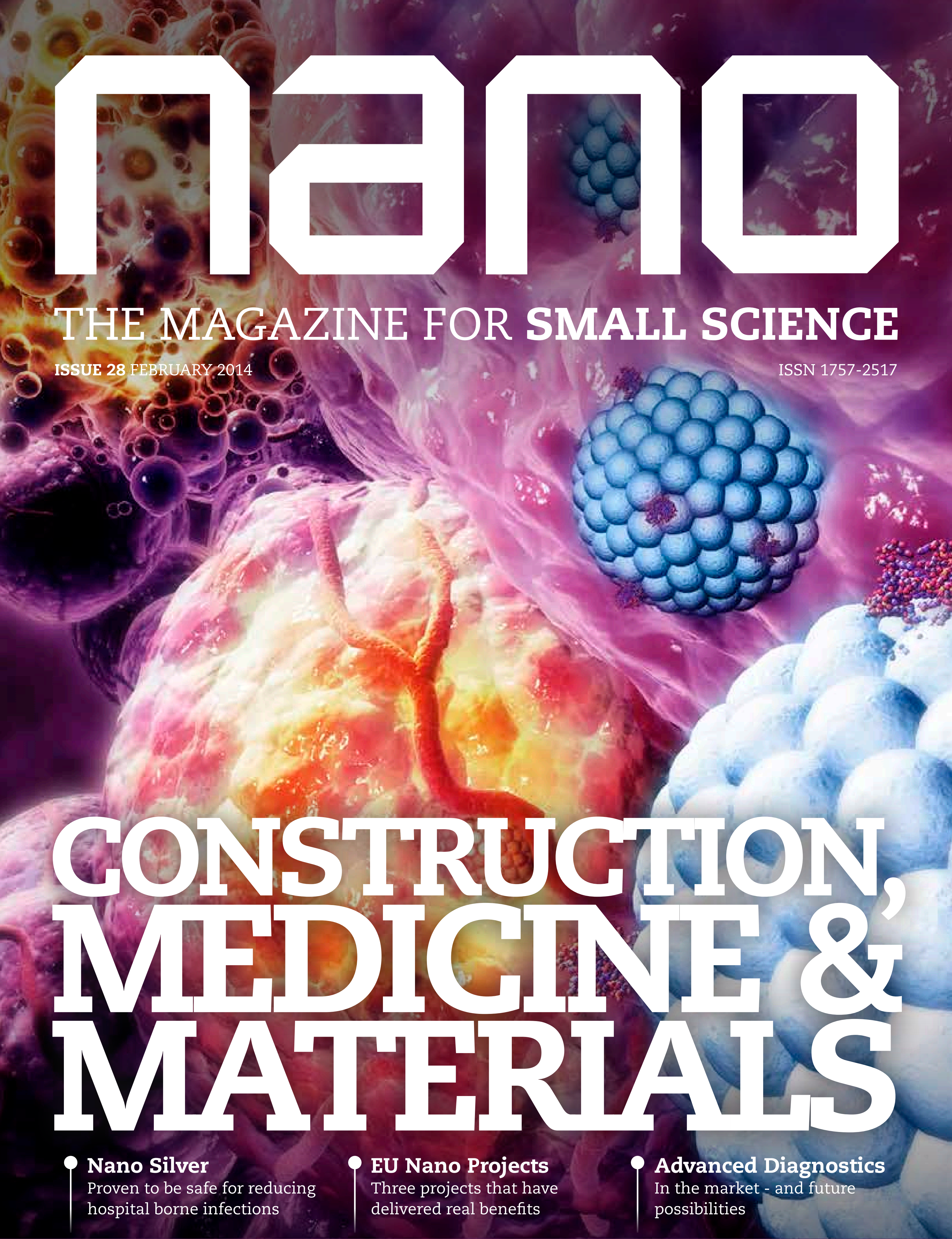

nano

THE MAGAZINE FOR SMALL SCIENCE

ISSUE 28 FEBRUARY 2014

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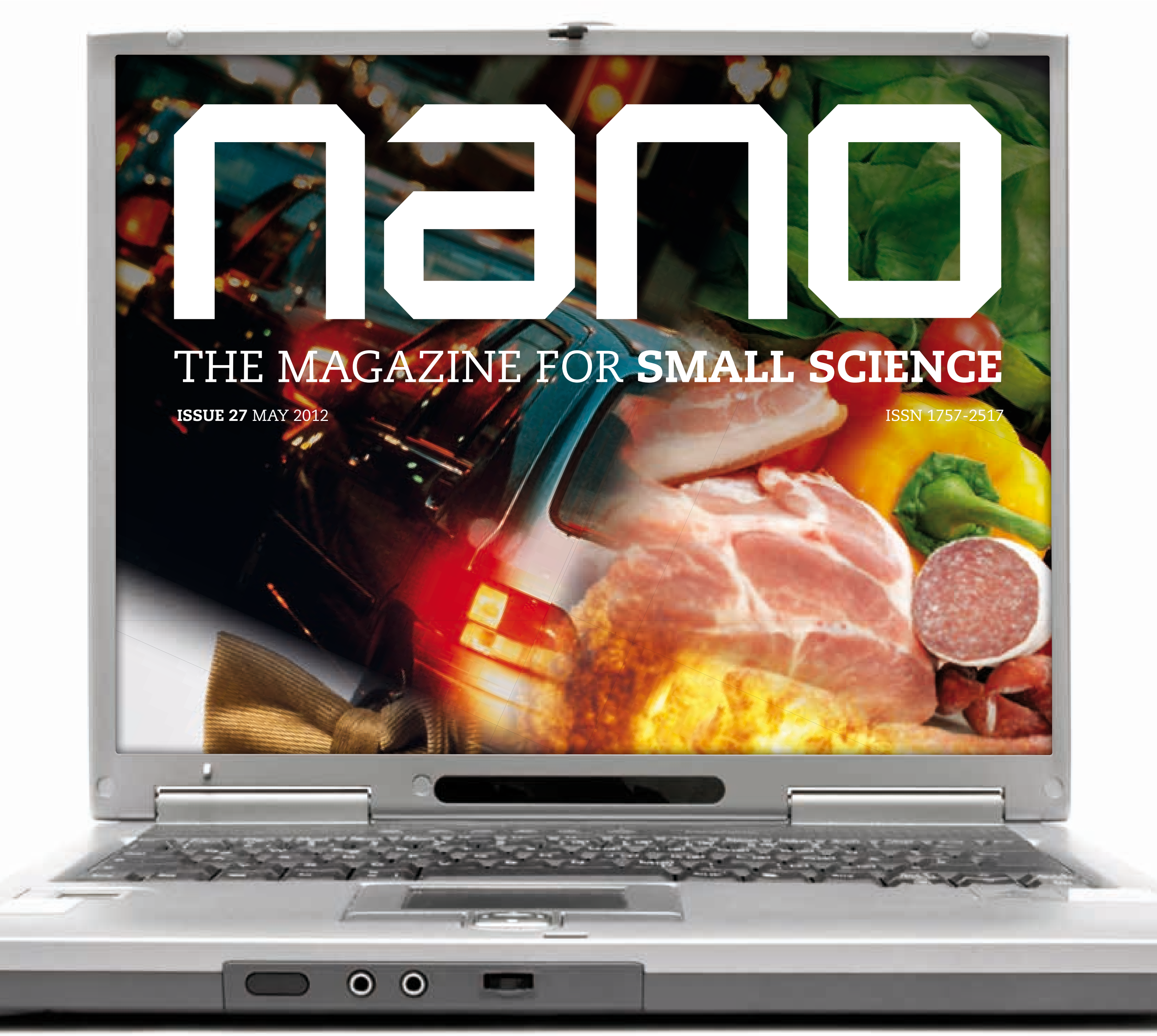
CONSTRUCTION, MEDICINE & MATERIALS

Nano Silver
Proven to be safe for reducing hospital borne infections

EU Nano Projects
Three projects that have delivered real benefits

Advanced Diagnostics
In the market - and future possibilities

Plus the latest and best news about nano for industry, healthcare and society, and NEW - an insight into EU-funded nano projects.



In the next issue, due out 15th May 2014:

Nano for advanced medical devices – the Star Trek effect; nano and encapsulation – be amazed at its multivarious applications; nanobiomimetics – how emulating nature leads to new and better products. Plus the best of the latest nano news and events.

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BEST OF NANO NEWS:

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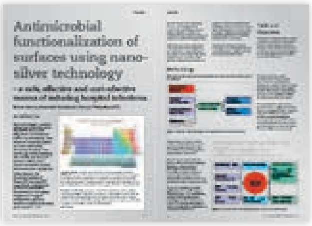
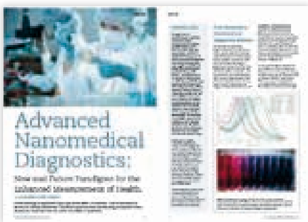
ARTICLES:



THREE EU-FUNDED NANO PROJECTS:



Nanotechnology – making a difference

There are always naysayers denying every promised technological advance – from the potential power of electricity to the usefulness of cars and trains to the impossibility of flight. Nanotechnology is no exception. But today's nano naysayers maybe haven't taken into account the presence of nano-inspired products that are already here, in mainstream use. And increasing almost by the day.

Ottilia Saxl, Director, NANO Magazine

Many people protest that nanotechnology has yet to realise its potential, while they are using their i-phones, almost absentmindedly. Or when they delight in the fact that their life was saved by an airbag when they were in a car accident. Some boast about the colour and ruggedness of the paintwork on their new car, or that the interior upholstery has been treated to be stain resistant. Some wealthier individuals and companies need to uniquely mark their products and use a barcode-type system, invisible to the naked eye. Others benefit from the latest in solar energy gathering technology, or in being able to store fruit and vegetables ready for export in ambient condition-maintaining packaging - which may also tell them when the contents has gone 'off' or been tampered with. On the subject of 'tampering', others are able to recognise illegally traded petrol by its unique chemical fingerprint.

All of these highly commercial products are courtesy of nanotechnology. They represent the tip of the iceberg, and don't even include the many nanomedical technologies that are already mainstream.

Nano advances are not serendipitous, as new developments have been in the past. Scientists know they can create customised materials from understanding how to create a novel composite with the necessary attributes for a specific product. For example, cars and aeroplanes in the past have been heavy and cumbersome, and fuel-hungry as a consequence. Today's materials, developed by understanding what makes a composite lightweight, but still reliable, rugged and resistant to fire has resulted in far more economical vehicles, where there has been no compromise on strength and safety.

Some of these nano advances have come directly from projects funded by the EU. In this issue, three EU projects are highlighted that are having, or will have, a significant impact on industry and society. One of these projects (Sonodrugs) is specifically aimed at improving the quality of life of the elderly, through quicker and better diagnosis of disease, a second (Light-Rolls) relates to the mass-manufacturing of devices requiring high functionalities, and the third (NanoInteract) on how nanoparticles interact with biological systems. Widely differing, but each vital to the sum of knowledge in this new and growing world of nano and micro products and processes. Each of these projects was on a shortlist of eleven for an award at EuroNanoForum, an event held every two years to celebrate EU projects during the 6-month presidency of a particular country. In 2013, that was Ireland, and the location for EuroNanoForum was Dublin. In 2015, EuroNanoForum will be held in either Latvia or Luxembourg.

Other articles in this issue include a well-argued paper on the importance of nanotechnology in making real improvements in the energy efficiency of buildings, and another scientific study on how the functionalization of surfaces using nano-silver can change the whole picture of hospital-borne infections. And further to my introduction, there is a major article on some mindblowing concepts for future nanomedical devices - for which the seeds are already sown.

A huge amount is happening in the nano world, and NANO Magazine is seeking news and articles that would be of interest to a broad community of readers.

Contact us at editor@nanomagazine.co.uk if you believe that some nano breakthrough, innovation or development deserves a wider audience.

Events Calendar

Every issue we highlight the leading conferences and summits where industry experts, academics and policy makers convene.

6-9 April, 2014

Nanomaterials for Industry 2014, Crowne Plaza San Diego, California, USA.

The conference is designed for business executives, engineers, and scientists to gain essential and wide-ranging knowledge about the science, technology and applications of nanomaterials. The three-day Congress includes:

- A special workshop on 'Graphene/Carbon nanotubes: properties, manufacturing techniques and applications'.
- Keynote speech by Nobel Laureate, Sir Harold Kroto.
- A series of comprehensive lectures by international leaders from industry, academia, and national laboratories. The presentations will review the state-of-the art in the rapidly expanding science and technology of nanomaterials.

See: http://www.executive-conference.com

30 September – 1 October 2014

Micro | Nano | Mems, The NEC, Birmingham, UK.

THE high precision manufacturing expo.

Micro | Nano | Mems is the event for manufacturers who make small parts - at every scale. The event will cover the full spectrum of technologies from laser micromachining through to micro injection moulding, and from MEMS fabrication, through to assembly, inspection and test equipment. It also will offer visitors a one-stop-shop for small and ultra-precision parts technology.

See: http://www.micronanomems.com/

Candle flames found to contain millions of tiny diamonds

Professor Wuzong Zhou, Professor of Chemistry at the University of St Andrews has discovered tiny diamond particles exist in candle flames.

Professor Zhou's investigation revealed around 1.5 million diamond nanoparticles are created every second in a candle flame as it burns. He revealed he uncovered the secret ingredient after a challenge from a fellow scientist in combustion. "A colleague at another university said to me "Of course no-one knows what a candle flame is actually made of." I told him I believed science could explain everything eventually, so I decided to find out".

Using a new sampling technique he invented himself,, and assisted by his student Mr Zixue Su, Professor Zhou was able to remove particles from the centre of the flame – something never successfully achieved before – and found to his surprise that a candle flame contains all four known forms of carbon. Professor Zhou said: "This was a surprise because each form is usually created under different conditions."

At the bottom of the flame, it was already known that hydro-carbon molecules existed which were converted into carbon dioxide by the top of the flame. But the process in between remained a mystery. Now both diamond nanoparticles and fullerenic particles have been discovered in the centre of the flame, along with graphitic and amorphous carbon.

The discovery could lead to future research into how diamonds, a key substance in industry, could be created more cheaply, and in a more environmentally friendly way. Professor Zhou added: "Unfortunately the diamond particles are burned away in the process, and converted into carbon dioxide, but this will change the way we view a candle flame forever."

Click here for more information

Scientists untangle nanotubes to release their potential in electronic inks

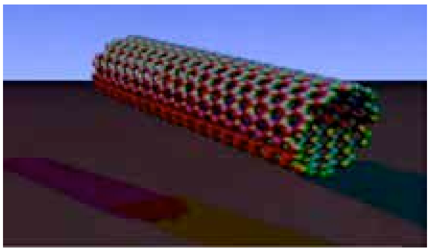
Researchers have demonstrated how to produce electronic inks for the development of new applications using carbon nanotubes.

Carbon nanotubes are lightweight, strong and conduct electricity, which make them ideal components in new electronics devices, such as tablet computers and touchscreen phones, but cannot be used without being separated out from their natural tangled state.

Carbon nanotubes are hollow, spaghetti-like strands made from the same material as graphene; only one nanometre thick but with theoretically unlimited length. This 'wonder material' shares many of graphene's properties, and has attracted much public and private investment into making it into useful technology.

By giving the nanotubes an electrical charge, Dr Stephen Hodge and Professor Milo Shaffer, both from Imperial's Department of Chemistry were able to pull apart individual strands. Using this method, nanotubes can be sorted or refined, then deposited in a uniform layer onto the surface of any object.

Working with an industrial partner, Linde Electronics, they have produced an electrically-conductive carbon nanotube ink, which coats carbon nanotubes onto



ultra-thin sheets of transparent film that are used to manufacture flat-screen televisions and computer screens.

This was developed by Professor Shaffer and colleagues from the London Centre for Nanotechnology, which includes fellow Imperial scientist Dr Siân Fogden, as well as Dr Chris Howard and Professor Neal Skipper from UCL.

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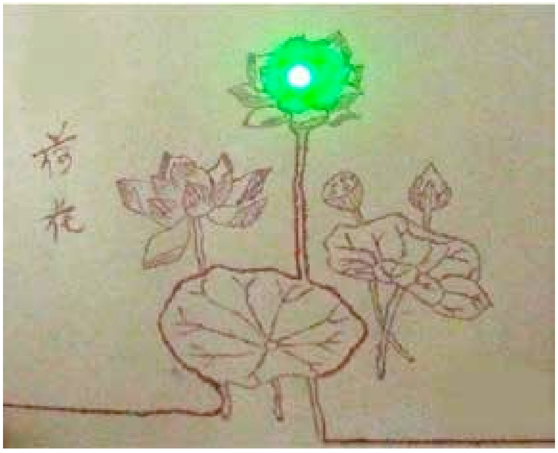
Metal ink capable of writing a functioning, flexible electric circuit on regular printer paper could ease the way towards flexible electronic displays



Scientists are reporting the development of a novel metal ink made of small sheets of copper. The conductive ink could pave the way for a wide range of new bendable gadgets, such as electronic books that look and feel more like traditional paperbacks.

Wenjun Dong, Ge Wang and colleagues note that the tantalizing possibilities of flexible electronics, from tablets that roll up to wearable circuits woven into clothes, have attracted a lot of attention in the past decade. But much of the progress toward this coming wave of futuristic products has entailed making circuits using complicated, time-consuming and expensive processes, which would hinder their widespread use. In response, researchers have been working toward a versatile conductive ink. They have tried several materials such as polymers and gold and silver nanostructures. So far, these materials have fallen short in one way or another. So, Dong and Wang's group decided to try copper nanosheets, which are inexpensive and highly conductive, as a flexible circuit ink.

They made copper nanosheets coated with silver nanoparticles in the laboratory and incorporated this material into an ink pen, using it to draw patterns of lines, words and even flowers on regular printer paper. Then, to show that the ink could conduct electricity, the scientists studded the drawings with small LED lights that lit up when the circuit was connected to a battery. To test the ink's flexibility, they folded the papers 1,000 times, even crumpling them up, and showed that the ink maintained 80 to 90 percent of its conductivity.

