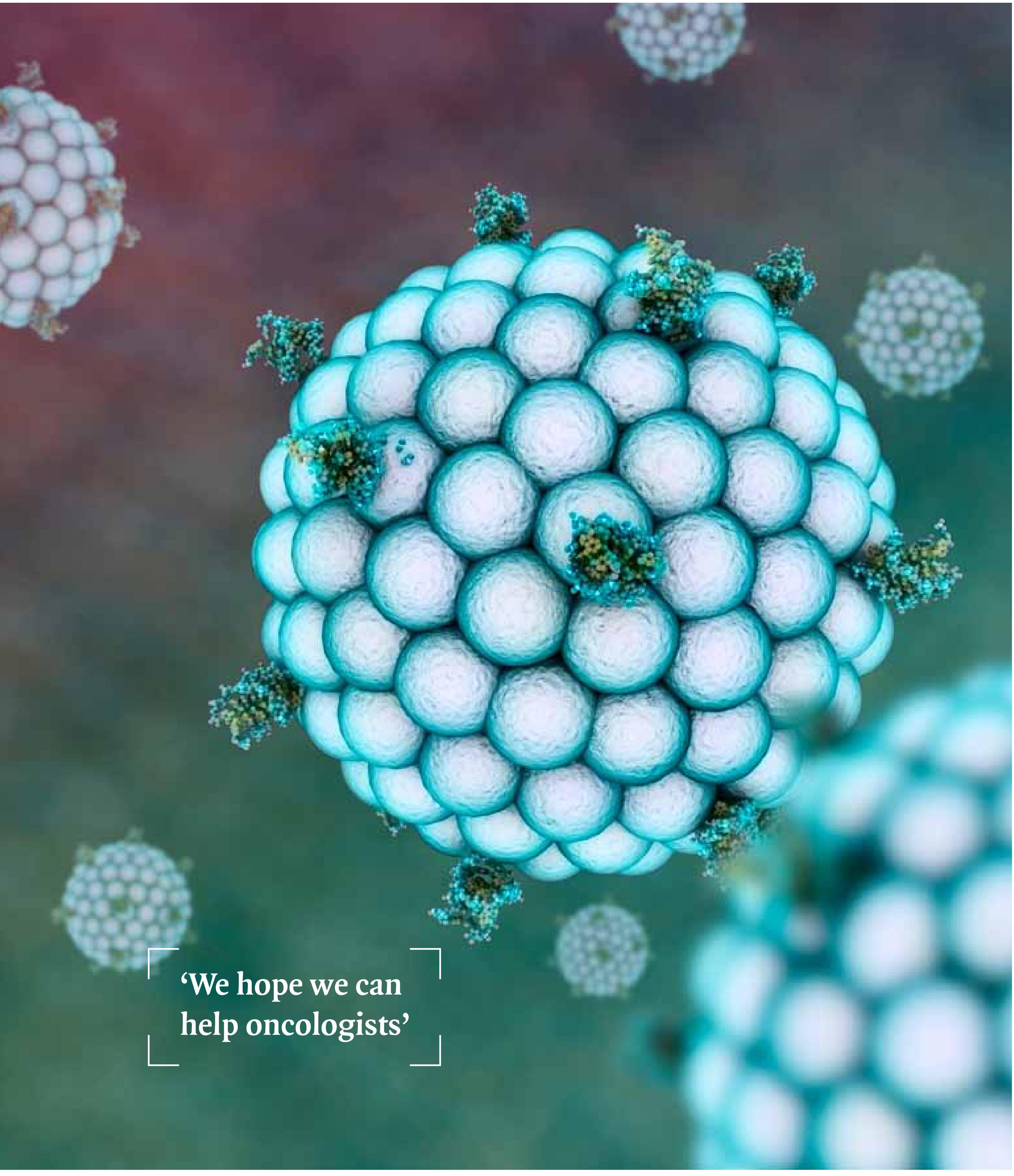
If it is up to Maarten Jongsma, tasting panels will soon be up against some stiff competition. They will not need to taste all the new products that food companies dream up because an electronic tongue will have done the groundwork. Jongsma, a researcher at Plant Research International, part of Wageningen UR, is working on creating a chip with miniscule human taste and odour receptors on it. It detects odours and tastes just as precisely as a real tongue does. Perhaps even more so. Because while a human being's sense of taste may be distorted by whatever he or she has just eaten, this electronic tongue stoically goes on registering whatever taste comes its way. A perfect tool for breeders or manufacturers who want to know how their new product tastes.
'We are not there yet, though,' says Jongsma. 'There are quite a few technical problems still to be solved. But if it is up to us, this electronic tongue will be in use in a few years' time.' And it won't stop with an electronic tongue, either. There may one day be an electronic bowel with all the receptors found in the human bowel, or an electronic brain with human brain receptors. Jongsma: 'Human beings have about 1000 receptors for chemical signals. The genes for these have already been mapped so in theory we could put those receptors onto a chip.' Such a chip can also be used to test potential medical drugs, says Jongsma: 'Now pharmaceutical companies use things called microtitre plates. This is a relatively expensive method because you need 1000 times more testing material than you need if you use these chips.'

