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Successful European Nanotechnology Research

Outstanding science and technology to match the needs of future society

STUDIES AND REPORTS

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Directorate-General for Research and Innovation
Directorate G – Industrial Technologies
Unit G.4 – Nano-and converging Sciences and Technologies

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Note of the editor: Matteo Bonazzi

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Interviews with: Christos Tokamanis and FP6/FP7 Project Coordinators

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Materiam superabat opus
The workmanship surpassed the material
(Ovidius Naso)

Ανθρωπος μέτρον
Man is the measure of all things
(Protagoras)

Note of the editor

'Nanotechnology' is the new frontier of science and technology in Europe and around the world, working at the scale of individual molecules. Top scientists as well as policymakers worldwide praise the benefits it would bring to the entire society and economy: most of them insist on the key role research would play in the value-creation process to develop exploitable portfolios of technologies leading to a choice of unique applications, products, markets and profitable revenue sources.

Additionally, nanotechnology is becoming ever more deeply embedded in today's life, so it is a critical moment for communicating the huge public effort that has been put into European research and its major outcomes and new directions, so that nanotechnology's crucial, potential opportunities and drawbacks for the whole society are properly explored and elucidated.

Clearly, this task cannot be left solely to scientists or technology suppliers. Dealing with new frontiers of technology calls for both the advantages and risks to be properly addressed and explained.

In the EU research on nanotechnology takes a very special place, to the extent that information, communication and fostering societal debate on nanotechnology research have already become an essential part of many European policy initiatives. Communicating nanotechnology research is critical for Europe and especially for European institutions, so selecting and structuring the relevant information to reach key audiences is essential.

In this light, setting up appropriate methodologies to display this information on nanotechnology research is the ultimate and most challenging step. This exercise has allowed identifying how information on EC-funded nanotechnology research can and should be effectively collected, structured and presented to be further communicated to relevant EU audiences.

For this purpose, almost 200 European projects on nanotechnology, funded both under FP6 and FP7, have been clustered into different thematic groups, described and explained by highlighting their scientific excellence and technological achievements and by focusing on the impact on industry, society and media they are likely to have.

Meaningful communication is especially needed in the case of nanotechnology as the public seems to be more sceptical and less deferential about it. This is the reason why creating a relationship and an exchange between stakeholders is regarded as being essential.

The present report is a true 'first': whereas communicating European research projects is a moral duty, communicating them well is a moral responsibility. We hope to have contributed to fulfilling this challenge, so that others may be inspired to pick it up.

Matteo Bonazzi

Programme Officer
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Directorate G Industrial Technologies
Directorate-General for Research & Innovation
European Commission

Inopem me copia fecit
To those whose abundance has not made them poor

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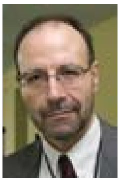
NANOTECHNOLOGY BECOMES A SOCIO-POLITICAL PROJECT

It is already much more than just an enabling set of tools, says Christos Tokamanis, and proactive governance should be the ultimate aim



Christos Tokamanis, Head Of Unit for Nano-and Converging Sciences and Technologies, Directorate G, Directorate-General for Research and Innovation

The current generation of European nanotechnology projects (funded by the EC both under FP6 and FP7), have generated a massive amount of exciting achievements for both research and policy-making. Could you describe the evolution of nanotechnology over this time?

Since the first "European Strategy for Nanotechnology", which goes back to 2004, and the Nano Action Plan that followed in 2005 we have been consolidating all our research effort in dedicated clusters and we also identified three major areas of societal interest into which we put a lot of effort, namely nanomedicine, energy/environment and ICT(Information Communication Technology). In addition to these, great progress was made in most fields of nano-sciences and laboratory infrastructure.

Today, other application areas are emerging, focusing on users of nanotechnologies. To the construction industry, nanotechnology can indeed offer great prospects to improve the energy efficiency of buildings and much more reliable construction methods and customization techniques. In the meantime, the use of nanotechnology has also spread within the textiles and cosmetics sectors, and of course there are some very important advancements in security.

In fact, six years down the road we understand that we cannot fund research without having a purposeful structure and system sustaining it. Nanotechnology is becoming so pervasive that if you don't structure it you are not likely to know exactly the level of progress you are making. You cannot simply rely on people being objective about their own achievements, as they may be overstating either the benefits or the risks.

The big issue is that we are now moving away from the idea that nanotechnology is just an enabling technology, or merely a method, or a process, or a means of controlling matter at the atomic level. What we are saying now is that nanotechnology is taking the form of a socio-political project whose trajectories extend into all spheres of life: from the cultural and ethical, all the way to the social, industrial and economical life. Furthermore, nanotechnologies generate a lot of different opinions and potential conflicts among the people who might use it.

It is, therefore, all the more necessary for us to have a "carrier platform" encompassing these various ideas, some of which could be conflicting, in order to avoid problems in the years to come. From the dialogue which we have encouraged, we know that parts of society are in favour of a moratorium on the use of engineered nano-particles before we fully know what the effects on the environment and health are, whereas others say that research and development is how society progresses and we may never know all the risks anyway.