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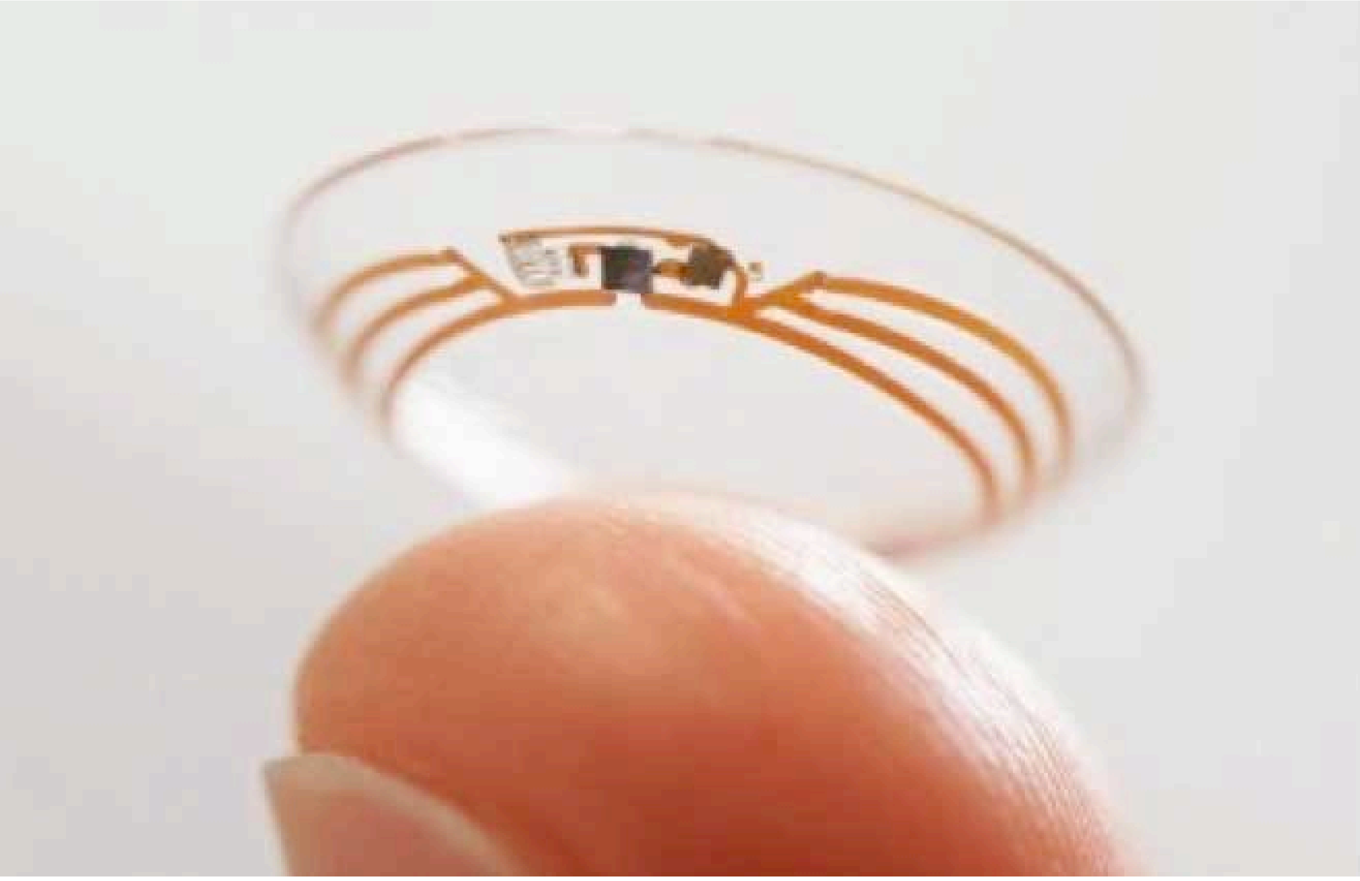
New sugar-sensing contact lens



Google has said it is testing a "smart contact lens" that can help measure glucose levels in tears. The lens includes a tiny wireless chip and a miniaturised glucose sensor embedded between two layers of lens material. The firm said it is also working on integrating tiny LED lights into the lens that could light up to indicate that glucose levels have crossed certain thresholds.

Google added that a lot more work needed to be done to get the technology ready for everyday use. "It's still early days for this technology, but we've completed multiple clinical research studies which are helping to refine our prototype," the firm said in a blogpost."We hope this could someday lead to a new way for people with diabetes to manage their disease."

Many global firms have been looking to expand in the wearable technology sector - seen by many as a key growth area in the coming years. Various estimates have said the sector is expected to grow by between $10bn and $50bn (£6bn and £31bn) in the next five years. Within the sector, many firms have been looking specifically at technology targeted at healthcare. Google's latest foray with the smart contact lens is aimed at a sector where consumer demand for such devices is expected to grow.

According to the International Diabetes Federation, one in ten people across the world's population are forecast to have diabetes by 2035.People suffering from the condition need to monitor their glucose levels regularly as sudden spikes or drops are dangerous. At present, the majority of them do so by testing drops of blood.

Google said it was testing a prototype of the lens that could "generate a reading once per second". Google also said it was working with the US Food and Drug Administration (FDA) to bring the product to mainstream use. It added that it would look for partners "who are experts in bringing products like this to market" to also help develop apps aimed at making the measurements taken by the lens available to the wearer and their doctor.

Click here for more information

How nanotechnology can trick the body into accepting fake bones

Altering the surface of orthopaedic implants has already helped patients – and nanotech can fight infections too. One of medicine's primary objectives is to trick the body into doing something it doesn't want to do. We try to convince our immune systems to attack cancer cells (our immune systems don't normally attack our own bodies), we try to convince neurons to regrow (another unnatural phenomenon), and we try to convince the body to accept foreign bits, such as someone else's kidney or a fake bone. In order to accomplish this, we try to make parts of our bodies we don't want, such as cancers, look foreign. We try to make foreign bits that we do want, such as orthopaedic implants, look natural. Nanotechnology, as you might have guessed, can help us do just that.

At the nanoscale, there aren't many smooth surfaces in our bodies. Cells are covered with bumpy molecules that help them recognise each other and stick together. Between the cells the extracellular matrix – a mesh of proteins, carbohydrates, and other molecules – helps migrating cells find their destination. Smooth, metal hip implants don't look anything like biological surfaces. Many companies now coat bone implants with nanoscale-textured hydroxyapatite, a mineral found in bone. This hydroxyapatite coating tricks the body into incorporating the implant as though it was a real bone.

Hydroxyapatite coating can make the implants "stickier", but to have a truly successful implant, the surrounding normal bone needs to grow around the implant. Titanium nanotubes, built to resemble the proteins that our bodies use to stick cells together, could encourage this kind of integration. In experimental models they encourage the growth of osteoblasts, the cells that synthesise bone. If osteoblasts grow around the new implant, they could produce new bone all around it. Titanium nanotubes are being developed by a number of groups, and could be used in future dental and orthopaedic implants. Researchers are also trying to embed drugs that encourage bone growth into hydroxyapatite coatings.

The antimicrobial properties of nanosilver have been discussed in a previous post, and post-operation bacterial infections are a serious and common problem in orthopaedics. Nanosilver is used in bandages and other wound-healing materials, and is being investigated for potential use on the surfaces of orthopaedic implants. One potential problem is that silver nanoparticles also inhibit the growth of osteoblasts, so fighting infection and encouraging bone growth might not be simultaneously achievable with silver. Other, more creative solutions are needed.

Companies such as Amedica coat implants with silicon nitride to simultaneously decrease bacterial growth and encourage the formation of bone. Unlike silver, silicon nitride seems to be able to do both at the same time. This could be because at the nanoscale the silicon nitride is textured in a way that attracts osteoblasts and repels bacteria.

Thomas Webster is one of medical nanotechnology's pioneers. NanoShield, one of the nine start-up companies that has sprung from Dr Webster's work, is developing a nanosensor that can measure how well an implant is doing. Carbon nanotubes on the implant detect what kind of cells are attached to the implant, and transmit this information through an embedded microchip. Each cell in the body has different electrical properties, and these properties can tell the nanosensor if an osteoblast, an inflammatory cell, or a bacterium is attached. A nanostructured film on the implant could then release drugs, such as antimicrobials or anti-inflammatory molecules, depending on which type of cell is detected by the nanosensor.

Altering the surface of orthopaedic implants with nanotechnology has already improved the kinds of fake bones patients receive today. Further trickery will undoubtedly make them even better, and convince our own bones to grow around the imposter implant.

Click here for more information

Carbon nanotube ‘sponge’ shows improved water clean-up

A carbon nanotube ‘sponge’ capable of soaking up water contaminants, such as fertilisers, pesticides and pharmaceuticals, more than three times more efficiently than previous efforts has been presented in a new study.

The carbon nanotube (CNT) ‘sponges’, uniquely doped with sulphur, also demonstrated a high capacity to absorb oil, potentially opening up the possibility of using the material in industrial accidents and oil spill clean-ups.

CNTs are hollow cylindrical structures composed of a single sheet of carbon. They have been touted as excellent candidates for wastewater clean-up; however, problems have arisen when trying to handle the fine powders and eventually retrieve them from the water.

Lead author of the research Luca Camilli, from the University of Roma, said: “It is quite tricky using CNT powders to remove oil spilled in the ocean. They are hard to handle and can eventually get lost or dispersed in the ocean after they are released. “However, millimetre- or centimetre-scale CNTs, as we’ve synthesised in this study, are much easier to handle. They float on water because of their porous structure and, once saturated with oil, can be easily removed. By simply squeezing them and releasing the oil, they can then be re-used.”

In the new study, the researchers, from the University of Roma, University of Nantes and University of L’Aquila, bulked up the CNTs to the necessary size by adding sulphur during the production process–the resulting sponge had an average length of 20 mm.

The addition of sulphur caused defects to form on the surface of the CNT sponges which then enabled ferrocene, which was also added during the production process, to deposit iron into tiny capsules within the carbon shells. The presence of iron meant the sponges could be magnetically controlled and driven without any direct contact, easing the existing problem of trying to control CNTs when added onto the water’s surface.

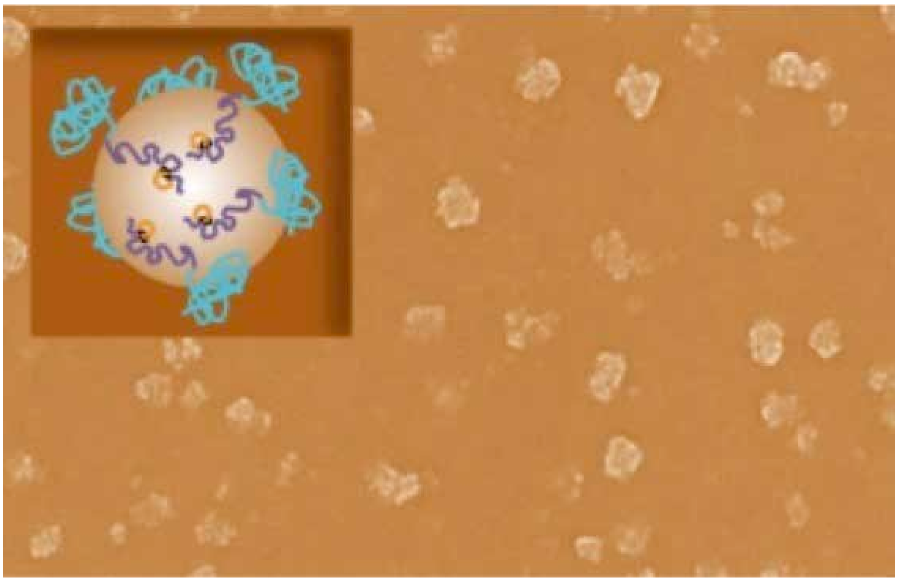
The researchers demonstrated how the constructed CNT ‘sponges’ could successfully remove a toxic organic solvent–dichlorobenzene–from water, showing that it could absorb a mass that was 3.5 times higher than previously achieved. The CNT ‘sponges’ were also shown to absorb vegetable oil up to 150 times of its initial weight and absorb engine oil to a slightly higher capacity than previous reported.

“The improved absorption properties of the sponge are down to the porous structure and the rough surface of the CNTs. Oils or solvent can easily be absorbed in the empty spaces amongst the CNTs, which is made easier by the rough surfaces,” continued Camilli. “The next stage of our research is to improve the synthesis process so that the sponges can be produced on a commercial scale. We must also study the toxicity of the sponges before any real-world applications can be realised.”

Click here for more information

On-demand vaccines possible with engineered nanoparticles

Vaccines combat diseases and protect populations from outbreaks, but the life-saving technology leaves room for improvement. Vaccines usually are made en masse in centralized locations far removed from where they will be used. They are expensive to ship and keep refrigerated and they tend to have short shelf lives.



University of Washington engineers hope a new type of vaccine they have shown to work in mice will one day make it cheaper and easy to manufacture on-demand vaccines for humans. Immunizations could be administered within minutes where and when a disease is breaking out.

"We're really excited about this technology because it makes it possible to produce a vaccine on the spot. For instance, a field doctor could see the beginnings of an epidemic, make vaccine doses right away, and blanket vaccinate the entire population in the affected area to prevent the spread of an epidemic," said François Baneyx, a UW professor of chemical engineering and lead author of a recent paper published online in the journal Nanomedicine.

In typical vaccines, weakened pathogens or proteins found on the surface of microbes and viruses are injected into the body along with compounds called adjuvants to prepare a person's immune system to fight a particular disease. But standard formulations don't always work, and the field is seeking ways to manufacture vaccines quicker, cheaper and tailored to specific infectious agents.

The UW team injected mice with nanoparticles synthesized using an engineered protein that both mimics the effect of an infection and binds to calcium phosphate, the inorganic compound found in teeth and bones. After eight months, mice that contracted the disease made threefold the number of protective "killer" T-cells – a sign of a long-lasting immune response – compared with mice that had received the protein but no calcium phosphate nanoparticles.

The nanoparticles appear to work by ferrying the protein to the lymph nodes where they have a higher chance of meeting dendritic cells, a type of immune cell that is scarce in the skin and muscles, but plays a key role in activating strong immune responses.

In a real-life scenario, genetically engineered proteins based on those displayed at the surface of pathogens would be freeze-dried or dehydrated and mixed with water, calcium and phosphate to make the nanoparticles.

This should work with many different diseases and be especially useful for viral infections that are hard to vaccinate against. However, the technique has only been proven in mice, and the development of vaccines using this method hasn't begun for humans.

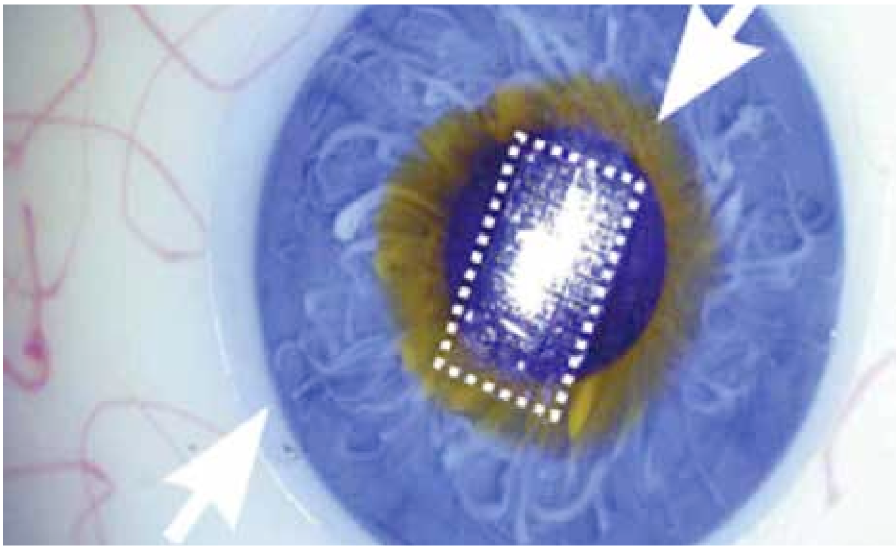
The approach could be useful in the future for vaccinating people in developing countries, especially when lead time and resources are scarce. It would cut costs by not having to rely on refrigeration, and vaccines could be produced with rudimentary equipment in more precise, targeted numbers. The vaccines could be manufactured and delivered using a disposable patch, like a bandage, which could one day lessen the use of trained personnel and hypodermic needles.

The research was funded by a Grand Challenges Explorations grant from the Bill & Melinda Gates Foundation and the National Institutes of Health.

Click here for more information

Ultra thin transparent sensors and 'smart' contact lenses

Researchers are developing electronic components that are thinner and more flexible than before. They can even be wrapped around a single hair without damaging the electronics. This opens up new possibilities for ultra-thin, transparent sensors that are literally - easy on the eye.



In Professor Gerhard Tröster's Electronics Lab, scientists have been researching flexible electronic components, such as transistors and sensors, for some time now. The aim is to weave these types of components into textiles or apply them to the skin in order to make objects 'smart', or develop unobtrusive, comfortable sensors that can monitor various functions of the body.

The researchers have now taken a big step towards this goal. With this new form of thin-film technology, they have created a very flexible and functional electronics. Within a year, Niko Münzenrieder, post-doctoral researcher at ETH Zurich, together with Giovanni Salvatore, has developed a procedure to fabricate these thin-film components. The membrane consists of the polymer parylene, which the researchers evaporate layer by layer into a conventional two-inch wafer. The parylene film has a maximum thickness of 0.001 mm, making it 50 times thinner than a human hair. In subsequent steps, they used standardised methods to build transistors and sensors from semiconductor materials, such as indium gallium zinc oxide, and conductors, such as gold. The researchers then released the parylene film with its attached electronic components from the wafer.

An electronic component fabricated in this way is extremely flexible, adaptable and – depending on the material used for the transistors – transparent. The researchers confirmed the theoretically determined bending radius of 50 micrometers during experiments in which they placed the electronic membrane on human hair and found that the membrane wrapped itself around the hair with perfect conformability. The transistors, which are less flexible than the substrate due to the ceramic materials used in their construction, still worked perfectly despite the strong bend.

Münzenrieder and Salvatore see 'smart' contact lenses as a potential area of application for their flexible electronics. In the initial tests, the researchers attached the thin-film transistors, along with strain gauges, to standard contact lenses. They placed these on an artificial eye and were able to examine whether the membrane, and particularly the electronics, could withstand the bending radius of the eye and continue to function. The tests showed, in fact, that this type of smart contact lens could be used to measure intraocular pressure, a key risk factor in the development of glaucoma.

However, the researchers must still overcome a few technical obstacles before a commercially viable solution can be considered. For instance, the way in which the electronics are attached to the contact lens has to be optimised to take into account the effects of the aqueous ocular environment. In addition, sensors and transistors require energy, albeit only a small amount, which currently has to be provided from an external source. "In the lab, the film can be easily connected to the energy supply under a microscope. However, a different solution would need to be found for a unit attached to the actual eye," says Münzenrieder.