HUMAN RECEPTORS

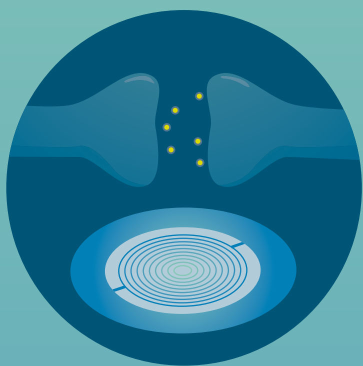
The development of a chip with human receptors is one of Wageningen's promising projects in the field of nanotechnology. In the past five years, Wageningen UR has made a big push into this new science. Last year NanoNextNL – a research programme in which universities, government and the business world invest jointly in micro- and nanotechnology – allocated 20 of its 250 million euros to Wageningen project proposals. This meant that, after the Technical University of Twente, Wageningen got the most funding in this programme.
Frank Kampers, coordinator of the Wageningen research programme that paved the way for this one: 'During the period 2007-2010 we very consciously built up the knowledge to be able to gain a position in this investment programme, especially in the area of food nanotechnology, one of the ten themes within NanoNextNL. And we succeeded.'
The group that gained the most funding was the one led by Han Zuilhof, professor of Organic Chemistry at Wageningen University, part of Wageningen UR. The funding enables him to set 10 fulltime scientists to work. 'Our core specialism is introducing layers one nanometre thick onto >



Visualization of a new organic nano molecule with other molecules attached to it.

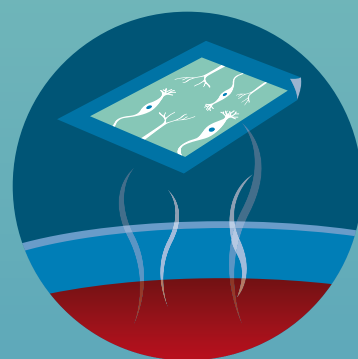
NANOTECHNOLOGY FOR FAST AND SUPER-PRECISE DETECTION

A major branch of nanotechnology research within Wageningen UR is the development of fast and super-precise means of detection. Using bio-molecules which detect harmful bacteria, for instance, and are embedded in a one-nanometre-thick layer of material. Or using human receptors on chips that identify the taste of foods, for example. Or even using newly created nanomolecules which look for specific cells in the body such as cancer cells.