However, at the moment we are in a much better position to manage uncertainty and risks, provided we understand them. Scientific knowledge and beneficial technology going into applications, products and services can only be put on its proper footing if we understand all the other aspects to be factored in: the policies, the regulations, the legal aspects, the standards. The very way we measure and characterize nano-entities is of crucial importance.

So the proposal that we are making compared to six years ago is that nanotechnology is not simply about creating or improving products, but we have to look at the whole process instead. People are very sensitive when you talk about single atom manipulation and control, which may have implications further down the line. All the more reason to consider issues of science and society jointly, as well as aspects of economic-environmental progress together with competitiveness. People expect us to treat this like a system.

Such a system has several components, such as research, innovation, infrastructure, the regulatory regime and the social-ethical-legal convergence. Social scientists and philosophers think of nanotechnology as being very important, so they do need to be part of the discussion as representatives of the wider society.

The new activities planned for 2011-2015 will outline the main trajectories: one is the research-innovation-commercialization route, the other one is the means ensuring the safety of consumers, workers and the environment, which must be of the highest standard; the third one is the proactive governance, which is really aimed to understand the points of view of all people, their respective roles and what kind of message they may want to bring.

The proposition elevates the whole issue to a socio-political project, which is really a proposal on the technical, social, economical innovation strategies to be followed, in which the governance and regulatory aspects are all brought together. All this has a bearing on how best to progress by not ignoring people's feelings and concerns and trying to engage citizens as early as possible in all developments and processes.

Clustering nanotechnology projects for the first time has focused attention around 13 core areas of science and policy-making. You once said that your ethical and social responsibility as Commission is to make sure that science is not rushed and that people can build up knowledge and confidence in nanotechnology. Is this publication part of the same public awareness effort?

That's correct. These clusters gather the most important projects within an investment portfolio exceeding one billion Euros of Research &Development. Collecting these projects according to the respective areas which they address is a good way to understand the intricate links and interactions among them. It would not be easy to make sense of the societal, economic or environmental impact by considering every single project by itself; but if you look at them together, people might be in a position to understand better where we are exactly. Also, we have foresight studies and road mapping, in which we already set our targets for the years to come; assessing and compiling the clusters helps us to form a precise picture of the progress we are making in order to compare it with what is happening in the rest of the world and in the other Member States. So it doesn't matter much whether these clusters cover everything, as long as we get the methodology right.

Nanomedicine with its Diagnostics, Drug Delivery and Regenerative Medicine sub-clusters, nanotechnology for Environment/Energy and Electronics / ICT are some of the main clusters on which the EC has invested heavily. Can you please sum up the main benefits that are expected of research in these fields?

We are spending a substantial amount of our budget on nano-biotechnology, which has the highest societal impact as it is mostly covered by nanomedicine, in order to try and understand how these biological interfaces can give an early warning of the onset of disease, be targeted and provide treatment inside the body as an alternative to flooding the human body with chemicals.

Energy production, storage and distribution are very important. Very interesting applications include high energy density batteries and super-capacitors, which can be used in cars or mobile devices and don't need to be charged for a long time, or more efficient, cost-effective, fourth generation photovoltaics. The first global environmental challenge for nanotechnology is water remediation, which could be used by water supply networks to eliminate unwanted traces, or by single hospitals and manufacturing plants to filtrate their own discharge waters. Another is monitoring pollution in air, water and soil. Yet another challenge is the capture of CO2 emissions, which with the aid of nanocatalysts could be turned into liquid fuel. We are going to have fossil fuels for quite some time, so this could be regarded as a recycling process.

In electronic/ICT applications the advantages would be in enhanced power to compute and lower power consumption, low cost microprocessors with huge memory capacity and organic large area displays with much higher resolution. If you go into nano-photonics, the aim is quantum computing.

On the basis of the projects' achievements described across these nanotechnology R&D clusters, what are the major public expectations in terms of nanomaterials, industrial applications, textiles and security?

The use of nanomaterials crosses over into every cluster. In the agricultural environment, nanotechnology can be especially useful to control and reduce the use of fertilizers and pesticides, so they may be applied only when necessary. Nano-sensors can be used for hydroponics, to monitor the insurgence of crop diseases. Animal welfare will also be increased, as viruses can be easily trapped by nano-sensors which can detect the early onset of epidemics early.

With regard to industrial applications, ultimately, the whole factory will eventually be the product itself. Nanotechnology will completely change the way we produce and consume because people will buy their own mobile factory according to the function they need: for instance they will be able to take their own blood sample and produce a pill according to their medical needs. Individual garments with incorporated nano-sensors will be able to take your blood pressure and give you an updated bill of health. Nanotechnology will allow for these manufacturing processes to be scaled up and down at will, depending on what customers want.