Professor Tröster's laboratory has already attracted attention in the past with some unusual ideas for wearable electronics. For example, the researchers have developed textiles with electronic components woven into them and they have also used sensors to monitor the bodily functions of Swiss ski jumping star Simon Ammann during his jumps.

Click here for more information

Nanoparticle that mimics red blood cell shows promise as a vaccine for bacterial infections

A nanoparticle wrapped in material taken from the membranes of red blood cells could become the basis for vaccines against a range of infectious bacteria, including MRSA (methicillin-resistant Staphylococcus aureus), an infection that kills tens of thousands of people every year.

Researchers at the University of California, San Diego, have shown that the nanoparticles, loaded with a common bacterial toxin and injected into mice, can induce an immune response that protects the animals against a subsequent lethal dose of the toxin. The toxins, which are proteins the bacteria secrete, are "pore-forming," meaning they target cell membranes in the host and poke severely damaging holes in them. The proteins are secreted by a class of microbes called gram-positive bacteria, which in addition to Staphylococcus aureus includes clostridium, listeria, strep, E. coli, and a range of other infectious bugs.

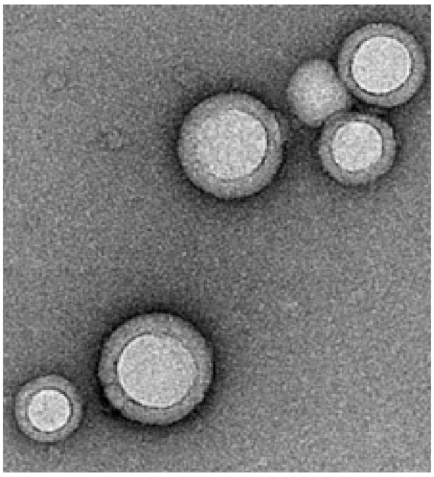
Liangfang Zhang, a professor of nanoengineering at the University of California, San Diego, had previously injected nanoparticles wrapped in membranes taken from red blood cells into mice that had been given large doses of toxin. The toxins targeted the decoy red blood cells; instead of forming deadly pores in real cells, they got themselves trapped and neutralized by Zhang's "nanosponges," which were then cleared from the body.

The nanosponges are so small that the membrane of a single red blood cell can supply enough material for 3,000 of them. According to Zhang, they can vastly outnumber the real red blood cells and divert toxins away from their natural targets, soaking up toxins from blood. Removing the toxin makes the bacteria more vulnerable to the immune system.

Now, Zhang has demonstrated that this same technology could be used to build vaccines similar to the "toxoid" vaccines used to inoculate people against diphtheria and tetanus. Whereas some bacterial vaccines work by inducing an immune response against the microbe itself (or parts of it), toxoid vaccines target bacterial toxins.

In experiments, Zhang and colleagues loaded alpha toxin, a type of pore-forming toxin produced by MRSA, into their nanosponges and injected them into mice. The "nanotoxoid" proved nontoxic and induced the production of antibodies that gave the animals protective immunity against the toxin. It also significantly outperformed an experimental vaccine made from a heat-treated form of the same toxin. The research is described in a recent paper in Nature Nanotechnology.

Whether a toxoid vaccine will work depends on the bacteria. Many bugs have other disease-causing factors in addition to their toxins. Staphylococcus aureus, for example, secretes the pore-forming toxin Zhang's group used in its vaccine, but it also has proteins on its surface that bind to and disable crucial

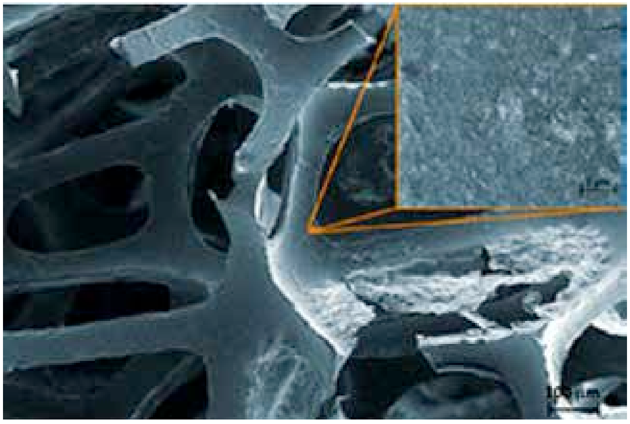


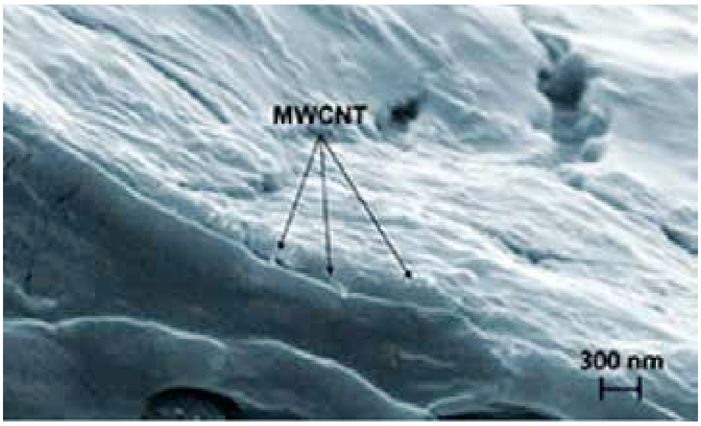
immune cells. After decades of research and many failed clinical trials, it's still not clear which targets, or combination of targets, a vaccine must attack to be successful. Currently, some large pharmaceutical companies are pursuing multitarget MRSA vaccines.

Making a new vaccine is a complicated process that can take over 10 years. Victor Nizet, a professor of pediatrics and pharmacy at UCSD, is now collaborating with Zhang to test the nanotoxoid vaccines in mice infected with various forms MRSA. Since Staphylococcus aureus secretes several different pore-forming toxins, it should be possible to load several toxins at once into the nanoparticle, says Nizet, and "potentially have more robust protection against multiple strains." Zhang's nanotoxoid also has the potential to lead to vaccines for multiple other bacterial species that rely on pore-forming toxins to harm their hosts.

Click here for more information

Carbon nanotubes promise flame-resistant coating





Using an approach akin to assembling a club sandwich at the nanoscale, researchers have succeeded in crafting a uniform, multi-walled carbon-nanotube-based coating that greatly reduces the flammability of foam commonly used in upholstered furniture and other soft furnishings.

The flammability of the nanotube-coated polyurethane foam was reduced 35 percent compared with untreated foam. As important, the coating prevented melting and pooling of the foam, which generates additional flames that are a major contributor to the spread of fires.

Fires in which upholstered furniture is the first item ignited account for about 6,700 home fires annually and result in 480 civilian deaths, or almost 20 percent of home fire deaths between 2006 and 2010, according to the US National Fire Protection Association.

The innovative technique, from the National Institute of Standards and Technology (NIST), squeezes nanotubes between two everyday polymers and stacks four of these trilayers on top of each other. The result is a plastic-like coating that is thinner than one-hundredth the diameter of human hair and has flame-inhibiting nanotubes distributed evenly throughout.

The brainchild of NIST materials scientists Yeon Seok Kim and Rick Davis, the fabrication method is described in the January 2014 issue of Thin Solid Films. Kim and Davis write that the technique can be used with a variety of types of nanoparticles to improve the quality of surface coatings for diverse applications.

The pair experimented with a variety of layer-by-layer coating methods before arriving at their triple-decker approach. All had failed to meet their three key objectives: entire coverage of the foam's porous surface, uniform distribution of the nanotubes, and the practicality of the method. In most of these trials, the nanotubes - cylinders of carbon atoms resembling rolls of chicken wire - did not adhere strongly to the foam surface.

So, Kim and Davis opted to doctor the nanotubes themselves, borrowing a technique often used in cell culture to make DNA molecules stickier. The method attached nitrogen-containing molecules - called amine groups - to the nanotube exteriors. This step proved critical: The doctored nanotubes were uniformly distributed and clung tenaciously to the polymer layers above and below. As a result, the coating fully exploits the nanotubes' rapid heat-dissipating capability.

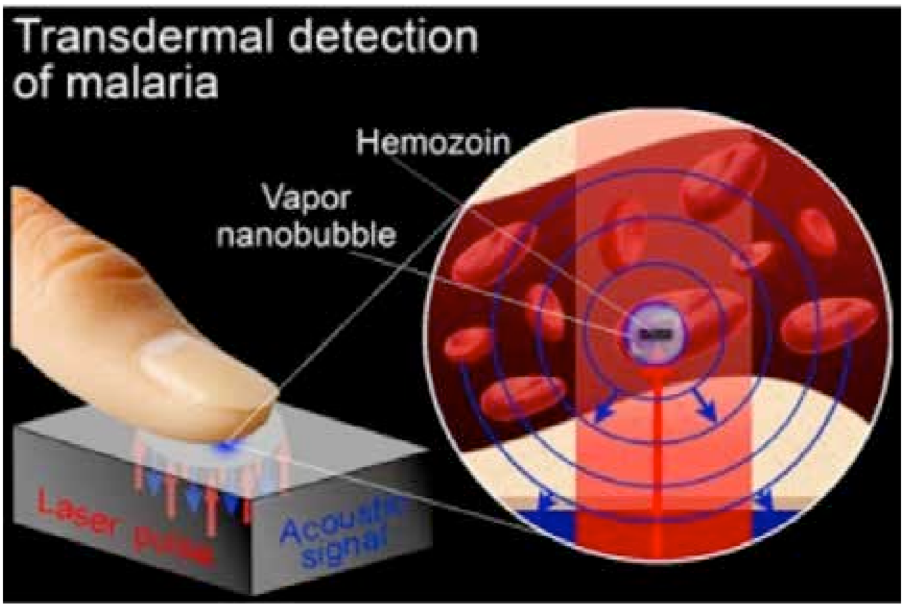
Gram for gram, the resulting coating confers much greater resistance to ignition and burning than achieved with the brominated flame retardants commonly used to treat soft furnishings today. As important, says Davis, a "protective char layer" forms when the nanotube-coated foam is exposed to extreme heat, creating a barrier that prevents the formation of melt pools.

"This kind of technology has the potential to reduce the fire threat associated with burning soft furniture in homes by about a third," Davis says.

Click here for more information

Vapour nanobubbles rapidly detect malaria through the skin

Researchers have developed a noninvasive technology that accurately detects low levels of malaria infection through the skin in seconds with a laser scanner. The "vapour nanobubble" technology requires no dyes or diagnostic chemicals, and there is no need to draw blood.



A preclinical study shows that Rice University's technology detected even a single malaria-infected cell among a million normal cells with zero false-positive readings. The new diagnostic technology uses a low-powered laser that creates tiny vapour "nanobubbles" inside malaria-infected cells. The bursting bubbles have a unique acoustic signature that allows for an extremely sensitive diagnosis.

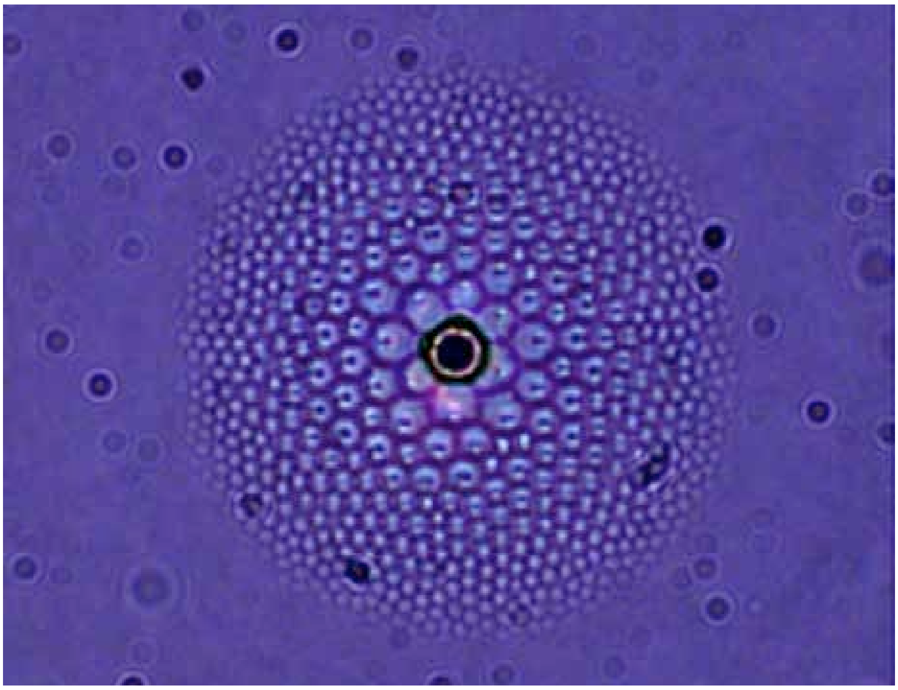
"Ours is the first through-the-skin method that's been shown to rapidly and accurately detect malaria in seconds without the use of blood sampling or reagents," said lead investigator Dmitri Lapotko, a Rice scientist who invented the vapour nanobubble technology. The diagnosis and screening will be supported by a low-cost, battery-powered portable device that can be operated by nonmedical personnel. One device should be able to screen up to 200,000 people per year, with the cost of diagnosis estimated to be below 50 cents, he said.

Malaria, one of the world's deadliest diseases, sickens more than 300 million people and kills more than 600,000 each year, most of them young children. The gold standard for diagnosing malaria is a "blood smear" test, which requires a sample of the patient's blood, a trained laboratory technician, chemical reagents and high-quality microscope. These are often unavailable in low-resource hospitals and clinics in the developing world. The vapour nanobubble technology has the potential to support rapid, high-throughput and highly sensitive diagnosis and screening by nonmedical personnel under field conditions.

The transdermal diagnostic method takes advantage of the optical properties and nanosize of hemozoin, a nanoparticle produced by a malaria parasite inside red blood cell. Hemozoin crystals are not found in normal red blood cells. Hemozoin absorbs the energy from a short laser pulse and creates a transient vapour nanobubble. This short-lived vapour nanobubble emerges around the hemozoin nanoparticle and is detected both acoustically and optically. In the study, the researchers found that acoustic detection of nanobubbles made it possible to detect malaria with extraordinary sensitivity.

"The nanobubbles are generated on demand and only by hemozoin," said Lukianova-Hleb, a research scientist in biochemistry and cell biology at Rice. "For this reason, we found that our tests never returned a false-positive result, one in which malaria was mistakenly detected in a normal uninfected cell." The first trials of the technology in humans are expected to begin in Houston in early 2014.

Click here for more information



Researchers grow liquid crystal 'flowers' that can be used as lenses

A team of material scientists, chemical engineers and physicists has made another advance in their effort to use liquid crystals as a medium for assembling structures.

In their earlier studies, the team from the University of Pennsylvania produced patterns of "defects," useful disruptions in the repeating patterns found in liquid crystals, in nanoscale grids and rings. The new study adds a more complex pattern out of an even simpler template: a three-dimensional array in the shape of a flower.

And because the petals of this "flower" are made of transparent liquid crystal and radiate out in a circle from a central point, the ensemble resembles a compound eye and can thus be used as a lens.

The researchers' ongoing work with liquid crystals is an example of a growing field of nanotechnology known as "directed assembly," in which scientists and engineers aim to manufacture structures on the smallest scales without having to individually manipulate each component. Rather, they set out precisely defined starting conditions and let the physics and chemistry that govern those components do the rest.

The starting conditions in the researchers previous experiments were templates consisting of tiny posts. In one of their studies, they showed that changing the size, shape or spacing of these posts would result in corresponding changes in the patterns of defects on the surface of the liquid crystal resting on top of them. In another experiment, they showed they could make a "hula hoop" of defects around individual posts, which would then act as a second template for a ring of defects at the surface.

In their latest work, the researchers used a much simpler cue. "Before we were growing these liquid crystals on something like a trellis, a template with precisely ordered features," Kamien said. "Here, we're just planting a seed." The seed, in this case, were silica beads — essentially, polished grains of sand. Planted at the top of a pool of liquid crystal flower-like patterns of defects grow around each bead.The key difference between the template in this experiment and ones in the research team's earlier work was the shape of the interface between the template and the liquid crystal.

In their experiment that generated grid patterns of defects, those patterns stemmed from cues generated by the templates' microposts. Domains of elastic energy originated on the flat tops and edges of these posts and travelled up the liquid crystal's layers, culminating in defects. Using a bead instead of a post, as the researchers did in their latest experiment, makes it so that the interface is no longer flat.

"Not only is the interface at an angle, it's an angle that keeps changing," Kamien said. "The way the liquid crystal responds to that is that it makes these petal-like shapes at smaller and smaller sizes, trying to match the angle of the bead until everything is flat."

Surface tension on the bead also makes it so these petals are arranged in a tiered, convex fashion. And because the liquid crystal can interact with light, the entire assembly can function as a lens, focusing light to a point underneath the bead. "It's like an insect's compound eye, or the mirrors on the biggest telescopes," said Kamien. "As we learn more about these systems, we're going to be able to make these kinds of lenses to order and use them to direct light."

This type of directed assembly could be useful in making optical switches and in other applications.

Click here for more information

Novel bio-inspired method developed to grow high-quality graphene for high-end electronic devices

A team of researchers from the National University of Singapore (NUS), led by Professor Loh Kian Ping, has successfully developed an innovative one-step method to grow and transfer high-quality graphene on silicon and other stiff substrates, opening up opportunities for graphene to be used in high-value applications that are currently not technologically feasible.

This breakthrough is the first published technique that accomplishes both the growth and transfer steps of graphene on a silicon wafer. It enables the technological application of graphene in photonics and electronics, for devices such as optoelectronic modulators, transistors, on-chip biosensors and tunneling barriers.

Graphene has attracted a lot of attention in recent years because of its outstanding electronic, optical and mechanical properties, as well as its use as transparent conductive films for touch screen panels of electrodes. However, the production of high quality wafer-scale graphene films is beset by many challenges, among which is the absence of a technique to grow and transfer graphene with minimal defects for use in semiconductor industries.

Said Prof Loh, "Although there are many potential applications for flexible graphene, it must be remembered that to date, most semiconductors operate on "stiff" substrates such as silicon and quartz. The direct growth of graphene film on silicon wafer is useful for enabling multiple optoelectronic applications, but current research efforts remain grounded at the proof-of-concept stage. A transfer method serving this market segment is definitely needed, and has been neglected in the hype for flexible devices."

To address the current technological gap, the NUS team led by Prof Loh drew their cues from how beetles and tree frogs keep their feet attached to fully submerged leaves, and developed a new process called "face-to-face transfer".