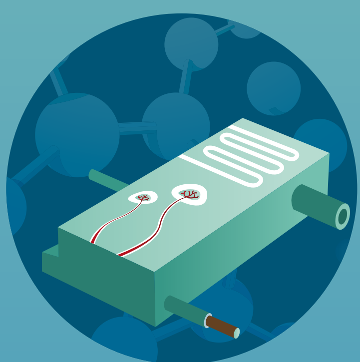


CHIPS WITH HUMAN RECEPTORS

Electronic brain
Chips with human brain receptors which detect neurotransmitters, growth factors and hormones: substances which regulate health and wellbeing. Pharmaceutical companies could use the chips to test whether a medicine really does block a particular signal substance.



Electronic tongue
Chips with miniscule human taste and smell receptors make it possible to find out whether a new food flavour will fulfil consumers' wishes, using very little testing material and without the aid of time-consuming taste panels.

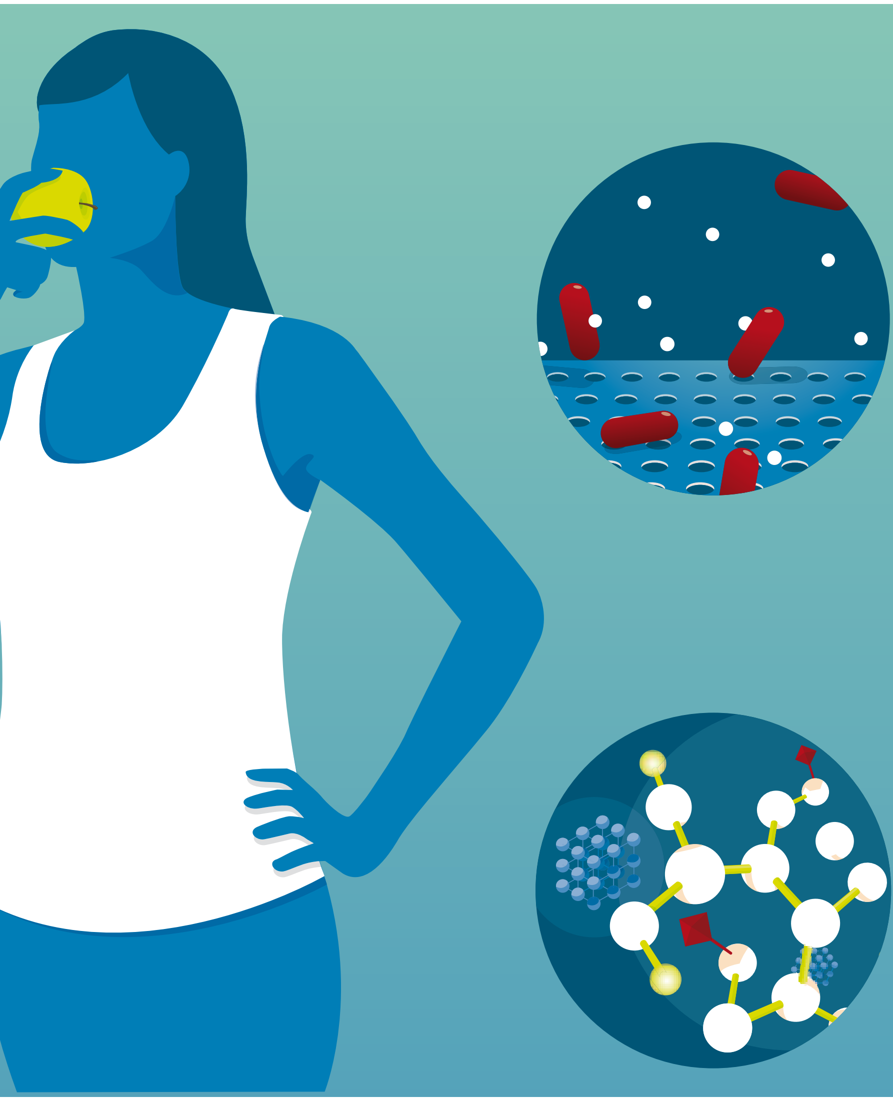


Electronic bowel
Chips with human bowel receptors which regulate such things as a feeling of satiety, inflammation responses and secretion in the bowel and related organs. Pharmaceutical companies could use the chips to test medicines that work through the signal substances and receptors in the bowel.