The use of nanotechnology in security covers four areas: detection of contamination from pathogens and chemicals or a hidden threat carried by someone; public protection from such threats; authentication purposes against commercial brand counterfeiting, or crime prevention and forensics. These advancements at the same time create huge ethical problems, as monitoring might not always serve a good purpose and regulation is needed to protect people from unwanted intrusion.

The EC's commitment to safe, responsible and integrated nanotechnology means that a lot of attention and funding has also been devoted to EHS (Environment, Health & Safety) research and care for ELSA (Ethical, Legal, Social Aspects) issues. The Outreach and CSA projects complete the picture. Will this contribute helping people to make their own most informed decision about nanotechnology, based on the most up-to-date facts?

Health and environment safety protection is a huge issue. That is why we are saying that EHS from its regulatory point of view, filling the knowledge gap and so on, boils down to managing the risks. The public is educated and people understand they are part of this process and they feel quite secure but governance must ensure that there are no additional risks which we are not aware of. The clustering is part of this information and engagement leading to dialogue on nanotechnology, so that people can focus on making the right decision based on their own benefit and the usefulness of the innovations.

Safety is just as important as the development of products and processes. In fact, it is part of the product itself; in other words, the product needs to be designed for safety. So we need to understand the individual behaviour of engineered nanoparticles, where they go, what their fate is during the use of the product or when they are recycled. Also, assessing the environmental impact and understanding the various levels of exposure are part and parcel of the developmental process.

EHS is obviously tied to ELSA, which is a combination of things. It includes the work of social scientists, philosophers, regulators but all this really bears on the significance one attaches to the way we manage risks and the risk assessment of each development stage. The Commission's Code of Conduct has provided the guidelines for responsible nanotechnology development.

ELSA gives you the means with which to engage the public in this socio-political project. Because nano is so new and can go anywhere, we don't take anything for granted, which wasn't the case for micro-technologies. So we need to validate every nano product, assess how we produce it and evaluate the lifecycle impact costs.

Outreach is just as important, as we probably are the only program in Europe that communicates directly to the public, especially with the education schemes for schools and universities and with the various initiatives we have set up to inform public opinion. Young people, especially, need specific care as we cannot get away from basic sciences, and in nanotechnology these disciplines need to be brought together. So outreach is something that needs to be continued, and the more we do so, the more benefits we will see overall.

ENERGY AND ENVIRONMENT

Sustainability with a smart green heart

From carbon capture to cheap and portable water purification, all the way to ultra powerful solar cells and super-batteries, nano names it.

ENERGY / ENVIRONMENT

Nanotechnology's great sustainability promise is to bring about the much needed power shift in renewable energy: a new generation of highly efficient photovoltaics, nanocomposites for stronger and lighter wind energy rotor blades, to name but two; but also a new class of nanomembranes for carbon capture at fossil fuel power plants. Energy savings could be made if the proper nanomaterials were used not just for more efficient distribution and power transmission (and nanosensors might lend a helping hand to the decentralised management of renewable energy grids), but also to build smart glass and electrochromic windows capable of maximising the use of solar power to heat buildings.

Energy storage could be greatly enhanced by optimised batteries and supercapacitors, while nanotacalysts could optimise fuel production.

Safe water purification, filtration and desalination through cheap and portable nanotechnology systems is a huge hope for a better future which could help developing countries to have their own clean and drinkable water.

Nanomembranes, which are organic polymer-based nanocomposites less than 100 nm thick, are effectively filters operating at the molecular level. They are a class unto itself since their work is copied from nature, and indeed living cells use a form of nanomembrane to function. Their properties and optimal use are actively being researched, as in the case of highly selective MIMs (Molecularly Imprinted Materials) with strong membrane permeability and the incorporation of natural aquaporins, which are naturally occurring proteins, into industrial membranes.

Nanotechnology is also focusing on researching nanoparticles as powerful adsorbents and nanoscale titanium dioxide as a catalyst to remove contaminants. Nanosilver ceramic filters have already found their way onto market applications due to their antibacterial and antiviral action.

SPOTLIGHT ON...

NANOGLOWA (NanoMembranes against Global Warming, http://www.nanoglowa.com)

Nanomembranes might potentially help meet Europe's CO2 reduction targets. NANOGLOWA's nano-structured membranes are built to separate CO2 from flue gases of coal-fire power plants, which make up for one third of Europe's power plant emissions, at a cost-effective price.

This means the project had to go down two paths: the development of optimal nano-structured membranes (three polymer, one carbon and one ceramic membrane), and the integration of the membranes into the power plants, which involves system engineering and transport modelling.

The main achievement halfway through the project was the development of suitable membranes and the increase of their surface by a factor of around 200 from 5-7 cm2 to 900 cm2.

Early on in the project, the focus was on the development of five membrane types. Halfway through the project, the consortium voted to select the two membrane types that were considered most likely to fulfil the project's requirements, such as high selectivity, high permeability and sufficient durability.

For these two membrane types, membrane modules were designed and developed for use in power plant pilot testing. The flue gas conditions are a challenge for all membranes because of the high temperatures and fly ash. The stability of such systems will be proven in the test in the power plants, which are in preparation.