Dr Gao Libo, the first author of the paper and a researcher with the Graphene Research Centre at NUS Faculty of Science, grew graphene on a copper catalyst layer coating a silicon substrate. After growth, the copper is etched away while the graphene is held in place by bubbles that form capillary bridges, similar to those seen around the feet of beetles and tree frogs attached to submerged leaves. The capillary bridges help to keep the graphene on the silicon surface and prevent its delamination during the etching of the copper catalyst. The graphene then attaches to the silicon layer.

To facilitate the formation of capillary bridges, a pre-treatment step involving the injection of gases into the wafer was applied by Dr Gao. This helps to modify the properties of the interface and facilitates the formation of capillary bridges during the infiltration of a catalyst-removal liquid. The co-addition of surfactant helps to iron out any folds and creases that may be created during the transfer process.

This novel technique of growing graphene directly on silicon wafers and other stiff substrates will be very useful for the development of rapidly emerging graphene-on-silicon platforms, which have shown a promising range of applications. The "face-to-face transfer" method developed by the NUS team is also amenable to batch-processed semiconductor production lines, such as the fabrication of large-scale integrated circuits on silicon wafers.

To further their research, Prof Loh and his team will optimise the process in order to achieve high throughput production of large diameter graphene on silicon, as well as target specific graphene-enabled applications on silicon. The team is also applying the techniques to other two-dimensional films. Talks are now underway with potential industry partners.

Click here for more information

Antimicrobial functionalization of surfaces using nano-silver technology

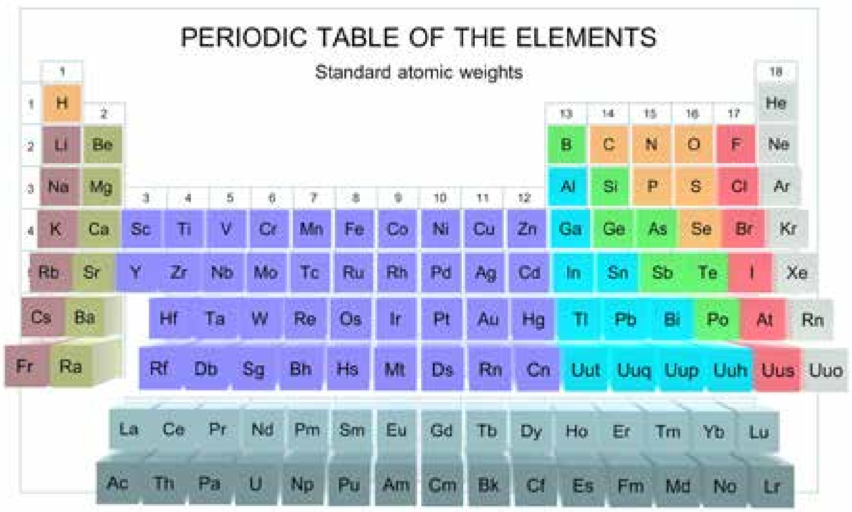
– a safe, effective and cost-effective means of reducing hospital infections.

Helmut Schmid, Fraunhofer-Institute for Chemical Technology (ICT)

Introduction

Nanotechnology is a particle technology where the active ingredients are in a size range from 1 to 100 nm (at least in one dimension) - and where the desired properties are dominated by size and not by chemistry. This technology enables suprising new volume-, surface- and quantum-effects, which can also be used for surface functionalization of polymers.

Within this area, the Fraunhofer-Institute of Chemical Technology (ICT) is specifically working in the production, stabilization, characterization and system integration of inorganic nanoparticles, especially transition metals and transition metal oxides /1/ - /14/.



Transition Metals: The International Union of Pure and Applied Chemistry (IUPAC) defines a transition metal as “an element whose atom has an incomplete d sub-shell, or which can give rise to cations with an incomplete d sub-shell”. Most scientists describe a “transition metal” as any element in the d-block of the periodic table (all are metals), which includes groups 3 to 12 on the periodic table.

Transition metal oxides comprise a class of materials that contain transition elements and oxygen. They include insulators as well as (poor) metals. Often the same material may display both types of transport properties, hence a Metal-Insulator transition, obtained by varying either temperature or pressure. A number of transition metal oxides are also superconductors.

Source: wikipedia

By means of nano-silver technology, surfaces can be equipped with antimicrobial, electrically conductive and heat reflective properties. For commercialization purposes, the focus is definitely on antimicrobial applications.

Firstly, the issue of nano safety needs to be examined. As the nanoparticles are embedded in a polymer by dipole interactions, so an uncontrolled release of single species is prohibited. This has been analytically checked by trace analysis. Secondly, the possible risk of building up resistance to the nano-silver must be investigated. As the nano-silver is acting by using several mechanisms simultaneously, the risk of resistance formation does not increased.

The general advantage of this new technology is in providing effective and sustainable surface catalysis, replacing tons of toxic standard biocides.

Tasks and Objectives

The task is to make nano-silver particles available and usable for antimicrobial additive functionalization of polymer surfaces. At the current level, the aim is to develop products to improve hygiene in consumer applications, in hospitals and in the food industry.

Methodology

From nano-particle synthesis to nano products, the same procedures always have to be performed.

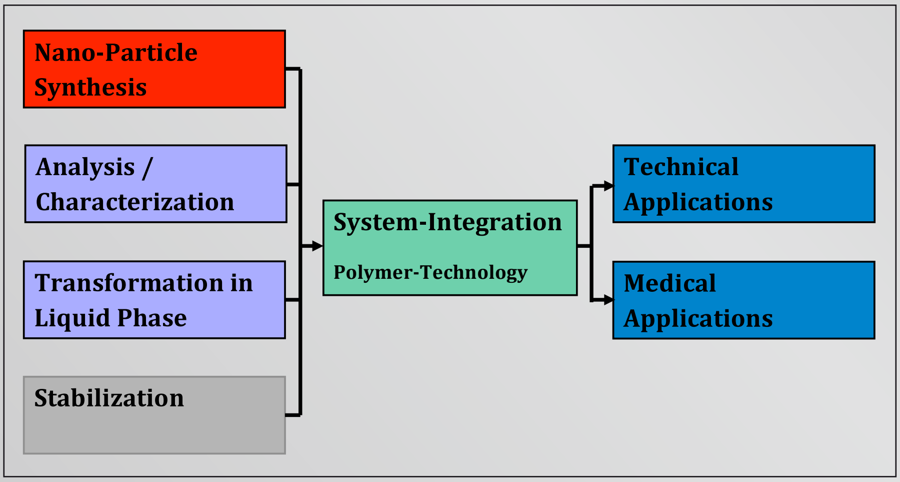


Figure 1: Overview of the main steps to get nano products out of nano-particles.

The first step is nano-particle synthesis which can be done top-down or bottom-up. Derived from experiments, nano-particles in the order of magnitude of around 10 nm exhibit the best effectiveness in nanomedicine applications. The **synthetic methods** should be optimized in this respect.

For thermodynamic reasons, nano-particles tend to re-agglomerate, which weakens the intended effects. To prevent this, **nano-stabilization** by chemical additives is required, imprinting resulting surface charges. The selection of suitable additives is carried out with potential calculations based on Poisson-Boltzmann differential equation (1).

Of importance is constant B, which correlates with the Hamaker constant of Van-der-Waals interactions. Only such additives are suitable, capable of minimizing these interactions.

$$\nabla^2 U(\eta,\theta) = \frac{(\cosh\eta-\cos\theta)^2}{B^2}\frac{\partial^2 U}{\partial\eta^2} + \frac{(\cosh\eta-\cos\theta)^2}{B^2}\frac{\partial^2 U}{\partial\theta^2} - \frac{\sinh\eta(\cos\eta-\cos\theta)}{B^2}\frac{\partial U}{\partial\eta} + \left(\frac{(\cosh\eta-\cos\theta)^2}{\tan\theta} - (\cosh\eta-\cos\theta)\sin\theta\right)\frac{1}{B^2}\frac{\partial U}{\partial\theta} = \sinh(U(\eta,\theta)) \qquad (1)$$

U: Reduced Electrostatic Potential, B: Constant in Bispheric System of Coordinates

The next step is to **characterize** the particles with selected **nano analytical methods** e.g. scanning electron microscopy, x-ray fluorescence, x-ray diffraction, photon correlation spectroscopy and atomic emission spectroscopy. The application of the last method is essential to ensure nano safety.

To provide an **interface to various applications** and to **enable system-integration** (Figure 1), the **combination of nanotechnology with polymer technology** is needed, with particular emphasis on **biocompatible polymers.** In this way **stable nano-suspensions** are available and ready for use.

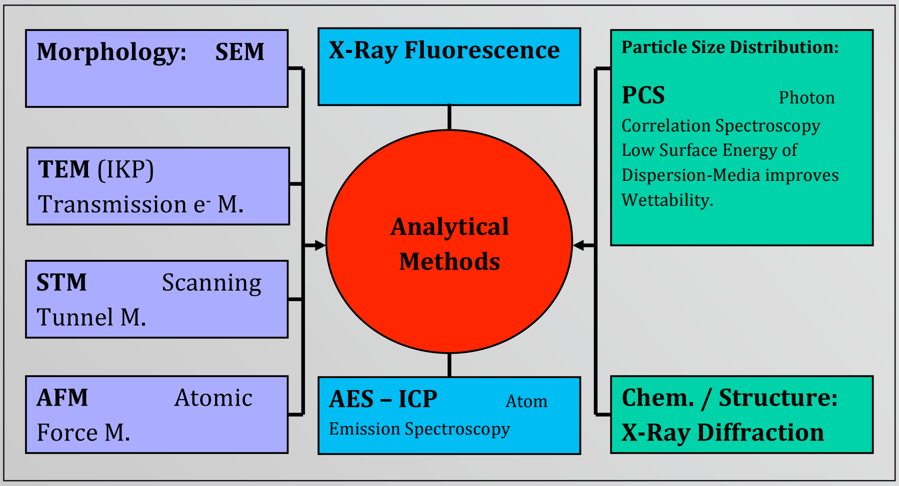


Figure 2: Overview of the nano analytical methods used for characterization.

Results and Discussion

As previously mentioned, for nano-particle synthesis, both top-down and bottom-up methods can be used, leading to intermediates that have a mean particle size of approx. 50 nm. This is demonstrated by the example of nano-silver, where Scanning Electron Microscopy images show very clearly particle-size, distribution, morphology and topography. Enabling antimicrobial interaction particles with an average size of about 10 nm for best effect, means that in this case, post-processing is required.

The optimization of processing parameters leads to a single-step synthesis. These methods of chemical nano-particle production are particularly suitable for the synthesis of inorganic nano-particles, enabling high production rates and economic, cost-effective process control. Even more specifically, we prefer to synthesise directly in liquid, because the handling of powders is avoided, which offers a tremendous safety advantage. Furthermore, the production of a nano suspension, which serves as an interface to polymer combination and system integration, is facilitated.

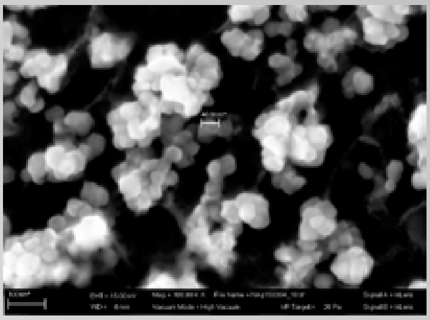


Figure 3: SEM-record of nano-Ag-particles. A stable suspension was applied to an Al-plate and investigated after drying. Particle size is approx. 50 nm.

For further production it is crucial to determine the particle size distribution in suspension. This is done using photon correlation spectroscopy (PCS), based on the measurement of Brownian movement of particles. The resulting diagram (Figure 4) shows the maximum distribution function at a particle diameter of 12,1 [nm]. This value will be more credible if it is possible to achieve the same or a similar result with a completely independent method. In this case X-ray diffraction is used,

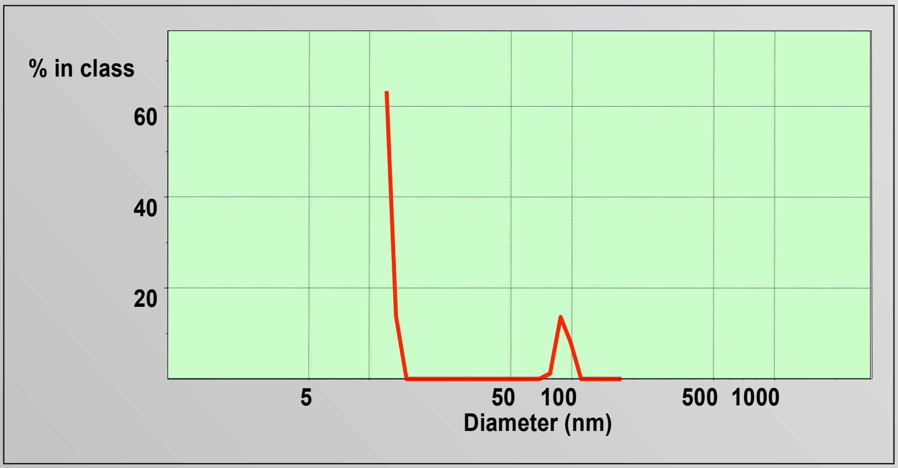


Figure 4: Particle size distribution results of PCS-Analysis of Nano-Ag, 1 vol.-% suspension in H2O (CAg00103).

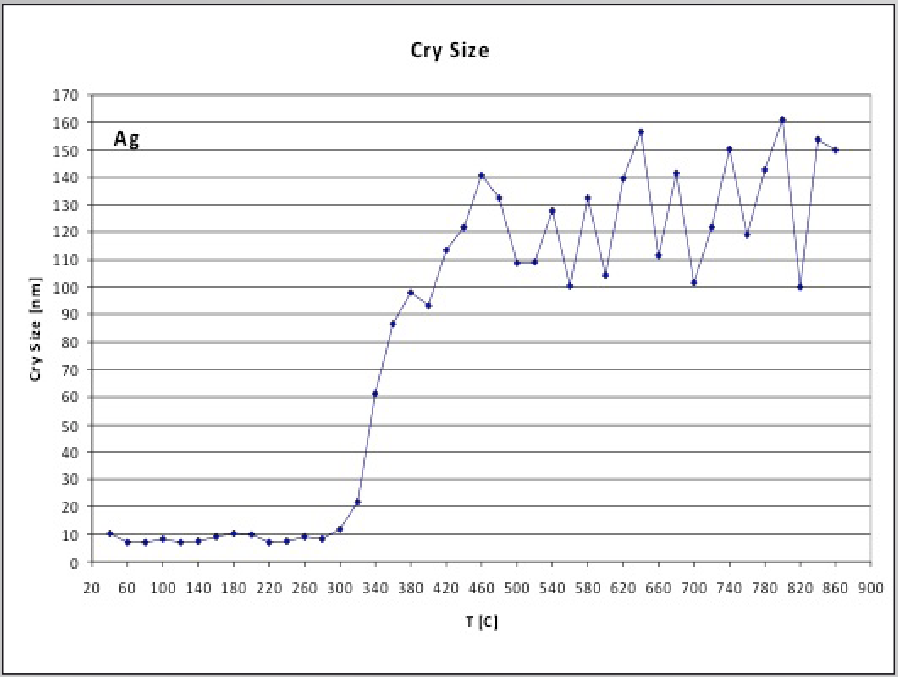


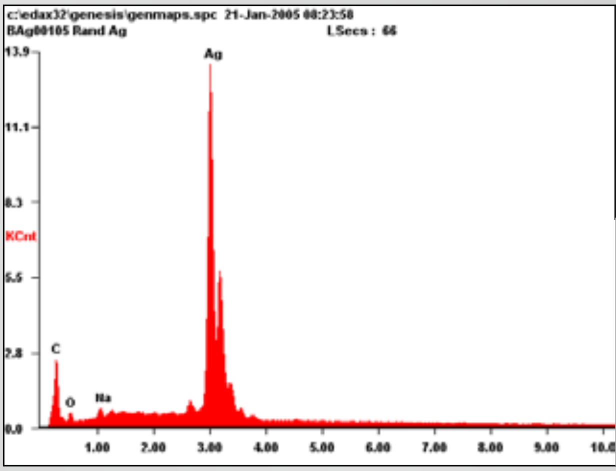
Figure 5: Temperature-resolved X-ray diffraction to determine average particle size of Nano-Ag sample.

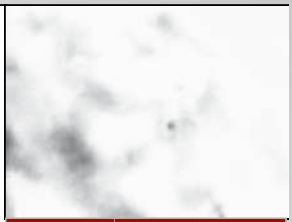
which is also very suitable, to estimate the primary particle sizes of starting materials.

Very close to application, the quality of surface coating must be checked especially in relation to the homogeneous distribution of active ingredients. In this case, the combination of methods may increase the power of tools substantially. SEM and EDX combinations allow an estimation of morphology as well as a quantitative chemical analysis (Figure 6, overleaf).

Next it is necessary to describe the principle working mechanism in our coating system. In opposition to known principles of standard biocides, we focus not on drug release of nano-silver but on surface catalysis. In brief - the partial charge of nano-Ag out of the lattice interacts with the structure proteins of cell walls and kills the microorganism. This dominating reaction mechanism is accompanied by various other working principles, so that the risk of forming resistance is not increased.

After sample preparation efficiency of antimicrobial effect on surface must be proofed.





Element	Wt%	At%
C K	41.08	78.57
O K	06.71	09.64
NaK	00.86	00.85
AgL	51.35	10.94

Figure 6: Quantitative Ag analysis in sample BAg00105 with X-ray fluorescence.

Figure 7: Result of incubated diluted crop-out of the samples. No fungal attack on treated samples BAg00601.

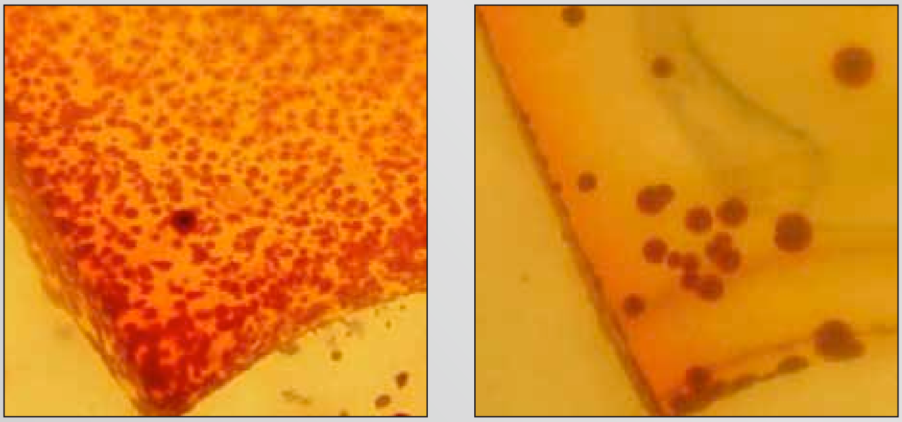


Figure 8: Nano-Ag in addition is very efficient against bacteria. Example of a nano-Ag-coated silicon polymer (on the right) compared to an untreated sample (on the left) with colonies of **Staphylococcus Aureus.** A reduction rate of factor 100 was detected based on the applied nanoAg content (Test-setup: Spray-test). **Depending on nanoAg content, reduction rates of 99.999 % (5 log-levels) are possible.**

These nano-silver systems are suitable for producing antimicrobial surfaces that have numerous medical applications, e.g. in hospitals, for medical devices, implants, etc.. Currently the commercially most successful products are dispersion paints for hygiene improvement in hospitals, killing even dangerous germs like MRSA.