material,' says Zuilhof. 'A specialism which paves the way for many new applications, such as the electronic tongue. This is because we can place on that layer all sorts of bio-active molecules which bind bacteria to themselves, or which intercept specific proteins or molecules.'
For example, his research group is working on microsieves with which it is possible to establish quickly which bacteria are present in a liquid. The sieves have a silicon nitride coating on them on which there are specific antibodies which only hold onto the target bacteria. 'This could be a useful tool for General Practitioners and hospitals. Like this they can almost instantly establish whether a urine sample contains a harmful bacterium and the patient can be started on the right antibiotic straightaway. Currently they first have to culture the sample, only seeing the result after four days. That is quite a gain,' says Zuilhof. 'The sieves can also be used to detect bacteria on other fluids such as blood or sputum.'

SALMONELLA IN SALMON

According to Kampers, then, much of the nanotechnology being developed in Wageningen will soon make faster and better detection possible. The detection of tastes and odours by means of the electronic tongue, for instance, and the detection of rotten packaged meat or fish in hospitals or the food industry. 'The dream of every food manufacturer is to have a dipstick which tells you within an hour whether your product is free of pathogens. With such a test, the recent outbreak of salmonella poisoning in the Netherlands, which came from infected salmon from a company in the town of Harderwijk, could have been prevented. I think nanotechnology can make that dream come true.'
The food industry also hopes to use nanotechnology to produce better quality and



BIO-ACTIVE MOLECULES

Microsieve
Minuscule sieves equipped with a coating of silicon nitride with a one-nanometre-thick layer of specific antibodies that only capture the target bacteria. This makes it possible to identify a harmful bacterium in a blood or urine sample almost instantly.

NEW ORGANIC MOLECULES

Dendrimers
Dendrimers are new nanoparticles: hollow organic molecules which branch out like trees. Other molecules or particles can be inserted into them or hung from them. These include proteins which only attach themselves to cancer cells. In future it may also be possible to equip dendrimers with drugs that are released as soon as they attach themselves to the cancer cells.

healthier food. Kampers puts a jar of 'nanonaise' on the table. 'It will never be put on the shelves like that of course. A name like that will not attract any consumers at all. But it spells it out that Wageningen is researching whether you can improve foods using nanoparticles.' In one project, the group led by Wageningen University professor of Agrotechnology and Nutrition Sciences Remko Boom is working on how to make water droplets with a nano coating of fat molecules. 'Because of the fatty outer layer, the product still tastes the same but it contains fewer calories.' These kinds of nano coatings can also be used for such ends as >

> 'We can track down a harmful bacterium almost instantly'

‘Nanoparticles can end up in the food cycle’

masking the nasty taste of healthy nutrients such as fish oil, or for getting health-promoting bacteria through the stomach without their being broken down there.

HELPING ONCOLOGISTS

Wageningen is also experimenting with nanoparticles outside the NanoNextNL programme. Funding from the Ministry of Education, Culture and Science, for example, made it possible to appoint Aldrik Velders, who came to Wageningen from the Technical University of Twente in April. One of the topics the new professor of Bionanotechnology will focus on in the Physical Chemistry and Colloid Science laboratory is the building of new nanoparticles. He has a lot of experience with hollow organic molecules known as dendrimers, which branch out like trees on the outside. ‘The nice thing about these molecules is that you can put other molecules or particles inside them, or hang them from them,’ says Velders. ‘They are very suited to medical uses. We hope we can help oncologists with them.’