For the lab tests, NANOGLOWA used new prototype modules. For the testing in the power plant, two membrane modules are in development that can contain around 1 m2 of membrane area. In the run-up to the start of the project the academic partners have already started work and filed two patents. During the course of the project a further patent has been filed.

In the simulator, the nano-structured membranes, looking like a bunch of straw or hundreds of fibres of the same size, bound together, are exposed to the gases of an artificial flue gas generator.

Carbon capture is an important part of EU's environmental strategy in order to reduce greenhouse gas emissions. In a document about CCS (Carbon Capture and Storage) from 2008, the European Commission said that 'the technology of carbon capture and storage has the potential to contribute to the EU's climate goals and to the security of its energy supply, but it must be deployed safely and with the support of the public and stakeholders.' The EU is committed to a 20% reduction by 2020 and 50% by 2050. CO2 capture by membranes is part of the technology race to hit these targets.

The potential industrial impact of a breakthrough in this field is enormous. When this is reached and the production of cheap and effective membranes becomes possible, a whole new membrane industry will be created and this technology will render existing coal-fired power production more environmentally benign. The development of the membrane modules is largely the domain of the small and middle-sized enterprise (SME) partners. One SME, for example, is looking to adapt its existing module products for use with the nano-structured membranes. Eventually, NANOGLOWA's applications could also be of interest to other industries, such as refineries, cement manufacturers and steel making. The project's nanomembranes could be an ideal alternative to the conventionally used and currently so-called 'scrubbing' technology whereby flue gases are made to flow through a solution in which CO2 binds with amines. These membranes would be much more energy-efficient, cleaner and cheaper.

Electrical energy storage has become a critical issue in the new clean energy economy needed to fight global warming and addresses the issue of dwindling fossil fuels. Where smaller, better distributed generators become indispensable, a substantial breakthrough in the performance of rechargeable lithium batteries, alongside other technologies, may have an important potential impact in this context.

The use of nanomaterials by **ALISTORE Network of Excellence (Advanced lithium energy storage systems based on the use of nano-powders and nano-composite electrodes/electrolytes, http://www.u-picardie.fr/alistore/)** has built on European progress in the field of lithium-ion batteries.

Rechargeable lithium batteries, which can be found in mobile phones, digital cameras and laptops, are struggling to meet current technological demands in terms of lifespan and performance, especially on a large scale. The technical problems stem from an imbalance between power input and power output, a process called hysteresis.

The project's partners, accounting for the majority of European leading research in the field, concentrated their efforts on developing an advanced lithium high energy and power storage system which is efficient and cost effective, based on the use of nanopowder and nanocomposite electrodes and electrolytes. This means stopping reliance on bulk materials and instead exploring the design of new charge-storage materials in nanometric forms.

This development can potentially make sure that market penetration of hybrid and electric vehicles can be strongly increased, ensure the quality of renewable solar and wind electricity and also improve the UPS (uninterruptible power supply) back-up system. All these factors could obviously help to reduce reliance on fossil fuel.

ALISTORE chose nanomaterials able to withstand structural strains and which ensure a longer battery life. Further advantages are a shorter diffusion path, which enhances electrode power capabilities; larger double layer capacitance and enhanced solid state reactivity that will enable kinetic limitations to be bypassed. As a result, new reactions offering staggering capacity gains are becoming feasible. Costs are decreased while safety is preserved.

Exploiting the properties of self-organising titanium oxide nanotubes with a specific focus on dye-sensitised solar cells is the challenge tackled by **TI- NANOTUBES (Preparation, Characterization and Application of Self-Organized Titanium Oxide Nanotubes)**. The project demonstrated that it is possible to develop new photo-active nanotube systems and the main innovative aspect is the application of new nanotube structures that have been produced by anodising under different experimental conditions.

The project achieved surface chemical modification of the Ti-Nanotubes by noble metal deposition and the doping is performed for direct application in photocatalytic processes, including fabrication, modelling and evaluation of photocatalytic reactors for efficient photodegradation of water and air pollutants. Eventually, super-hydrophylic surfaces with self-cleaning and anti-fogging properties will be developed.

The project achieved the design and processing of new systems consisting of titanium or other valve-metals with enhanced properties for their application and use in the field of nanotechnology. It also generated new knowledge by fundamental research on the TiO2 nanotube structures, including self-organisation effects together with their mechanisms. A new photoactive nanotubes system has been successfully developed.

This clearly has potential for the environmentally safe production of a new generation of highly efficient, cost-effective solar cells. Although there is no company participation in the project, the industry is already very keen on **TI- NANOTUBES technology**.

Another effort in nano-photonics was led by **N2T2 DEVICES (Novel Nano-Template Technology And Its Applications To The Fabrication Of Novel Photonic Devices)**, which aimed at developing novel nanoforming technologies based on the patterning of porous anodised alumina (Al2O3) and their application to the construction of organic solar cells, quantum dot-based photonic LEDs/Lasers and photonic crystal structure elements. The project produced some demonstration prototypes of these devices. There was a high industrial presence in the consortium, leading to the commercialisation of the project's results.