Figure 9: Al Wasl Hospital, Dubai, U.A.E., where the nano-silver coating system is applied.

Outlook

- New technical nano-products will be soon be available to buy (Nano-silver wallpaper "Microna" has already been successfully produced by Dresden Papier GmbH).
- Nanomedicine is identified as an outstanding field of further applications.
- Recognizing the overall benefit, investment in this technology makes sense. Fraunhofer-ICT therefore is looking for international partnerships.

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Note: *References for this paper are available on request to Nano Magazine*

Summary and Conclusion

For some technical and medical applications, the additional functionalizations of surfaces in order to achieve antimicrobial effects are useful and desirable /1/ - /14/. State-of-the-art standard biocides like thiazolinones are used as active ingredients, but have disadvantages of toxicity and lack of sustainability of effect.

A new approach, avoiding these disadvantages, is the use of nano-silver as an active substance. With this technology, cost-effective solutions are possible, because the required concentrations can be kept small. Even the concept of action is fundamentally different: there is no drug-release, but only provision of the active substance on the surface in the extended sense of a catalyst. In technical applications, mould formation can be prevented. In medical applications, dangerous bacteria and even multi-resistant germs like MRSA are killed. This leads to a general improvement in hygiene. The risk of resistance formation is the smaller, the more numerous the response mechanisms are. Product safety throughout the life cycle is guaranteed by a combination of nanotechnology and polymer technology. The nano-particles are chemisorbed in the polymer via dipole-interactions.

Just how is your money spent?

The best EU-funded research project is selected from 11 finalists at EuroNanoForum 2013.

EuroNanoForum is a biennial conference and exhibition usually located in the country which holds the Presidency of Council the EU at that time (a rolling position). EuroNanoForum is aimed at showcasing EU-funded research projects and enabling networking amongst grant holders and others – especially industry, and the dissemination of results. The venue was Dublin.

Over 50 projects were submitted covering areas as diverse as industrial technologies, life sciences, environment, energy and transport. At the Awards Gala, the spotlight was on 11 finalists who presented their achievements on stage.

A ballot was then held at the Gala Dinner, and the result was that the **Sonodrugs project on Image-Controlled Ultrasound Induced Drug Delivery** was chosen as the winner. What do you think? Click the links on the right to find out more.

The 11 finalists, including Sonodrugs, are listed below, with links for further information:

BIOELECTRICSURFACE; Electrically Modified Biomaterials' surfaces: From Atoms to Applications. *Watch the BioElectricSurface pitch for best project.*

EUMET; Design, Development, Utilization and Commercialisation Of Olefin Metathesis Catalysts. *Watch the EUMET pitch for best project.*

FEMTOPRINT; Develop a printer for microsystems with nano-scale features fabricated out of glass. *Watch the Femtoprint pitch for best project.*

FLEXONICS; Ultra-high barrier films for r2r encapsulation of flexible electronics.

IP NANOKER; Structural ceramic nanocomposites for top-end functional applications.

LIGHT-ROLLS; The development of a roll-to-roll production platform for the manufacturing of micro-structured flexible LED displays – "Light where you want it" The future of retail lighting. *Watch the LIGHT-ROLLS pitch for best project.*

MUST; Multi-Level Protection of Materials for Vehicles by Smart Nanocontainers. *Watch the MUST pitch for best project.*

NANOINTERACT; The aim of NanoInteract was to ensure that nanotechnologies do not cause inadvertent harm to human or environmental health at any stage of their lifecycle. *Watch the NanoInteract pitch for best project.*

NANOTHER; Integration of novel NANOparticle based technology for THERapeutics and diagnosis of different types of cancer.

SONODRUGS; Image-Controlled Ultrasound Induced Drug Delivery. *Watch the Sonodrugs pitch for best project.*

STONECORE; The use of nanotechnology materials for the refurbishment of buildings as well as the conservation of natural and artificial stone, plaster and mortar. *Watch the STONECORE pitch for best project.*

In this issue of Nano Magazine you can read about the winning Sonodrugs project, plus the background to two more, LIGHT-ROLLS, and NanoInteract.

The Winner: Sonodrugs Project

– towards improving healthcare for an ageing population

Introduction

The demographics in Europe which are moving towards an aging society, also coincides with increasing morbidity of the population. Cancer and cardiovascular diseases are the most common causes of death, and cancer is expected to be the main cause in the foreseeable future. As such, citizens will increasingly need access to state-of-the-art medical care especially in oncology and cardiology. This requires both improvements in the medical care itself, as well as measures to keep expenditures on healthcare affordable and thereby accessible to all.

The Project

Several aspects of the concepts investigated within the **Sonodrugs** project were aimed at realizing these unmet needs. These include:

- Local delivery of drugs to where they are needed - to improve treatment efficacy, and reduce toxicity in the rest of the body.
- Image guidance of treatment - to allow for personalized therapy, leading to improved individual outcomes.
- Non-invasive treatments - to avoid taxing surgical procedures and/or general anaesthesia, which are known to be a large burden and hazard especially to ageing patients.

Background

The **Sonodrugs** FP7 project ran from November 2008 to October 2012. Led by Philips Research in Eindhoven, the consortium comprised 14 partners from seven EU countries. **Sonodrugs** focused on investigating new concepts aimed at personalizing and targeting drug treatment, focussing on oncology and to a lesser extent on cardiovascular disease.

Currently, most drugs are administered systemically, and while a portion of the dose reaches the site of action and brings about the therapeutic effect, most of the administered drug is taken up by other tissues or excreted, and as such only contributes to side-effects. Especially in oncology therapy, doctors work a fine balance between therapeutic efficacy and severe side-effects. Other treatment options, such as surgery, are often highly invasive and may also lead to unwanted effects.

Research Activities

In the **Sonodrugs** project, researchers explored possible future treatment options in which drugs are encapsulated within tiny particles (nanocarriers). These particles circulate throughout the body, and can be activated very precisely at the diseased site by an ultrasound pulse applied from outside the body. In this way, a high concentration of the drug may be achieved at the diseased site, with lower concentrations elsewhere, thus reducing adverse effects on healthy tissue. Moreover, the complete treatment can be planned and monitored non-invasively by imaging, i.e. ultrasound and/or MRI, and also the triggering of the therapy by ultrasound is non-invasive, together leading to a concept of minimally invasive, image-guided ultrasound-triggered drug delivery. This may decrease the burden to the patient, promote faster recovery, and reduce hospitalization rate and duration.

Sonodrugs investigated 4 different concepts for ultrasound mediated drug delivery:

- **Microbubbles for co-administration.** Microbubbles are tiny (only a few micrometres) gas bubbles, stabilized by an outer shell, which are responsive to ultrasound. They are therefore used in the clinic as contrast agents in diagnostic applications, but at higher ultrasound intensities they can be forced to implode. For drug delivery, microbubbles are injected together with a drug. Upon local ultrasound activation inside the blood vessels of the targeted organ, the blood vessels become transiently more porous. This is named sonoporation, and the drug in circulation in the bloodstream will then enter tissues at the treated site at a much higher concentration.
- **Drug-loaded microbubbles.** Liposomes, usually 100 to 200 nanometres, can be loaded with drugs and attached to microbubbles. These nanocarriers are injected, and upon ultrasound activation, sonoporation with concurrent local release of the drug occurs. Drugs reach the target tissue at higher concentrations, and exposure of the rest of the body to potentially toxic drugs is limited.
- **Hyperthermia-induced drug delivery.** Ultrasound at even higher intensities can be used to cause localized, controlled hyperthermia, a mild heating of the target tissue to about 42°C. For this, high intensity focussed ultrasound (HIFU) is used. HIFU is combined with novel temperature-sensitive liposomes, engineered to release the loaded drug upon mild heating. The liposomes are injected, circulate in the body, and when they reach the heated target tissue, release the drug. The effect is that drugs reach the target tissue at higher concentrations, and exposure of the rest of the body to the drug is limited. The liposomes can be loaded with drugs and MR contrast agents such as gadolinium or iron oxides for image guidance of drug release.
- **Combined or 2-step approach.** Co-administration and hyperthermia can be combined for a synergistically improved local delivery. First, microbubbles are activated by ultrasound to cause sonoporation at the target site. Then temperature-sensitive liposomes are injected and the target tissue is heated to induce local release of the drug from the liposomes. This results in a high increase of exposure of the target organs to the drug.

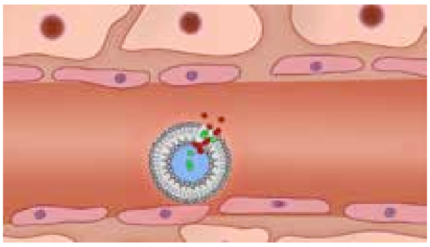


Fig 1: Local release of drug from a nanoparticle after ultrasound activation.

Such developments are technologically challenging, and require a multidisciplinary approach. The EU **Sonodrugs** project brought together multiple partners with specific expertises, and partially covered the costs for the first steps towards proof-of-concept, and was thus an ideal tool to bring such a novel concept forward. The success of **Sonodrugs** resulted from synergistic advances in nanomedicine drug delivery vehicles; imaging systems hardware and software; and protocols for planning, executing and monitoring treatment.

Sonodrugs brought together expertise in:

- Materials research (Philips Research Eindhoven, Eindhoven University of Technology, Ghent University, Nanobiotix, Aalto University)
- Material production (Nanobiotix, Lipoid)
- Clinical knowledge in oncology (University of Tours, University of Cyprus) and cardiology (University of Muenster)
- In vitro and preclinical validation (University of Tours, Erasmus Medical Center, University of Cyprus, University of Muenster, University of Bordeaux/University Medical Centre Utrecht, Philips Research Eindhoven, Eindhoven University of Technology)
- Imaging techniques (University of Cyprus, Philips Healthcare, Philips Research Hamburg, University Bordeaux/University Medical Centre Utrecht, Philips Research Eindhoven)
- Pharmacokinetics, toxicology and biodistribution (University of London, Eindhoven University of Technology).

Conclusions

Significant advancements were made towards improved and expanded medical treatment options in oncology and cardiology by providing image control for externally triggered drug release.

The following results were achieved by the **Sonodrugs** project:

- Preclinical proof-of-concept of local delivery for three concepts of ultrasound-mediated drug delivery: co-administration, MR-HIFU hyperthermia with temperature-sensitive liposomes; and the combined approach.
- Increased therapeutic effect was shown in preclinical studies for two of these concepts, addressing oncology and cardiovascular diseases using the hyperthermia approach and the co-administration approach, respectively.
- A fundamental understanding was obtained of the drug release process, mechanism of action of ultrasound activation, and the relationship between material properties, release kinetics and the effect of ultrasound. These insights have been leveraged within **Sonodrugs** and will also be used in follow-up projects.

Extrapolating the results, the platform can potentially be used for many different drugs and disease areas, and increases the options for a combination of pharmaceutical and imaging research.

Dissemination

The project members shared the generated knowledge with the scientific and clinical world via publications and presentations. Moreover, within **Sonodrugs**, three courses have been (co-) organized during which **Sonodrugs** researchers were educated, and also external scientists. Finally, the concept of ultrasound-mediated drug delivery and the project results were presented at a dedicated **Sonodrugs** session of the ESCDD conference (European Symposium on Controlled Drug Delivery, Egmond aan Zee, April 2012).

Outcomes

- 8 patents resulted from the project, on nanocarriers, treatment protocols, and methods for therapy monitoring.
- Results were disseminated as 44 manuscripts in high-impact peer-reviewed journals and 100+ conference presentations so far.
- During the project, four press releases were circulated, which culminated in interviews on TV, radio and in newspapers, as well as coverage on the web. **Sonodrugs** partners also participated in community outreach programs.
- Many promising European young researchers have been educated. The project has contributed to 5 PhD theses so far, with at least 5 more expected. **Sonodrugs** researchers have found new positions in medical device companies, universities and hospitals.

Although the consortium has made significant progress, the final goal of improved therapy options cannot be reached in the lifetime of a single project. Fortunately, collaborations between the partners have continued after the project end. Several fruitful collaborations have been initiated or strengthened in the past four years, and these will remain active. Illustrative of this are the collaborations between some of the partners in follow-up projects that are currently running, as well as several new applications for EU funding. Some of these include or work towards clinical trials, which are the pivotal steps towards clinical adoption.

The consortium believes that nanomedicine, the application of nanomaterials and nanotechnology to healthcare, may potentially lead to cost-effective treatments with fewer side effects, less burden on the patient and faster recovery time. The EU project **Sonodrugs** allowed enabled significant steps to be taken towards achieving this goal.

Click here for more information

Light-Rolls:

A Novel Manufacturing Technique For Flexible Lighting And Display Systems.
- A European success story

Introduction

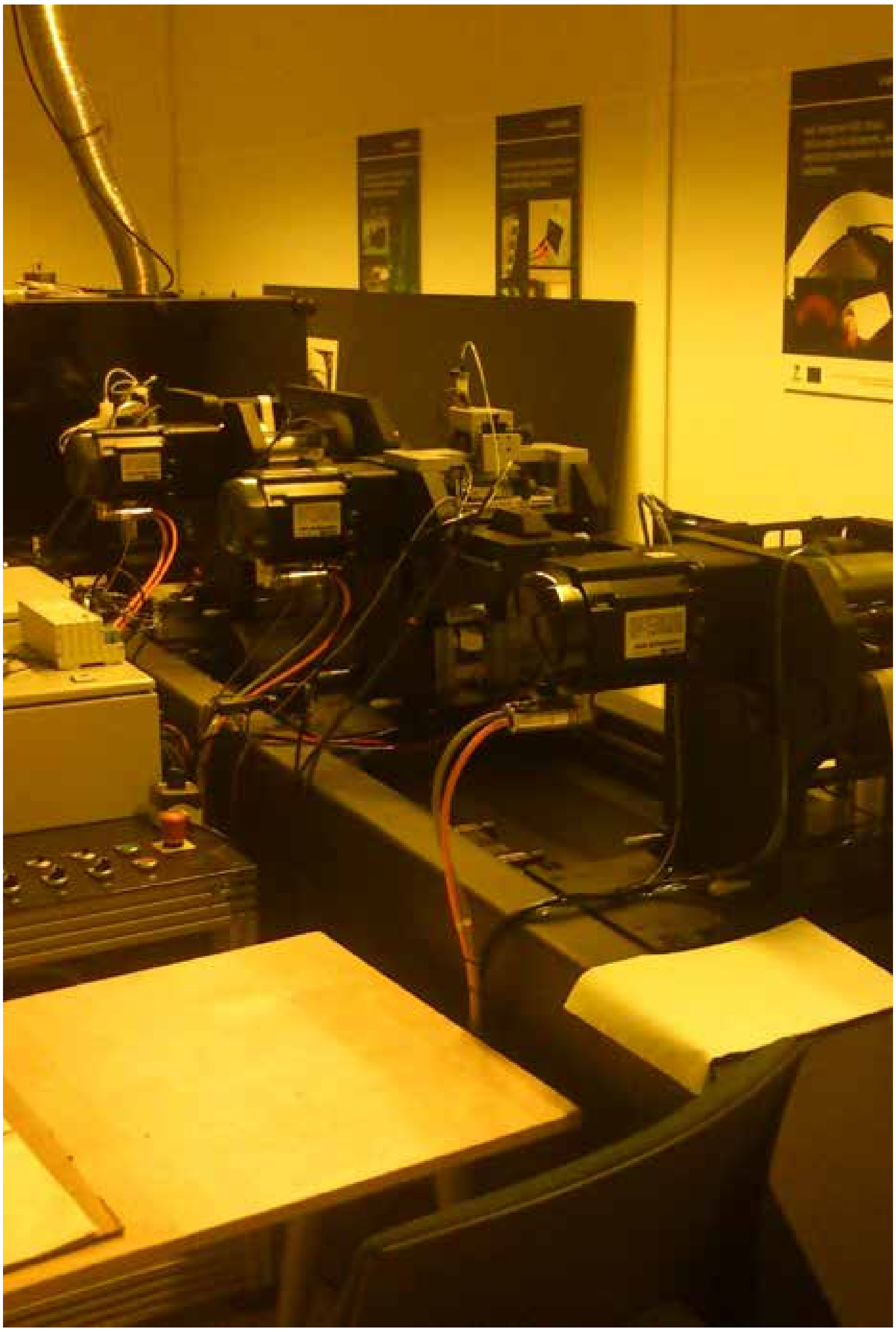
Micro-products have become increasingly important in the medical, biotechnology, consumer and automotive sectors. However, products in these sectors, such as innovative display solutions and light emitting panels, require the integration of different functionalities and demand new mass manufacturing methods and technologies.

The Light-Rolls (http://www.light-rolls.eu) project resulted in a novel manufacturing technology pilot line, integrating highly innovative production modules, based on a roll-to-roll manufacturing concept (the process of creating electronic devices on a roll of flexible plastic or metal foil), for the seamless, high throughput manufacture of micro-structured, polymer based components and microsystems.

The Light-Rolls project focused on the development of modular based production line units for the high throughput manufacture of micro-structured systems, in particular LED-based lighting and display systems, for applications in the automotive, consumer and life sciences industries. The scientific objective of the project was aimed at realizing structures in the micron range and also integrating dies to be assembled at high-speed and in parallel. The approach was based on a modular roll-to-roll philosophy, in such a way that the manufacturing modules are exchangeable, making it easy and cost-efficient to adjust the sequence of process steps for the production of different products.

The main market addressed was lighting applications. Thin "light sheets" are very attractive in automotive applications or in building lighting because they require little space, are potentially more reliable, cheaper, include several functionalities and offer a high degree of freedom to fulfil designers´ needs. Potential applications in other markets include diagnostics, applications based on functional printing, such as flexible active RFID tags, flexible solar cells and batteries or in simple consumer products.