Rather in the way we might decorate a Christmas tree with baubles and lights, Velders hangs molecules containing metals and specific proteins from the branches of the dendrimer. The proteins ensure that the nanoparticles only attach themselves to tumour tissue; thanks to the metal compounds, the nanoparticles are visible in the body. Because of their magnetic or fluorescent characteristics, they can be tracked with the radio waves in an MRI scanner before the operation, or with the naked eye during the operation. ‘By injecting cancer patients with these dendrimers, the oncologist can track down the tumour very precisely and remove it,’ explains Velders, who is doing this researcher together with his colleague Fijs van Leeuwen of Leiden University Medical Centre. ‘We design the nanoparticles; he gets them ready for application in the clinic by first testing them on cells and on lab animals.’ Eventually they hope to be able to equip the dendrimer with a drug that is released as soon as it attaches itself to the cancerous tissue.

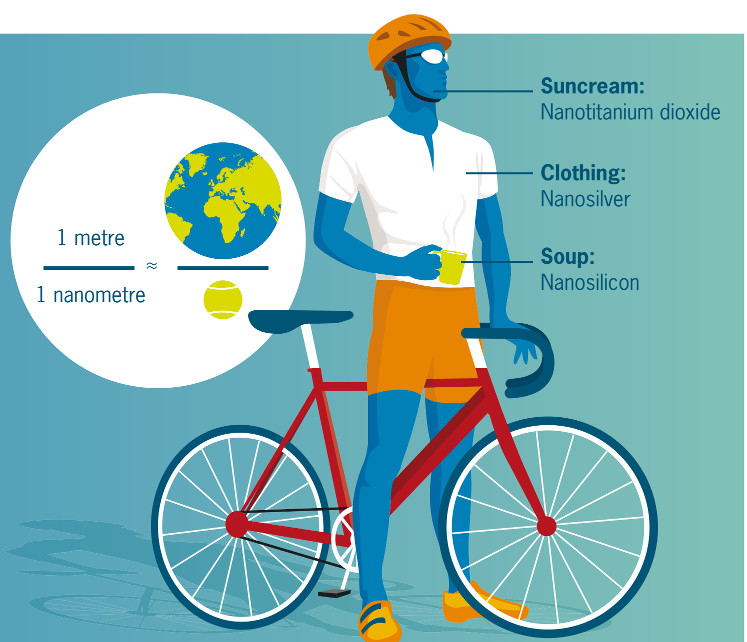
NEW CHEMISTRY

‘In nanotechnology we are actually developing an entirely new chemistry,’ declares the new professor with enthusiasm. ‘A sort of periodic system of nanoparticles with new characteristics and functions.’ But he is also the first to stress that these new chemicals entail risks. ‘We are making particles whose characteristics are harder to define than they used to be in traditional chemistry. Then we knew right down to the atomic level precisely

WHICH PRODUCTS ALREADY CONTAIN NANOPARTICLES?

Nanoparticles are human-made structures smaller than 100 nanometres (= one billionth of a metre). To give some idea: a human hair is 60,000 to 80,000 nanometres in diameter. There are very many different kinds of nanoparticles. They can be made up of metals (silver, gold and iron), of silicon, titanium and carbon, of biological molecules such as DNA, proteins, antibodies, lipids or a combination of such particles. On a nano scale, materials sometimes gain new characteristics: they might become super-strong or water-resistant, for example. In the Netherlands, manufacturers are already putting nanoparticles into about 120 products, mainly cosmetics and packaging. They use nanosilver, for instance, as an antibacterial substance in sportswear or packaging, nanosilica (E551) as an anticoagulant in milk powder, soups and sauces, or nanotitanium dioxide in sun cream to protect against UV light.

Source: www.rijksoverheid.nl/nanotechnologie.



which molecules we were making and how they functioned. Now we don't know. Not all the molecules hanging on to one of those supermolecules are attached with sturdy compounds and under some conditions they can become detached. That is not just a nuisance for us – because we then have less idea what we are making – but also for monitoring organizations such as the Food & Drugs Administration, the Dutch Food and Consumer Product Safety Authority or the Medicines Evaluation Board. They are not yet sure where the dangers lie and what exactly they should measure.'