Nano-etching may look like patterning the very fabric of the future, as the nanodesign is bonded into a given surface. However nano-structuring technology extends to coatings too, and its possibilities are so exciting that a project like **N2P (Flexible production technologies and equipment based on atmospheric pressure plasma processing for 3D nano structured surfaces, http://www.n2p-project.eu/)** brought them together in an integrated way.

Outstanding progress has been made in recent years in developing novel structures and applications for direct fabrication of 3D nanosurfaces. However, exploitation is limited by lack of suitable manufacturing technologies. N2P develops innovative in-line high-throughput systems based on atmospheric pressure surface and plasma technologies. The two identified approaches to direct 3D nano-structuring of surfaces are etching for manufacturing of nanostructures tailored for specific applications, and coating.

The project focused on four major areas: structures for solar cell surfaces, biocidal surface structures, carbon nanotubes on electrode surfaces and tailored interfaces. The applications range from solar cells, infection control, energy storage and interface control for the automotive and aeronautics industry.

Solar cell performance is significantly affected by an optimised 'light management' to improve the energy harvesting properties of the solar cells. Nano-structured surfaces have the potential to improve efficiencies of cells by up to 25%, with a dramatic impact on their commercial viability.

In biocidal surfaces N2P combined nanosized antibacterial materials with 3D surface nanostructures, which will both immobilise and deactivate pathogenic organisms on surfaces. These have been shown to kill dangerous bacteria such as E Coli, Clostridium difficile and MRSA (Methicillin-resistant Staphylococcus aureus), and they could eventually be used on hospital equipment.

The project has achieved results in the direct growth of aligned carbon nanotubes on electrode surfaces that could be used in capacitors with high power density, which are seen as key components for energy storage systems, with possible applications in hybrid electric vehicles. The main objective is the development of such economic growth processes on metal electrode surfaces.

Tailored interfaces can achieve durable adhesion on polymer surfaces by 3D nano-structuring and coating, which means reduced energy consumption by introducing lightweight materials, for aeronautics and automotive. The beneficial effect of SiOx-based coatings as an adhesion-promoting interface has been demonstrated for titanium. Long-term stability of bonds has been improved compared to industrial standard wet chemical treatment, which needs to be replaced in due course.

The project is developing prototypes and materials demonstrators in all impact areas. The vertically integrated consortium has a major industrial presence including seven technology-leading SMEs, four multinational companies from the photovoltaics, aeronautics, automotive and steel sectors and nine institutes for industrial research.

Summoning the forces in action on the nanoscale, with a view to measuring and using them to assemble objects, was the goal of **PARNASS (Parallel nano assembling directed by short-range field forces).** In the macro world, forces such as gravity can be used to manipulate objects. However, different forces occur on the nanoscale. Although this was a fundamental challenge, this work could lead to better sensors, smaller and faster computers.

In order to overcome certain disadvantages deriving from current nano-object assembly, such as their difficulty in being used in complex arrangements and the slowness of manipulation of single atoms and molecules by using microscopy, theoretical studies were carried out on these forces at first, followed by the design and execution of experiments to ensure the theoretical models were correct and to measure the forces. In these experiments, the project used carbon nanotubes and carbon nanowires (CNWs).

Finally, PARNASS developed carbon nanotubes-based sensors by using its own techniques, which have been integrated into devices capable of sensing chemicals at very low levels. The project filed one patent and developed a modified scaling force microscope.

Nanotechnology could bring about a life-changing revolution in water treatment. The cross-over Nano4Water cluster (http://nano4water.eu/) hosts a coalition of research projects, funded by the European Commission following an Seventh Framework Programme (FP7) Joint Call on nanotechnologies for water treatment together with the Directorate-General (DG) Environment of the

European Commission. The aim of this action is to support research and technological development (RTD) in this field by applying developed or adapted nano-engineered materials to some very promising separation, purification and detoxification technologies.

Out of the water treatment projects mentioned here, MONACAT, MEMBAQ and WATERMIM are funded by the NMP (nanosciences, nanotechnologies, materials and new production technologies) Theme, whereas NEW ED is funded by the Environment Theme together with Nametech and Clean Water.

MONACAT (Monolithic reactors structured at the nano and micro levels for catalytic water purification, http://www.monacat.eu)

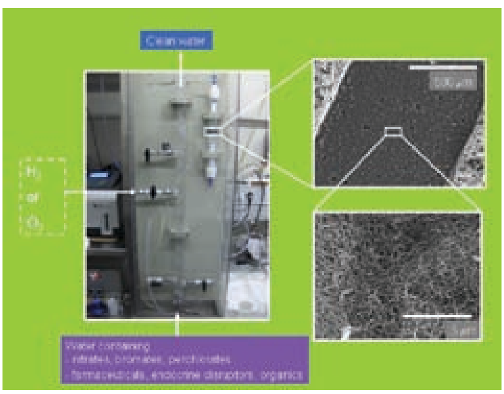
The project is developing a catalytic process to destroy or remove persistent pollutants such as pharmaceuticals, endocrine disruptors, perchlorates, bromates and convert organic matter into CO2. Nitrates are converted to nitrogen. The big advantage is that MONACAT doesn't get any residues, so it is a more sustainable process.