The manufacturing pilot line is already available for exploitation. This exploitation includes the use of the innovative pilot line for the development of high added-value products, as well as designing, constructing and selling ad-hoc roll-to-roll machines, or in consultancy on the technology. An exploitation agreement with the intellectual property owners was reached after the research project was completed. A business plan is being implemented as from March 2013. Initial investment for the commercialization was identified. First customers have now been achieved.



Moreover, the project has been selected by the European Commission as a Success Story. The manufacturing platform was co-funded by the European Commission (FP7) under grant agreement n° CP-TP 228686. The total budget used for the development and construction of the platform was 5.1 M€.

Light-Rolls Partners: Prodintec Spain, microTEC Gesellschaft für Mikrotechnologie mbH Germany, Norbert Schläfli Maschinen Zofingen Switzerland, Centro Ricerche FIAT S.C.p.A. Italy, Design LED Products Ltd United Kingdom, ACP-IT GmbH Austria, Fraunhofer IPA Germany, Xaar Jet AB Sweden, microelectronica S.A. Romania.

The Social / Economic Relevance And Impact

The impact of the project is potentially very large, and related to domains as diverse as technology, consumer and health markets and societal issues. More generally, it is believed that Light-Rolls will enable Europe to be a step ahead of leading competitors in the field of micro-manufacturing and its applications.

With regard to its impact on lighting systems and displays, the Light-Rolls solutions in the field of lighting are manifold, including display backlighting, brand animation, point of sale & interactive switching etc. Typical markets are electronics, auto-motive, medical, consumer & industrial.

It is also a new medium for creative product designers. The European Technology Platform "Photonics21" calculated a 6.5 billion euros market for lighting applications in 2011 in Europe. The annual worldwide market for lighting-based products will have exceeded 100 billion €, while the European market will be greater than 20 billion € by then. It is predicted that LEDs will be the light source for all automotive lightings by 2016, although there are major challenges including reducing manufacturing costs. The LED market is expanding into new and profitable sectors, for example, automotive lighting, architectural lighting and general illumination, in addition to the LCD backlighting market.

According to Yole Developpment, "To capture the profits in these application sectors new approaches in manufacturing technologies are required at all levels: materials, design, front-end, back-end and packaging". This is exactly where Light-Rolls offers commercial solutions as it is a manufacturing process which allows solid state LED chips to be packaged in a more versatile way for a specific range of applications.

Another attractive impact on lighting would be in "light emitting wallpaper". Because of the low power consumption and low production costs of LEDs, Light-Rolls technology has the potential to access the indoor lighting market.

Regarding the impact of Light-Rolls on polymer based microsystems. These play an important role for high volume – low cost product applications. Markets include life-sciences (medical and biotech), consumer goods, environment, security, etc. Light-Rolls for micro-fluidics would provide an important key to access these attractive markets.

In the high tech packaging and in the lab-on-chip industry, an innovative product will allow tapping into potentially a very large market. Global Industry Analyst (www.strategyR.com) were quoted as saying the worth of the annual biochip market (where a Light-Rolls based fluidic chip could enter) is around 3 billion of US$ in 2010.

A new product in the (bio)sensor industry will allow access to another very important market. Frost & Sullivan estimated the total annual biosensor market revenues to be about 4.4 billions of US$ in 2011. A penetration of 15% in this market will imply annual revenues for the companies involved in such a business above 600 million US$ by 2011.

Today the growing market for micro-systems based products is still dominated by few so-called killer applications, which millions of pieces per year are produced (pressure and acceleration sensors, print heads are examples). But many microsystems-based solutions exist as prototypes, waiting to be commercialized. Light-Rolls´s impact is that the platform reduces the time-to-market for polymer based microsystems. Light-Rolls thus provides a clear strategic contribution to the goal of Europe to stay competitive in the fields of manufacturing. This will be possible, since the roll-to-roll platform provides a flexible tool for integrating different components in one product. Light-Rolls based packaging and assembly opens an opportunity to bring assembly back to Europe.

Innovative originality

The main innovation of the Light-Rolls project is enabling the manufacture of electronic micro-components on flexible substrates. To achieve this, Light-Rolls had to tackle the following challenges:

- Development on RMPD®, self-assembly and ink-jet printing/sintering technologies to translate them into functional manufacturing solutions.
- Development of advanced control systems.
- Integration of process modules into a seamless equipment platform for a high throughput manufacturing of lighting and displays products.

The design and development of the three main units integrated in the Light-Rolls production line (RMPD) viz the Rotation module, Self Assembly and Printing/Sintering, involved the exploration of innovative micro-fabrication technologies and their technical implementation.

The state of the art regarding the self-assembly module is to take the dies from the wafer by the sequential pick-and-place process. The Light-Rolls approach brings the dies into a feeder unit and places many dies in parallel onto the seamless polymer interim substrate for precise and fast assembling, resulting in the integration of chip self-assembly methods into roll-to-roll production, which has not been implemented before. Light-Rolls partners focused on solutions for:

- Dispensing small volume of fluid on specific nano-functionalized areas for the self-assembly process.
- Developing solutions for feeding and transporting the chips.
- Developing solutions for sorting the chips to detect their orientation and to discern whether they are in right position or not.

These results involved a major leap forward in the state of the art, breaking down the barriers to the implementation of the technology at industrial level. The project also chose ink-jet technology to produce the electrical interconnection between individual electrical devices because it is easily integrated into a roll-to-roll environment. It is fast, flexible, and easy to configure for various applications. High tolerances when combined with production control systems and reduced waste are additional advantages considered to the selection of ink-jet as printing technique for conductive track generation. An innovative method for non-invasive sintering of the nano-inks was also investigated and implemented.

Practical applications

The most important applications are found in the following areas:

Lighting: Lighting is the main market

Figure 1.

focus. Thin "light sheets" are very attractive since they require little space, are potentially more reliable and cheaper, include several functionalities, and offer a high degree of freedom to fulfil designers´ needs with respect to e.g., fashion trends. The move from using packaged LEDs and low precision screen printing methods for assembly and interconnection towards high-volume, low-cost application would push the commercialization of Light-Rolls lines to new horizons. One particular application which derives large cost/performance benefit from LED "light where you want it" is retail lighting.

Automotive: In the automotive industry, Light-Rolls exploited LED processes know-how not only for new interior lighting and accessories, but also for other applications, e.g. LEDs for interior lighting and accessories. Lighting systems are taking retail shelf space away from traditional components (i.e. neon, inorganic emissive sheets) at an accelerating pace. The fastest growing segments are LEDs that replace the small filament bulbs found in tail lights and interior dome lights like courtesy lights. However, there are more applications with respect to lighting or even other applications, where Light-Rolls solutions – if seen as a technology platform - may play an important role (see Figure 1)

Life Sciences: For disposables at high volume production quantities, it is expected that Light-Rolls production modules can be chained, and result in competing "costs per component". For low volume production, a sufficient number of modules must be available to be able to switch between different product designs. Since the RMPD®-Rotation technologies allow the manufacture of polymer microstructures and are able to use foils as a substrate, integrate electrodes etc., this field of application is a potential candidate for future product development. Several emerging applications particularly enabled by the use of thin foils are, for example, temperature controlled biological reactions, such as the polymerase chain reaction (PCR), taking advantage of fast heat transfer through thin materials. Applications such as centrifugal microfluidics in which a microfluidic chip is accelerated, can profit from low mass and thus low moment of inertia of foil cartridges.Foil-based Lab-on-a-Chip systems are perfectly suited to be disposable consumables because they only require a minimum of material volume

Functional printing: Thin, light-weight, flexible and environmentally friendly processes and products – these are some of the key advantages organic and printed electronics can offer. They also enable the production of a wide range of electrical components that can be directly integrated in low cost Roll-to-Roll processes. Intelligent packaging, low cost RFID (radio-frequency identification) transponders, rollable displays, flexible solar cells, disposable diagnostic devices or games, and printed batteries are just a few examples of promising fields of application for organic and printed electronics based on new large scale processable electrically conductive and semiconducting materials. There are many other ideas like printed humidity sensors printed on paper to be placed in, e.g., cement bags indicating a wet – dry status, applications in smart packaging to support marketing to promote certain products. The market for functional printing is still in its infancy, with flexible active RFID tags, flexible solar cells and batteries or simple consumer products and games only a few examples according to the OE-A roadmap.

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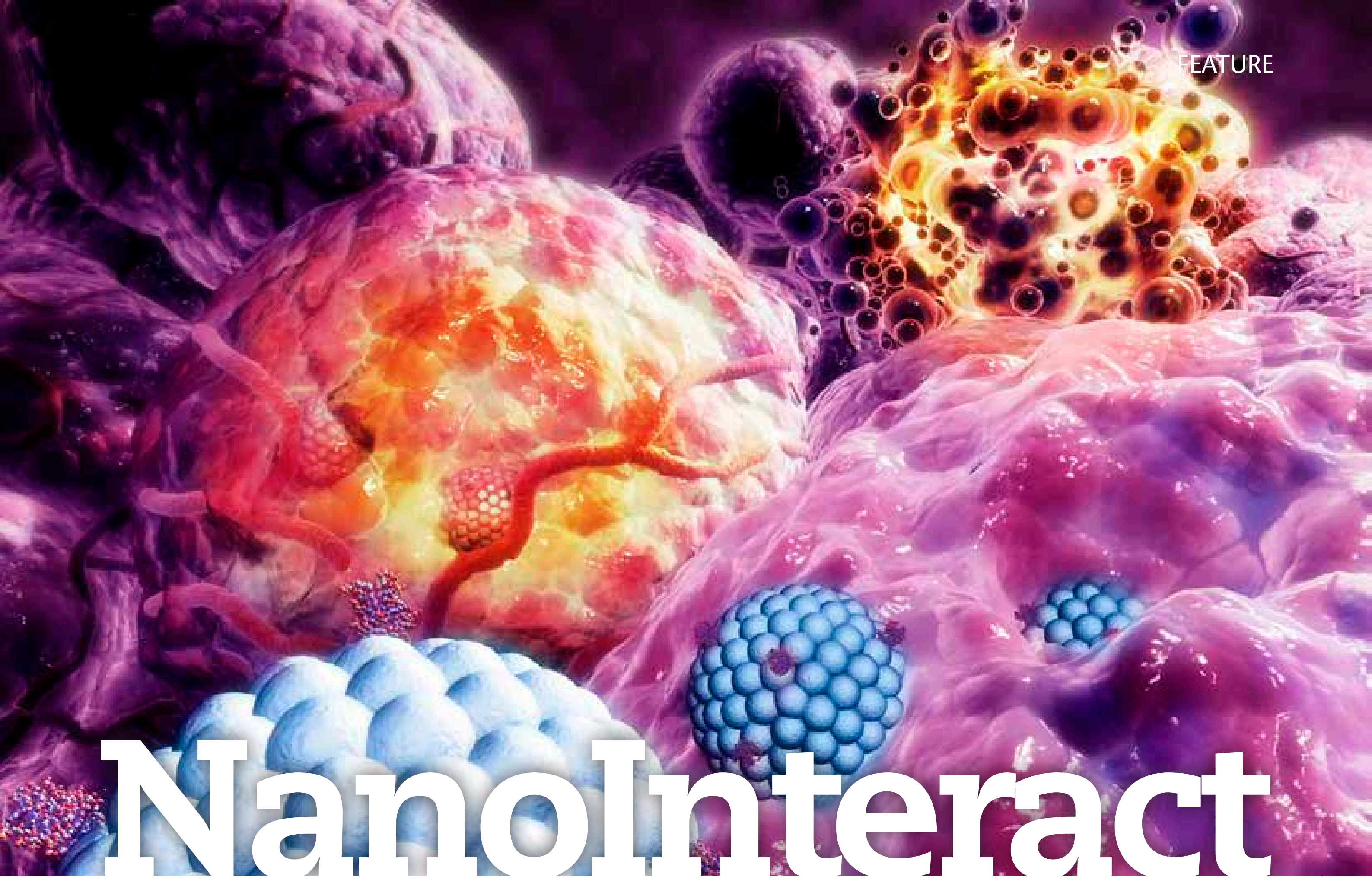


NanoInteract

- A first step in establishing how nanoparticles behave in a biological environment

When NanoInteract was first proposed (early 2006) the field of nanointeractions and nanosafety was in its infancy, and the principle goal of NanoInteract was to help frame the field, and to ensure that it emerged as a quantitative science based on the principles of physical and biophysical chemistry.

The depth and breadth of the scientific issues being addressed within NanoInteract was unique, and the foundation of the field on a rational and quantitative basis was of such importance for all stakeholders, from governments to NGOs to industry and beyond, that the consortium decided to use round robin approaches for some of the early studies, to ensure that all laboratories were performing to a similar standard, and to show the applicability of the approaches for quantitative reproducibility of biological assays using nanoparticles. Thus, the first interlaboratory study using an assay for genotoxicity applied to nanoparticles was performed within NanoInteract: the Comet assay was applied to a range of SiO2 nanoparticles and quantitative reproducibility was achieved (Barnes CA et al., Nano Lett. 2008, 8:3069). A similar approach was taken for the first studies on nanoparticle-induced protein fibrillation, whereby three laboratories reproduced data showing that nanoparticle can modulate the rate of protein fibrillation in solution (Linse S et al., Proc Natl Acad Sci U S A. 2007, 104:8691).

A key aspect in the success of the NanoInteract project was the development of secure processes for controlling the systems used across all partners. Due to the considerable variability in terms of experience and facilities across the partner institutions in terms of dispersing and characterising nanomaterials, all particles were held centrally by the coordinator, and cleaned and dispersed for periodic shipment to the partners in the appropriate solutions (concentration, pH, etc.). Shipments were timed such that dispersions would not be left sitting for long periods of time, as no dispersants were used. Much of this experience and infrastructure was subsequently integrated into the International Alliance for NanoEHS Harmonisation (www.nanoehsalliance.org), and later into the QNano (now QualityNano) research infrastructure (www.qualitynano-ri.eu).

The main exploitable scientific results from NanoInteract include:

- The nanoparticle protein (biomolecule) corona as a basis for characterising what cells (organisms / animals) actually "see" and interact with. It is now well accepted that in typical biological environments, nanoparticle surfaces are covered by ambient proteins, resulting in a well-defined long lived 'hard corona', which obscures the bare surface in early nanoparticle. Adoption of this concept will facilitate a re-thinking of current approaches to characterise and categorise nanoparticles on the basis of their bare physico-chemical properties towards an approach with takes account of the evolution of nanoparticle dispersions in biological milieu and reflects the fact that the nature of the nanoparticle corona changes depending on the environmental conditions.

- Support for the concept of rational 'safety by design' for nanomaterials, via control of the nanoparticle-biomolecule interface. Thus, by learning to connect precise physical and biological mechanisms underlying nanoparticle interactions with living organisms to the nature of the protein corona will enable surfaces and biological interfaces to be designed with specific responses in mind.

- Attention to the issue of nanoparticle bioaccumulation. Given that the lysosome appears to be the final destination of many engineered nanoparticles, and that we have not yet observed any exit process for nanoparticles, the issue of nanoparticle bioaccumulation becomes important, and suggest that extensive evaluation of lysosomal signalling and disruption, including those too subtle to manifest in cell death, may be a key step in understanding nanoparticle biological responses, and nanosafety issues.

- The need to address issues around nanoparticle quality control and batch-to-batch variability as a matter of priority, as does the question of agreed standard nanoparticles as positive and negative controls for a range of biological end-points. NanoInteract has made some significant progress towards these goals, and this is being built upon in the QualityNano research infrastructure via the development of positive and negative control nanoparticles for apoptosis, cell cycle regulation and other biological end-points.

- The use of round robin (inter-laboratory comparisons) for identifying sources of different in results from different groups. This has been shown to be an extremely useful process, and highlighted a range of issues that need to be controlled for, such as changes in dispersion quality during nanoparticle shipping; the considerable variability in cells at different passage numbers and in serum from different lots, both of which can easily be resolved by having common batches distributed to all partners; and the potential for interpretation in even detailed protocols, which is usually resolved by performing a few iterations of the experiment and discussing to identify where differences occurred in order to improve the protocol. Quantitative reproducibility can be achieved in biological assays in this manner.

Additionally, NanoInteract protocols and methodologies are being incorporated into several other ongoing international efforts, such as being incorporated into the FP7 NanoImapctNet protocols database (www.nanoimpactnet.eu), the International Alliance for NanoEHS Harmonisation (www.nanoehsalliance.org) and the FP7 Research Infrastructure for NanoSafety assessment (QualityNano, http://www.qualitynano.eu/). Members of the NanoInteract consortium have been actively involved in dissemination of the outputs from the project to regulatory bodies and policy makers, via representation of the OECD working party on manufactured nanomaterials, via ISO and CEN, via the DG Sanco Scientific Committee for Emerging and Newly Identified Health Risks (SCENIHR) and via the European Medicines Agency (EMEA) and the European Food Safety Authority (EFSA).

The concepts have progressed significantly since the first paper was awarded the Cozarelli prize in 2008, and indeed a recent review of developments was written by the project coordinator and current postdoctoral colleagues at University College Dublin in Nature Nanotechnology (Monopoli MP et al., Biomolecular coronas provide the biological identity of nanosized materials, Nature Nanotechnology, 2012, 7: 779, also featured on the cover image of the Journal). This shows the enduring impact of the concept of the protein corona as determinator of nanoparticle face and behaviour in living systems. Indeed NanoInteract was cited as having contributed significantly to the ideas presented in the review.

Among the longer term implications for the protein corona, beyond its role in determining nanoparticle fate and behaviour for safety assessment, is the fact that understanding the corona is also central to the development of key applications, including improved drug delivery by targeting nanoparticles. Unless they are specifically designed to avoid it, nanoparticles in contact with biological fluids are rapidly covered by selected biomolecules to form a corona that interacts with biological systems, which can mask engineered targeting moieties and hamper the targeting processes (an example of this has been recently published by Dawson and colleagues, Salvati et al Transferrin-functionalized nanoparticles lose their targeting capabilities when a biomolecule corona adsorbs on the surface, Nature Nanotechnology 2013, 8, 137-143).

The NanoInteract project resulted in over 60 publications in high quality journals. The knowledge and experience gained is now forming the basis for other projects, both in the EU and across the world, including incorporation into several other EU projects. These include: NeuroNano, which investigated the potential role of nanomaterials in the onset and evolution of neurodegenerative diseases; QualityNano, the EU Infrastructure for nanosafety assessment; NanoTransKinetics, a modelling project that aims to develop a predictive tool for determining uptake, localisation and impact of nanomaterials based on their physico-chemical characteristics and their subsequent biomolecular corona. Additionally, inclusion of bionanointeractions is now standard in EU FP7 call texts and projects, with most large projects now including a dedicated workpackage addressing this issue, including MARINA, NANOMILE and NanoSOLUTIONS and several others.