So five years ago, the ministry of Economic Affairs, Agriculture and Innovation (EL&I) and the Dutch Food and Consumer Product Safety Authority asked RIKILT, part of Wageningen UR, to find out whether the current testing procedures are adequate for a reliable assessment of the risks of nanoparticles in food or in the human body. Are the in-vitro tests which imitate the behaviour in the human body adequate? And the animal tests that accompany them? 'Both issues are now under research here,' says researcher Hans Bouwmeester. 'For two types of nanoparticles – silver and silica ones, both of which are already used a lot in products (see box) – we have now looked at how they behave in animal tests and cell cultures. As far as silver is concerned, the result is clear. Silver nanoparticles, some of which dissolve, appear to pose no additional risks.' It is not as clear in the case of silica. 'In our in-vitro model – which imitates the digestive tract in the human body – it turned out that nanoparticles of silica clumped together to form bigger particles in the stomach, but fell apart again to go back to their original size in the intestines,' explains Bouwmeester. 'We are now doing animal tests to see whether intestinal cells absorb them, which would mean they could end up in the blood. The results of these tests have not come out yet.'

Through these studies, RIKILT aims to gain insight into the risks of nanosilver and nanosilica, as well as the risks of nanoparticles in general. Bouwmeester: 'Each type of nanoparticle behaves differently, but we may soon be able to estimate in advance roughly where the dangers lie, on the basis of particular characteristics.'

ACCUMULATING OR BREAKING DOWN

It is not just the behaviour of nanoparticles in the human body that is still unclear. Very little is known either about what goes on in the natural environment. Do they accumulate or do they get broken down? Are they a problem for living organisms and, if so, in what quantities? A few ongoing exploratory studies by Alterra and IMARES, both part of Wageningen UR, are showing negative effects. For example, Alterra showed that buckyballs – promising carbon nanoparticles that are still only used in laboratories – are harmful to earthworms. Exposure to these particles slows down the growth and the rate of reproduction of the worms and causes them to die earlier. Meanwhile, IMARES showed that mussels exposed to plastic nanoparticles eat less. Bart Koelmans, attached to IMARES and professor of Water and Sediment Quality at Wageningen University: 'We gave the mussels huge concentrations of nanoparticles, so the results do not tell us anything yet about what happens to mussels in the sea. The concentrations are probably much smaller – but we do not yet know how to measure them. But we have shown that there are effects and that these aquatic organisms can suffer from them. Other studies have shown that plastic nanoparticles are absorbed into the tissue of the mussel. So in theory they could also end up in the food cycle, and the consequences of that are unknown.'

For this reason Koelmans thinks we should treat nanoparticles with caution. 'I fully support all the applications, and we can create fantastic new products with nanoparticles. But we must make sure we do not regret it later.' A thorough risk assessment should take place before we start producing them on a large scale, in Koelmans' view. What does exposure to nanoparticles mean for workers who will be making them, what does it mean for consumers, and what happens when all these particles end up in the water, the air or the soil? 'We should deal with nanoparticles in the same way as we do all new materials that come onto the market. First do our homework, and only then give the go-ahead.' ■

CONSUMER IS STILL IGNORANT

Consumers are critical of nanotechnology but they do not reject it out of hand, according to results of two studies by Wageningen UR Food & Biobased Research for the ministry of Economic Affairs, Agriculture and Innovation. In fact the technology does not mean much to them yet: they can hardly imagine its applications or its implications. Remarkably, when they consider nanotechnology in general consumers tend to emphasize the risks, whereas for particular applications they focus more on the advantages. Their attitude varies according to the application. Consumers are positive about a nanotechnological sticker that indicates the freshness of a product, but are critical of drinks to which healthy substances are added using nanotechnology.