The original methodology consists in the preparation of novel materials based on carbon structured at the nano- and macro-levels. MONACAT has developed catalyst nanoparticles which are very well attached to macroscopic structured reactors (ceramic and metallic honeycomb monoliths, metallic filters, carbon cloth). The water is made to flow through the reactor.

The nanocarbon materials (NCMs), namely carbon nanofibres (CNFs) and carbon nanotubes are porous, but not loose, so they are resistant to attrition and stress. This also means there cannot be any nanoparticle leaks whatsoever. By the control of the preparation at different scales, it is possible to intensify catalytic water treatment processes, such as reduction of nitrates and catalytic oxidations, thereby decreasing energy consumption and by-product generation.

Some partners prepare and characterise the catalysts, others build the plants to test them and others deal with the modelling and optimisation. The catalysts are tested in the developed reactors and the best performing ones are selected. The project has devised this system of knowledge transfer in order to bring together some of the best experts in coating, catalyst preparation, process design and final users.

The structured reactor intensifies the process, as a lower pressure drop and energy consumption and enhancement of the destruction rate of the pollutants are reached. Also, the selectivity is increased in the sense that the occurrence of undesired secondary reactions is reduced. A mathematical model of the treatment process has been developed.



Design of the oxidation or reduction reactor using a nanostructured catalyst

MONACAT's technology is relatively inexpensive. In fact, the project uses hydrogen or ozone gas as reactants; also, the structured reactor is very robust and compact and easy to transport, which would make it ideal in the case of developing countries.

The potential use of this technology is enormous because nowadays there is no established technology for the removal of emerging pollutants. The potential of this technology is being validated by one of the project's industrial partners, which is an international company specialised in water treatment worldwide.

Aquaporins are ubiquitous proteins in living cells and have often been described as one of the great promises for the future of water treatment, although the smaller quantities of the ultra-pure water they can potentially produce, and the frequent need to replace them, at the moment might appear to be more suitable to the needs of the pharmaceutical industry than to those of the developing world. But they are capable of removing obstinate poisons like arsenic and mopping up any nasty pathogens from water, so their future potential use needs to be carefully evaluated.

Incorporating them into nanomembranes would replicate the way plants draw water from the soil and animal kidneys control the flow of water through them. MEMBAQ (Incorporation of Aquaporins in Membranes for Industrial Applications, http://www.membaq.eu) synthesised aquaporins from spinach DNA and engineered them into a nanomembrane made of lipids and a synthetic polymer. The result is a 3 nm-thick transparent film densely dotted with pore-like structures.

The spinach DNA is expressed in yeast or bacteria and aquaporins are subsequently harvested. Each functional aquaporin protein is made of 4 identical sub-units and set out in an almost square-like shape of about 64 nm2. MEMBAQ's nanomembranes have an almost zero permeability for salt, so they have very good salt separation properties. This is one of the aims of this ultra-pure water filter. The other thing is the very high water flux: a billion water molecules move through each aquaporin protein every second.

This would potentially make them cheaper to use than other normal membranes as they need much less applied pressure to purify the water membrane so they consume much less energy. MEMBAQ believes that aquaporins could trap just about any impurities, however small, which would normally seep through other conventional decontamination processes. There are only one or two lipid molecules between each aquaporin inside the membranes, so they are quite dense in protein. Potentially, this might mean hundreds of litres per hour per square metre of aquaporin membrane per bar.

TWO RECENTLY STARTED PROJECTS IN WATER TREATMENT

WATERMIM (Water Treatment by Molecularly Imprinted Materials, http://lpre.cperi.certh.gr/watermim) addresses the need for a new class of novel 'tailor-made' membranes and filters with high selectivity and long-term performance stability, capable of recognising and separating organic compounds such as pesticides, pharmaceutical active compounds and endocrine disruptors.

Therefore WATERMIM is focusing on the production of molecularly imprinted polymers (MIPs), one of the most promising classes of new and highly selective adsorbing materials to be used in water treatment, detection and monitoring of pollutants at very low concentrations (below 0.1 ppb). In fact, conventional methods for pollutant removal are normally non-selective and may result in secondary pollution.

So far, some novel experimental and computational tools have been developed in order to optimise the synthesis and molecular function of MIPs in an aqueous environment. The results obtained from the theoretical study have been combined with experimental data.

The gained knowledge will be also applied for the development of improved monitoring techniques based on the MIP technology for pollutant detection at very low concentration and the development of bifunctional MIP adsorbents and catalysts for the selective separation and decomposition of the target pollutants.