Advanced Nanomedical Diagnostics:

New and Future Paradigms for the Enhanced Measurement of Health.

A. Domschke[1] and F. Boehm[2]

Nanotechnology is expected to have a profound effect on medicine. Several nanomedical devices are already mainstream. The authors present some mindblowing concepts for future devices that they insist are well within the realms of possibility.

Introduction

The application of nanotechnology to medicine (nanomedicine) has a strong potential for shifting myriad paradigms in the field of medicine. Although nanomedicine is still in its very formative stages, we are already seeing the development of specialized nanoparticles, such as gold nanoshells and SPIONs (Superparamagnetic Iron Oxide Nanoparticles (Fe3O4), ~300 nanometers to 3.5 microns in diameter) that are utilized to specifically target and thermally destroy cancer cells via hyperthermia, without imparting collateral damage to surrounding healthy cells and tissues. Hollow nanocarriers such as liposomes or hollow metallic nanoshells have the capacity to deliver powerful anticancer drugs and a host of other drugs specifically to diseased cells. This translates to remarkable improvements in efficiency and a dramatic reduction in the side effects that we see when patients are "flooded" with conventional toxic chemotherapeutic drugs.

In this paper a number of exciting emerging and conceptual technologies that relate to unique and efficacious nanomedical strategies for the enhanced diagnoses of human disease are briefly surveyed. These and others can be found described in detail in a new book entitled: Nanomedical Device and Systems Design: Challenges, Possibilities, Visions, edited by Frank Boehm. http://www.crcpress.com/product/isbn/9780849374982

The book explores many aspects of nanomedical device and systems design, which may assist in inspiring and facilitating the development of advanced therapeutics and diagnostics

First Generation Nanomedical Diagnostic Devices

First generation nanomedical diagnostic "devices", intended for use in vivo, consist primarily of variously composed nanometric contrast agents, such as magnetic nanoparticles, gold and other metallic nanoshells, or polymeric nanocomposites. These may be precisely targeted to diseased cells and tissues by "decorating" them with customized monoclonal antibodies or other chemical targeting agents. Some of the latest developments in this area involve "smart" nanoparticles that integrate multifunctional "theranostic" capabilities, where diagnosis and therapeutic drug delivery may be induced to occur simultaneously. Following their introduction into the human body via injection (though future modes may include ingestion as a pill, inhalation via a puffer, transdermal patch, or topical gel), these nanodevices circulate through the bloodstream until they automatically bind with the specific proteins that are displayed on the surfaces of affected cells.

In the case of magnetic nanoparticles (e.g. SPIONs), ~2 to 200 nanometers in diameter, an external magnetic field, e.g., via MRI, may be applied to visualize them in dramatic contrast to local tissues. This imagery may assist physicians and surgeons by spatially demarcating, for example, cancerous tumors in high

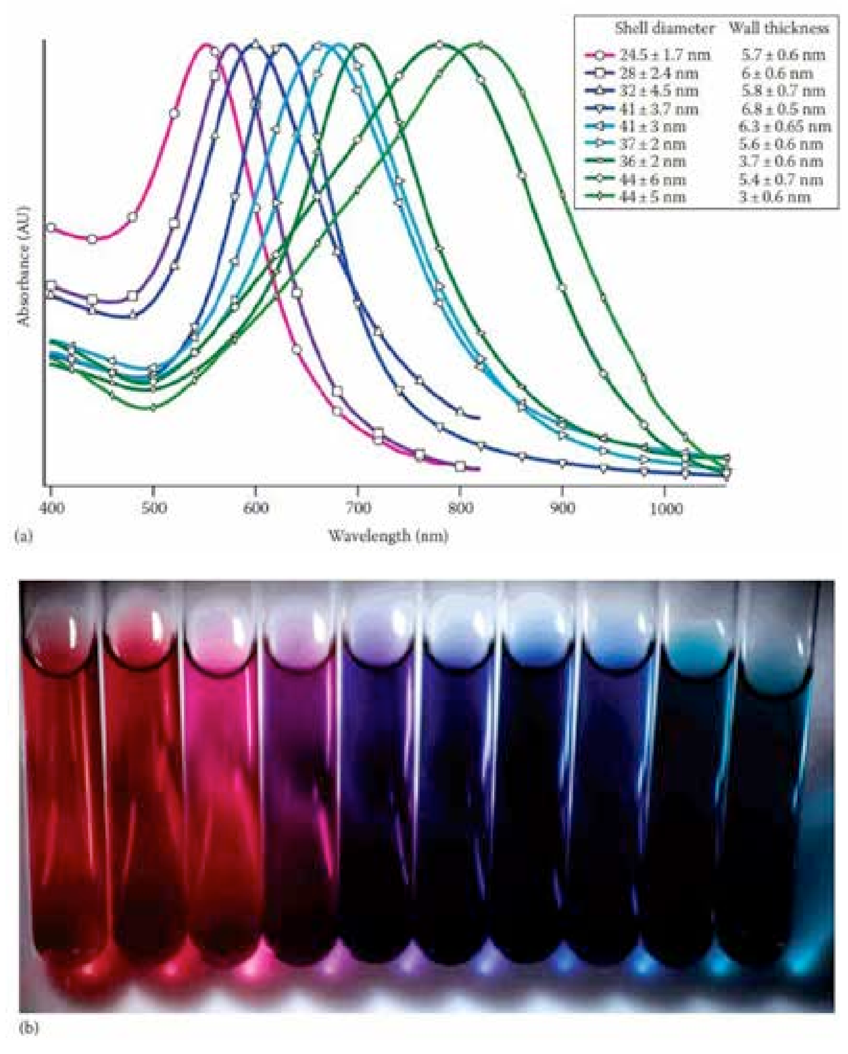


Figure 1: (a) Absorption spectra (via UV–Vis–NIR) of nine hollow gold nanoparticle samples with different diameters and wall thicknesses. (b) Color range of hollow gold nanoparticle samples with different diameters and wall thicknesses (vial on far left contains solid gold nanoparticles.

resolution. This enables an increased level of accuracy insofar as the planning and performance of subsequent surgical interventions.

In the case of gold nanoshells, ~10 to 200 nm in diameter, which have "tunable" dielectric cores of silica coated with thin skins of gold, near infrared laser light, which can pass safely through "transparent" soft tissues at these wavelengths at up to 10 cm in depth, is used to activate a process termed "localized plasmon surface resonance". (Figure 1) This phenomenon involves the oscillation of electrons at the gold nanoshell surfaces, where reflected photons can be detected and contrasted against local tissues.

A growing number of nanomaterials-based bioimaging probes may be employed for the diagnostic imaging of cancerous tumors. These may include highly fluorescent quantum dots (QDs), e.g., CdSe/CdS/ZnS, ~2-10 nanometers in diameter, which are semiconductor nanocrystals that are endowed with unique spectral properties. Quantum dots may also be synthesized to fluoresce under near-infrared laser light, which enables diagnostic imaging in vivo. Because of their extremely small size, upwards of two billion QDs might inhabit the nucleus of a single cell without negatively impacting its functionality! (Y. Xing and J. Rao, "Quantum dot bioconjugates for in vitro diagnostics and in vivo imaging", Cancer Biomarkers 4, (2008), 307–319, 307 IOS Press).

Ophthalmic Glucose Nanosensors for Diabetes Management

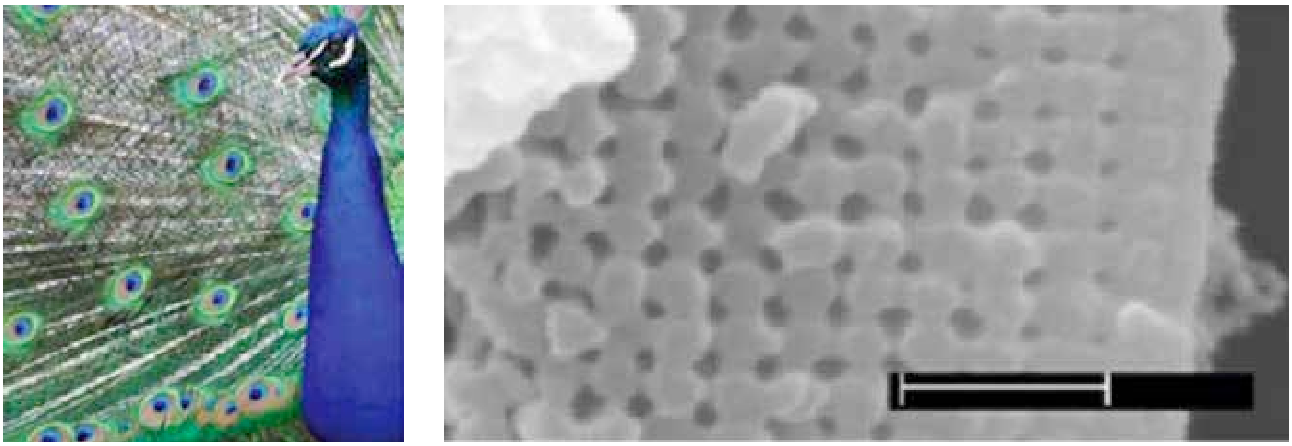
Distinctive medical applications of diagnostic nanosensors that spark considerable interest are ophthalmic glucose sensors for the management of diabetes. One groundbreaking example of these advanced ophthalmic technologies is what is known as a "holographic glucose sensor", which comprises a class of colorimetric sensors that are based on periodic optical nanostructures, designed to influence the movement of photons. The interaction of light photons within these nanostructures results in a distinct color phenomena that may also be observed in nature, where it is termed as "structural" color. A well-known example of structural color is found within the feathers of the peacock (Figure 2). Stacked melanin rods are interspersed with air pockets, cumulatively resulting in periodic optical nanostructures, with differences in color being achieved when the lattice spacing between the rods is altered.

Lattices consisting of points, spheres, or other structures have found widespread use in thin film optics, with applications that range from low and highly reflective coatings on lenses and mirrors, to color-changing inks. Under white light illumination, such lattices diffract light and produce a characteristic spectral peak with a wavelength that is governed in approximation to the Bragg equation. Even the most subtle variations in the spacing of nanolattices initiate color shifts that may easily be detected by a spectrophotometer. Ease of fabrication, high sensitivity, and ease of integration with read-out devices, make optical nanostructures particularly suitable as ophthalmic sensors.

A collaborative team, led by Angelika Domschke and Chris Lowe[3], have developed a holographic platform that was based on periodic optical nanostructures, which is suitable for contact lens applications. The platform combined a simple reflective hologram that was recorded within the hydrogel sensor matrix of the contact lens. The matrix contained covalently bonded glucose binding ligands that had the capacity to specifically and reversibly bind with glucose, which caused the hydrogel to swell. This swelling in turn altered the fringe distances. The resulting color shift could therefore be employed to sensitively quantify glucose concentrations using a simple spectrophotometer that is integrated into a hand held readout device. (Figure 3)

This novel holographic glucose sensor technology demonstrated the ability to continuously and reversibly

Figure 2:



(a) Example of iridescent peacock plumage.

(b) Scanning electron microscope image of peacock periodic optical barbule nanostructures.

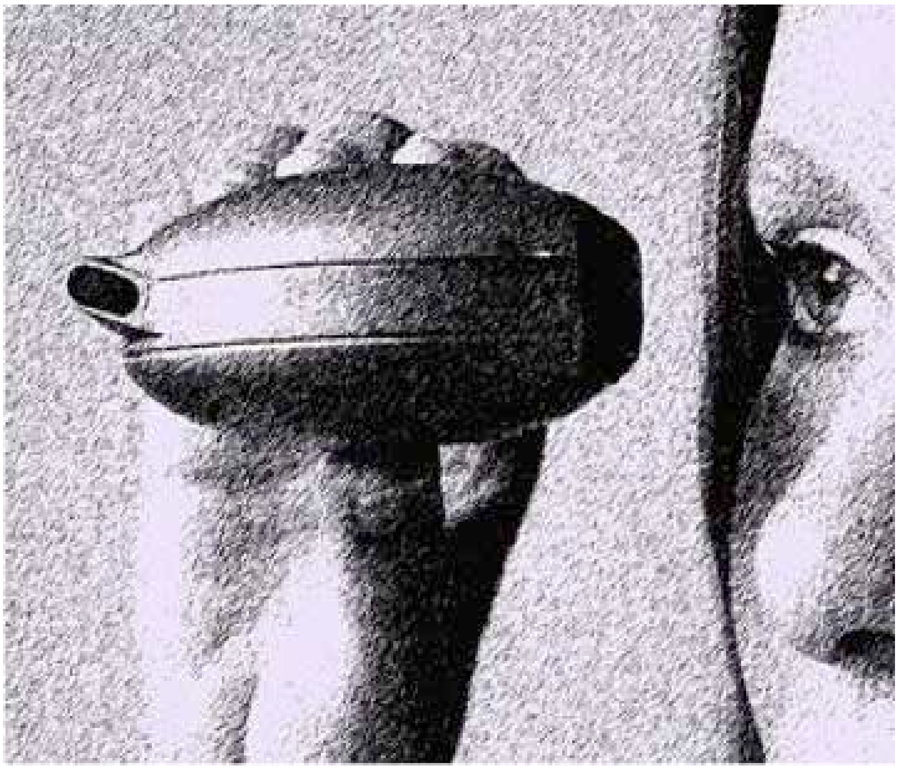


Figure 3: Contact lens glucose sensor and hand held readout device. 2008 International Conference on Nanoscience + Technology (ICN+T), Angelika Domschke, July 22, 2008.

function in complex biological media at physiological pH, ionic strength, and glucose concentrations. Initial clinical studies indicated the capacity for tracking glucose responses in vivo, and these results formed the foundation of subsequent exciting technology platforms[4].

Nanomedical Visions

Looking further into the future (~10-30 years), with the advent of mature molecular manufacturing capacities that work in conjunction with advanced Artificial Intelligence, AI, we may see the emergence of sophisticated, fully autonomous nanomedical devices, albeit still under the complete control of "outbody" computers that are overseen by human physicians and surgeons.

Some examples of such conceptual nanomedical devices/systems include:

In the mouth: Unique classes of hybrid (diagnostic/therapeutic) "dentocytes" may serve as long indwelling nanodevices, whose tasks within the human oral cavity would include the continual cleaning of gums and teeth, keeping breath fresh by eradicating associated bacteria, undertaking the repair of cavities before they have a chance to cause problems, coating teeth with superhard diamondoid materials, and even rebuilding teeth from scratch. Existing cavities might be repaired painlessly as specialized nanodevices would be charged with the task of temporarily blocking the nerves that are associated with the tooth, or teeth to be repaired. All of these procedures would proceed completely unnoticed by user-patients, as these nanodevices would be so diminutive, smaller than the thousands of bacterial species that already commonly inhabit our bodies.

As support to the immune system: Another far reaching and powerful application might involve the long-term implantation of millions of so-called "sentinel" nanodevices, (Figure 4) which would cumulatively function as 24/7/365 physiological monitors. They could serve as a potent immune system augmentation, with the capacity for administering an array of nanomedical diagnostics and therapeutics that would rapidly identify and neutralize virtually any perceived "non-self" chemical toxin or pathogenic micoorganism that the human body might be exposed to. These envisaged autonomous micron-scale nanodevices, programmed with comprehensive data on all known toxins and pathogens, might continually "patrol" the human vasculature and lymphatic system for the presence of invasive species. They may also be enabled with the capacity for penetrating into tissues via a process called diapedesis. As we articulate in the book "Instances where the identity of an intrusive agent is unknown, a default

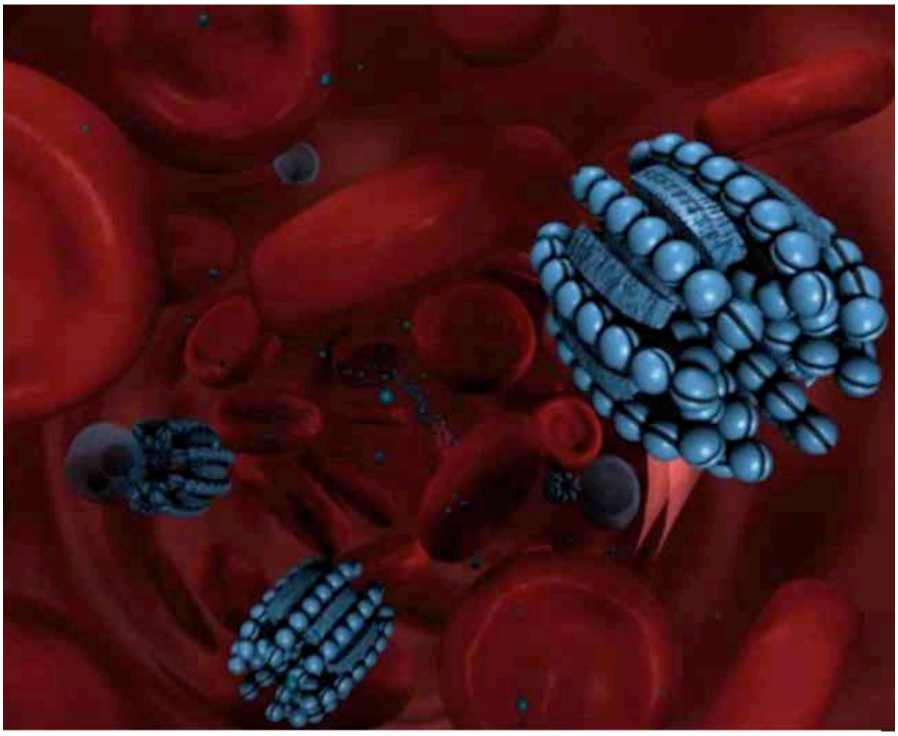


Figure 4: Artistic representation of Sentinel class nanomedical device.