WATERMIM's expected prototypes are related to the production of composite membranes utilising pre-formed MIP nanoparticles. Also, MIP composite filters based on organic and inorganic support are under preparation via novel grafting techniques. Ultra-thin MIP films are intended to be used for the development of sensor devices for pollutants monitoring, since MIPs can be easily employed as recognition elements with the addition of appropriate signal transduction elements. Additionally, MIPs are combined with catalysts that are expected to provide an alternative composite separation/catalytic degradation system able not only to remove the pollutants from the water but also to convert the pollutants into harmless compounds.

This work on the development of novel and efficient MIMs is expected to promote the protection of the environment and to improve the health and safety of citizens through the use of better separation and purification systems.

It is expected that the use of MIPs will provide new opportunities and challenges to European water treatment industries, as well as to chemical, pharmaceutical and other industries.

NEW ED (Bipolar Membrane Electrodialysis for Remediation of Highly Saline Waste Streams, http://www.new-ed.eu) addresses the treatment of saline effluent waste streams from chemical production sites, which conventional technologies cannot perform in such a way that the constituents of the effluent are recovered. Instead, the saline waste streams are often discharged directly into surface waters. NEW ED aims to obtain the cost-effective conversion of salt wastes into more valuable components.

This will be achieved by the development of a new bipolar membrane technology that will enable the economical recovery of acid and base from saline wastewater streams.

Acids and bases are among the most popular commodity chemicals of the world with more than 50 million tonnes of them produced annually and converted into salt at the end of their life cycle. NEW ED electrodialysis with bipolar membranes will be able to recuperate acids and bases from their salt.

The project is developing several new manufacturing approaches to the production of these new bipolar membranes. The aspect that all these have in common is that by the combination of new materials with a well directed modification of membranes and membrane materials on the nanoscale, it is possible to produce tailor-made membrane films displaying new advanced properties regarding water transport and ion conductivity, thus overcoming the current limitation of bipolar membrane technology.

Furthermore, NEW ED looks at the whole process towards energy efficient technology, such as the optimisation of the current module technology. The products of the project will be tested and integrated into relevant production processes to prove their environmental and economic feasibility.

It is expected that the project will reduce waste production and energy consumption in various industrial production processes, which will bring a direct positive impact on water utilisation and CO2 emission. The improved technology will enable new environmentally compatible processes, strengthen industry and create new jobs.

The beneficial impacts of the project will be felt in the chemical industry, food and beverage industry, power generation and industrial production processes. NEW ED is further expected to enhance the productivity of salt splitting and to reduce investments and operating costs for acid and base production

OTHER RECENTLY STARTED PROJECTS

COMETNANO (Technologies for Synthesis, Recycling and Combustion of Metallic Nanoclusters as Future Transportation Fuels) is introducing a novel approach in the challenging field of zero-emission Internal Combustion Engines (ICEs) development. According to this approach, metallic nanoparticles are considered as potential energy carriers and transport fuels.

The project is proposing an integrated approach that deals with the entire 'fuel cycle', including: suitable raw materials, with an emphasis on the exploitation and recycling of relevant industrial by-products; efficient and environmentally-friendly processes for the production of tailored metallic nanoparticles as new fuels; studies on the feasibility and characteristics of the combustion of these new fuels under engine-like and real engine conditions; efficient onboard collection of combusted nanoparticles and recycling of the spent fuel via processes that utilise renewable means, with an emphasis on solar hydrogen technologies.

COMETNANO has demonstrated experimentally that the combustion of metallic nanoparticles under both engine-like and real engine conditions is feasible. In terms of energy release, pressure and temperature characteristics during combustion, the phenomenon occurs in a way that is quite similar to the combustion of conventional liquid fuels.

The project also proved that the collection of oxidised particles is possible with the use of filter technology with extremely high efficiency (>99%), and even higher for the very fine nanoparticles, which are regarded with more concern regarding their health effects. The recycling of spent/combusted nanoparticles has been efficiently demonstrated already for one candidate metal. The project already produced high-purity (99.5-99.9%) metal oxides from metal industry waste that can subsequently be used for the production of tailored metal nanoparticles.

A small prototype engine running on metal nanoparticles is under development and represents an end deliverable of the project. The main impact of COMETNANO will be in the field of green mobility and the development of zero-emission ICEs. Another major contribution is expected to be related to the development of technologies that will allow for the efficient transformation of industrial by-products and waste into value-added products. The use of tailored metal nanoparticles and the recycling of the respective combustion products is also a major contributor towards a zero-emission future. A good industrial involvement in the project is expected to generate further interest from the automotive and metallurgical sectors.

Improving the efficiency of solar cells through the use of organic dyes, down to single molecule photobehaviour, is at the core of **NANOSOL (Organic dyes in solar cells)**. The project is focusing on the study of the femtosecond to millisecond dynamics of some selected triphenylamine dyes in solutions and confined within a mesoporous silica material in absence and in presence of titanium dioxide. The dyes are being proposed as potential candidates for solar energy conversion with an efficiency in classical configuration up to 5.33%.