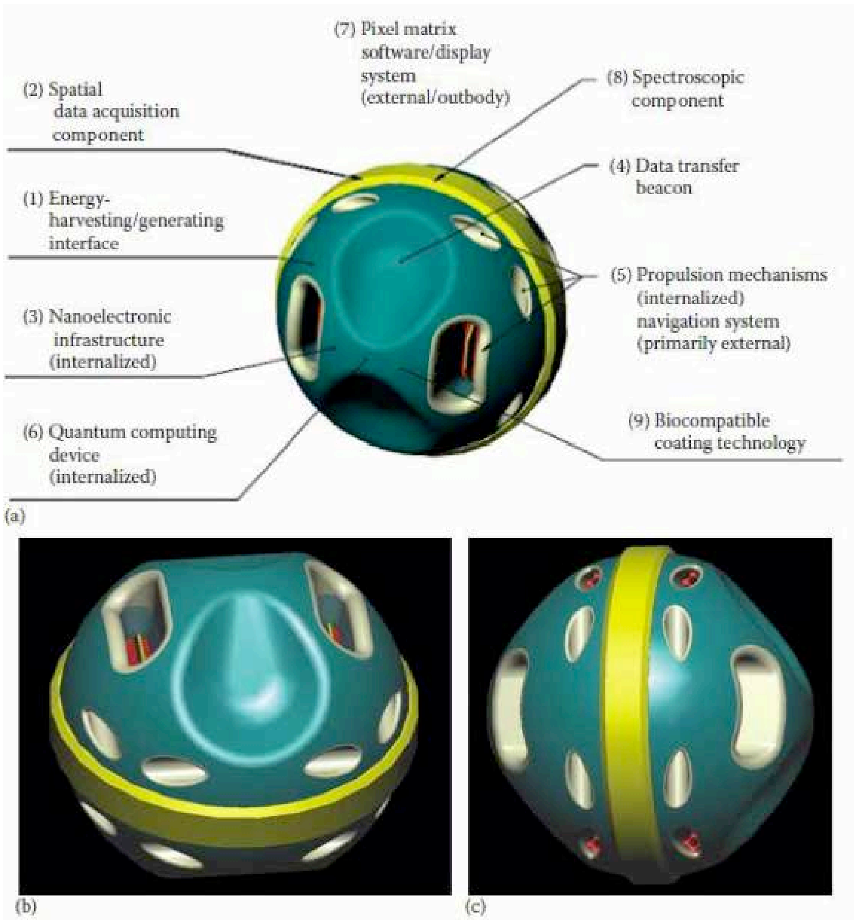


Figure 5: (a) Artistic anatomic representation of conceptual Vascular Cartographic Scanning Nanodevice (VCSN) (b,c) Alternate VCSN orientations.

protocol would be spontaneously instituted to ensure their complete destruction via chemical, oxidative, hyperthermic, or highly localized nanomechanical disassembly."

Within the blood system. A Vascular Cartographic Scanning Nanodevice (VCSN) (Figure 5) would constitute a fully autonomous nanoscale in vivo medical imaging device and system. The ~1 μm in diameter nanodevice, or more likely, many thousands of identical such nanodevices working in parallel, would function to scan/image the entire human vasculature down to the level of the smallest capillary lumen (e.g., ~3 μm diameter) in high-resolution three-dimensional (3D) digitized format. The primary capabilities of such a nanodevice, as well as its precursor, the Gastrointestinal Micro Scanning Device (GMSD), would be:

- Capacity for the generation of a very high-resolution (less than ~1 μm) 3D rendering of the complete human vasculature down to the capillary level. It may also be applied to the imaging of the lymphatic system, and in a simplified form (e.g., GMSD – [described below]), the gastrointestinal tract (GIT).

- Ability to distinguish and superimpose vascular and neurological plaque deposits

- and lesions with high accuracy against the topographically rendered backdrop of healthy endothelial wall surfaces.

- Quantification of vascular wall thicknesses along with the identification and highlighting of "hot spots" at any site within the vasculature, such as imminent blockages or aneurysms that are at risk of rupturing. This capacity will be of particular value when enabling the clear elucidation of such risk sites for subsequent mitigation in situ, within the brain.

- Capacity for physicians to "fly-through" all scanned areas via a joystick and computer display for the highly detailed inspection of any desired site within the system. The acquired spatial data may also enable holographic rendering and virtual travel through all imaged systems.

- Ability to facilitate the targeting of tumors by revealing instances of nascent angiogenesis in close proximity to tumor growth sites."

Within the digestive system. A Gastrointestinal Micro Scanning Device (GMSD) (Figure 6) which will serve as a formative and far less complex precursor to the VCSN in that it will not have the capacity for propulsion or navigation. It will, however, utilize nascent forms of the quantum computing, nanoelectronics, spatial data acquisition, and PM technologies that are envisaged for the VCSN. Hence, the GMSD, in addition to serving as spatial data acquisition device, may also have utility as a test bed of sorts that is employed to identify and resolve technical, integrative, and functional issues toward the further evolution of the VCSN. The GMSD system will consist of three distinct components working in unison to generate a very high-resolution 3D topography of the entire internal surface of the GIT. The GMSD would accomplish this task by employing:

- An internalized (via ingestion) scanning device (BB)

- An external pulse generator/data transfer unit (PGDT)

- A Pixel Matrix (PM) display element

The setup for the GMSD operational procedure would be relatively simple to implement. Initially, the BB would be administered orally to the patient in the same manner as a pill. Next, an adhesive and waterproof PGDT thin film patch would be affixed to the skin of the patient's abdomen. At this juncture, a systems calibration would be performed to assure that the communication link between the BB and the PGDT is functioning properly. A test scan would also be performed to configure the image resolution. Following these

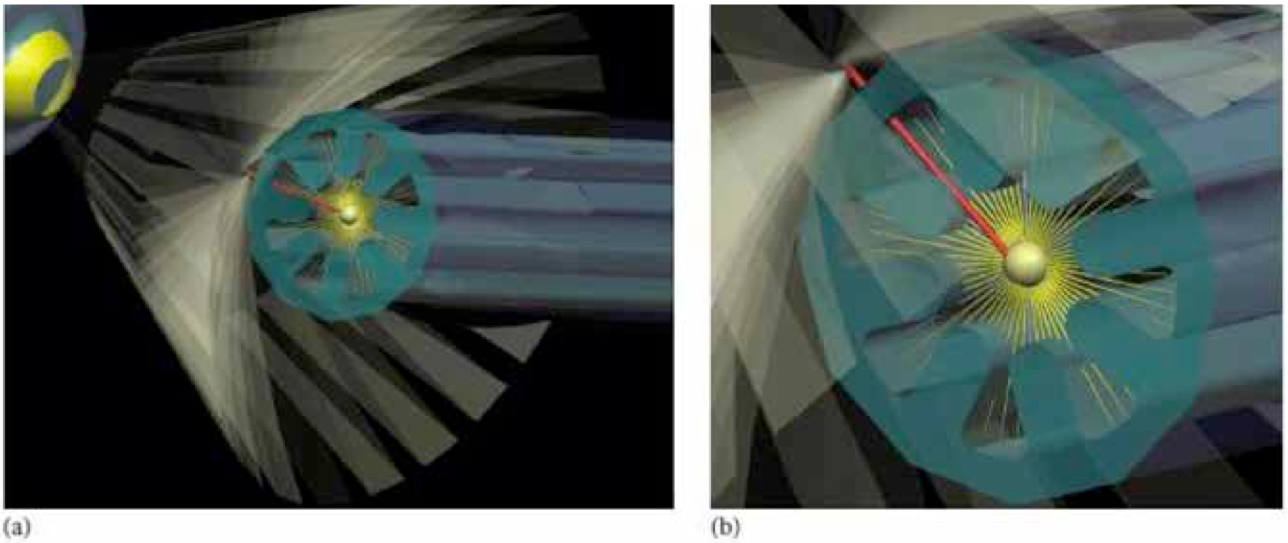


Figure 6: (a.b) Artistic representations of conceptual Gastrointestinal Micro Scanning Device (GMSD) depicting communication link between the pulse generator/data transfer unit (PGDT) and the bright ball (BB) internal scanning device.

procedures, the patient would be allowed to leave the physician's office, clinic, or hospital to go about his/her normal routine. The internalized BB would now progress along with the natural peristaltic rhythms of the GIT and be naturally eliminated at the conclusion of the transit duration. The patient would subsequently return to the facility in two or three days (contingent on the assessed GIT transit time) to have the PGDT patch removed. The PGDT will have continually accumulated all of the data acquired by the BB during the designated scanning period. This device would then be interfaced with a computer via a USB port to stream all of the acquired data to the PM software housed within the computer.

The data would now be translated into high-resolution 3D imagery on a display. The interrogating signals emitted by the BB would have the capacity for passing through the contents of the small and large intestines, as if transparent, through the utilization of a selective signal filtering algorithm. The scanning signals would have no harmful effect on any cell or tissue, even with prolonged exposure. The PGDT would emit a unique pulsed signal (e.g., ultrasonic, near-infrared), which when received by sensors embedded within the surface of the BB would trigger all of the embedded Emitter/Receiver units to fire and emit their scanning beams simultaneously in every direction. The PM software would calculate BB orientation and would correlate the hits obtained within predetermined parameters to construct a cross section of the GIT representing its internal topography. These digitized segments would be sequentially pieced together to form a seamless spatially accurate rendering of the system."

Conclusion

The rapidly emerging and exciting discipline of nanomedicine has strong potential for enabling dramatic paradigm shifts in medicine. Medical diagnostics is an area where nanomedical devices might impart significant beneficial impacts for patients, in terms of enhanced diagnostic resolution (e.g., sensitivity and selectivity). This may subsequently facilitate more precise therapeutic assessments, which translate to overall improvements in patient outcomes. First generation nanodiagnostic devices are already demonstrating considerable enhancements in efficacy. Over the next few decades we may well witness a revolution in diagnostics, as autonomous AI-enabled nanomedical devices probe the depths of the human body in a valuable future step in the quest for optimal healthcare for all.

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4. Many of these are presented in Dr Domschke's chapter in Nanomedical Device and Systems Design: Challenges, Possibilities, Visions, in addition to the ophthalmic sensing opportunities that lie beyond diabetes.

Nanotechnology - towards real improvements in the energy efficiency of buildings

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Introduction

The building sector is responsible for about 40% of the worlds primary energy consumption, and 30% of the greenhouse-gas emissions - a major portion of this energy being used to achieve thermal comfort conditions for the occupants. The International Energy Agency has identified the building sector as one of the most cost-effective for reducing energy consumption worldwide, and is encouraging the search for and use of new technological solutions.

Phase change materials (PCMs) in energy efficiency.

A technology that might contribute to reducing energy consumption in buildings is based on the use of phase change materials (PCMs) for temperature control and for heat or cold storage. When applied in the building envelope, PCMs have the ability to increase the thermal mass of the building due to their controlled phase transition characteristics, thus reducing uncomfortable temperature fluctuations, and collecting free solar energy. This characteristic becomes even more important in modern buildings since they also tend to have a low thermal mass.

Nevertheless, having temperature fluctuations controlled does not mean that the temperature will be at the ideal level. Therefore, to ensure a comfortable temperature for the occupants, it is necessary to have heating and cooling systems in the building. Although these systems do not need to tackle the temperature peaks, diminished by the presence of PCMs in the building envelope, they also require to be significantly improved.

One interesting way to improve the performance of heating and cooling systems is through the production and storage of thermal energy during the most economically and energetically favourable periods. This can be addressed through latent heat storage units using PCMs. However, from a thermal point of view, PCMs offer poor thermal conductivity, limiting the performance of such systems. A high thermal conductivity of both solid and liquid phases of the PCMs would assist the energy load and discharging processes.

The performance of the heating and cooling systems of buildings is also limited by the low thermal conductivity of the conventional fluids used for heat transport between the production (or storage) plant and the building zone to be heated or cooled. Regarding Fourier's law of thermal conduction, the improvement of the thermo-physical properties of the heat transport fluids will enhance the effectiveness of the heat transfer, enabling miniaturization of the devices and therefore contributing to a more sustainable system.

Carbon nanotubes (CNTs) and the enhancement of thermal properties

An innovative strategy for the thermal conductivity enhancement of fluids and PCMs is based on the addition of solid nanoparticles with considerably higher thermal conductivity resulting in a new complex material with enhanced thermal properties. This mixture is known as nano-enhanced phase change materials. Among the various nanoparticles available, perhaps the most interesting are carbon nanotubes (CNTs) which are cylindrical nanostructures that exhibit extraordinary thermal properties. It is expected that the suspension of such particles will enhance the overall thermal conductivity of the obtained mixture.

In addition to their high conductivity, the elongated shape of the CNTs combined with a high aspect ratio, allows the formation of dynamic spanning nanostructures with a high degree of connectivity, even at lower concentrations, as depicted in Figure 1. These nanostructures create a more efficient means for heat transport than that of the original medium. It is recognized that the physical

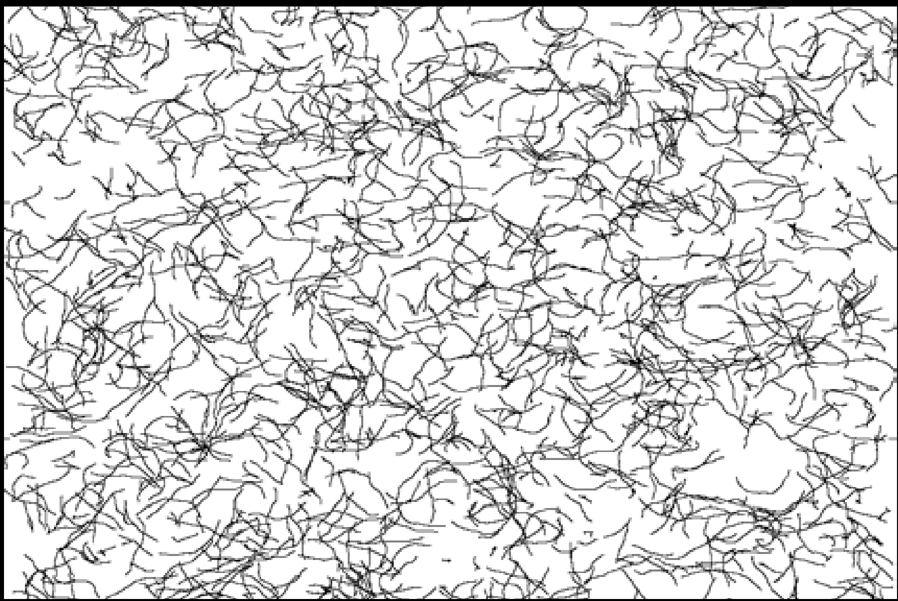

Figure 1: Spanning nanostructure formed by well-dispersed CNTs.

Figure 1: Spanning nanostructure formed by well-dispersed CNTs.

interaction between the nanoparticles induces a further increase on the thermal conductivity of these mixtures. Therefore, CNT dispersions present the highest known thermal conductivity enhancement.

Additionally, it is possible to engineer the thermal conductivity of the dispersions for each specific situation, as well as other thermo-physical properties. It is known that the intimate inclusion of nanoparticles in a medium can significantly change several other thermo-physical properties, such as its viscosity, density and heat capacity, amongst other parameters - not necessarily all of which are according to the desires of the design engineer. For instance, the dispersion of nanoparticles in conventional working fluids raises both thermal conductivity and viscosity. The latter is a known disadvantage, since it will increase the pressure drop and pumping power. Therefore, it is necessary to balance the overall thermo-physical properties of the nanodispersions for the required outcomes and conditions.

The dispersion nanostructure shown in Figure 1 represents an ideal case. At the nanoscale, the percentage of atoms at the surface becomes significant, increasing the surface-to-volume ratio of the particles. This characteristic induces strong attraction forces between the nanoparticles leading to the formation of local clusters, like yarns. These clusters of increased size tends to settle down rapidly, leading to the degradation of the thermo-physical properties of the mixture. Moreover, regarding nanofluids, the clusters may also produce other problems, such as clogging of the flow channels and abrasion of device components, among others. In summary, it is an undesirable, unstable mixture.

One way to prevent this from happening is through modifying the surfaces of the CNTs, decorating them with special chemical compounds that interact with each other. These compounds have the ability to produce repulsive forces between the CNTs, preventing their agglomeration. However, this modification is not problem free, requiring an appropriate selection of the chemical compounds. For instance, the selection of an inappropriate compound may lead to the formation of foams or even to their fast degradation, due to the thermal cycles thst the nanofluids and the nano-enhanced phase change materials are subjected.

These compounds must also be chemically compatible with the medium in which the CNTs will be dispersed. In chemistry, the expression "like dissolves like" is often used. This means that, in general, polar substances will dissolve in polar solvents, and non-polar substances will dissolve in non-polar solvents. Therefore, if the solvent is water or an aqueous solution of ethylene glycol, the carbon nanotubes must be modified to behave as a polar substance. In this case, a typical used compound is the carboxylic acid group. Carboxylic groups are polar weak acids, with an acceptable resistance to thermal degradation, being commonly used in the modification of CNTs for the production of nanofluids and nano-enhanced organic PCMs. Furthermore, these chemical groups possess ion-exchange properties, having both hydrogen acceptors and donors, improving the wettability of the particle and increasing the electrostatic repulsion forces between the dispersed modified CNTs.

Despite the fact that the instabilities introduced by nanoparticles' agglomeration may be overcame through the modification of the particles, it should still be taken into account that these particles are permanently subjected to gravitational or other centrifugal force fields. These force fields will induce the separation of the phases. This effect is stronger when the difference in the specific density of both materials is larger. However, in the case of non-agglomerated CNTs, the rate of phase separation can be significantly reduced or even annulled. As it can be seen from Figure 1, the CNTs interact and easily collide, producing opposing reactions to the separation phase motion. In addition, when a particle moves, it displaces fluid in the opposite direction to its movement, affecting the motion of the surrounding particles. Other mechanisms may also reduce sedimentation, for instance, every particle suspended in a fluid presents a natural random motion, known as Brownian motion. When this motion is more intense than that of the phase separation, the mixture is stable regarding sedimentation.

Nanotech and 'green' buildings. The future.

As described above, nanotechnology may help the production of heat exchange fluids and latent heat storage units with improved thermal conductivity. However, it is of the utmost importance that the engineered thermo-physical properties endure over time and cyclical usage, a fact directly linked to the colloidal stability of the developed mixtures. Nevertheless, through the appropriate modification of nanoparticles available in the market, it is possible to ensure long-term stabilities for such mixtures.

Recent technological developments are quite enticing and the nanoscale seems to be providing the means to breach through barriers in what concerns better energy usage. The incorporation of the herein presented technologies will enable the reduction of the energy consumption and greenhouse gas emissions in buildings. For instance, nanofluids could reduce the size of the heating and cooling systems, for the same amount of thermal energy. These lower rated systems are less expensive, require less power, and may also present a reduced carbon footprint. Moreover, latent heat storage units with improved thermal conductivity enable faster heat charge or discharge, which consequently provides a faster response to thermal comfort needs. Combining these technologies may assist buildings to become greener and more eco-friendly.

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