The results will be used to design confined systems for a new generation of photovoltaic cells. The expected results will be of great interest to the nanotechnology research and development (R&D) sectors working with nano LEDs, nanoswitches, drug delivery and clean energy, with particular attention paid to the branch that is developing dye-sensitised solar cells.

Nanotechnology can bring benefits to the modern paper-making industry too. **SUNPAP (Scale-Up Nanoparticles in Modern Papermaking, http://sunpap.vtt.fi/sunpap.htm)** is aiming to find new applications in this field, for instance by using nanocellulose, functionalised nanoparticles or other technologies based on nanomaterials to add value and increase efficiency to the whole process.

The project has already developed pilot manufacturing and production lines and it eventually aims to upscale its lab scale prototypes. Increased efficiency in this sector will reduce costs and use of resources like wood, water and energy, thereby reducing the greenhouse gas emissions and the environmental impact of the paper industry.

There is a huge industrial involvement in the project, including large companies as well as SMEs. By adding value to European paper products the project might strengthen the competitiveness of European industry.

ELECTRONICS AND ICT

The ever smaller, getting ever faster

Molecular electronics and supercomputers are throwing the doors open to a hyper-tech era

The ever smaller is all focused on ever bigger, ever faster achievements. Molecular electronics, nanolithography, extremely thin films and transistors are rapidly propelling research and technology towards spectacular accomplishments. Nanotechnology is throwing the doors open to a hyper-tech era in which electronics and information and communication technology (ICT) are going to become ubiquitous.

Nanoelectronics are paving the way to miniaturised supercomputers and bringing about the development of pervasive computing all the way down to the so-called 'smart dust'. It is already generating ultra-fast semiconductors and microprocessors, not to mention low voltage and high brightness displays. Nanotechnology can now realistically look forward to a much longed-for quantum computing breakthrough.

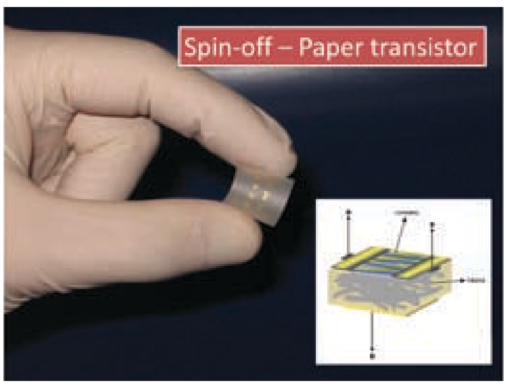
SPOTLIGHT ON...

MULTIFLEXIOXIDES (Multicomponent oxides for flexible and transparent Electronics)

The paper transistor is already here among us; a transparent computer is just around the corner. The achievements of MULTIFLEXIOXIDES represent a major move away from silicon, which can be expected to have a significant impact on European industry and society. The project addressed the need for Europe to develop novel materials and processing techniques which will facilitate the sustainable and competitive manufacture of new displays with low-cost, non-fab continuous-write technology and open up big opportunities for numerous potential long-term applications due to the availability of materials with high electrical performance.

The project focused on the development of new ceramic thin films containing multi-component oxides (amorphous or nano-structured) to be used as transparent materials, conducting, semiconducting or insulating components in rigid and flexible electronic devices. Their inorganic nature will result in environmentally stable and long-lifetime devices using existing and novel room temperature deposition

Multiflexioxides Prototype of "Paper Transistor"



techniques and non-fab–based patterning. The central focus was the design, synthesis and processing of novel multi-component oxide materials in terms of electronic, mechanical and optical properties.
The challenge of obtaining multi-component oxides for flexible and transparent electronics processed at room temperature has already brought many benefits. The electrical performance of this technology was much better than that of amorphous silicon or organic semiconductors. For large area electronics, these thin films fare much better than poly silicon, as they have a homogeneous surface, not to mention the fact that processing at room temperature allows for the use of very low-cost substrates, such as polymers.
The most recent discovery, and subject of a spin off, is the use of paper as a dielectric, which has the added advantage of being recyclable. A prototype of this paper transistor has been developed. MULTIFLEXIOXIDES also succeeded in producing test vehicles such as TFT (thin film transistors) and passive and active matrices based on the set of materials developed. For passive applications, the materials developed were used to build a fully functional chip LED flexible test vehicle. Further, fully functional and fully transparent 128x128 pixel arrays (active matrix) on glass and flexible substrates were produced. This represents a major European breakthrough.
Among the main technological achievements, there was the development of physical vapour deposition (PVD) at temperatures lower than 150°C compatible with flexible substrates. The new target materials and deposition methods used allowed the achievement of electrical performance on films and devices exceeding the state-of-the-art for low temperature processing. Novel multi-component amorphous dielectrics based in the combination of high band gap and high k-dielectrics were also developed and processed at room temperature and annealed at 150ºC, exhibiting very smooth and homogeneous surfaces, as required for device applications.
The use of oxygen to passivate the vacancies to control resistivity was a success. The project hit a world record in providing proof of concept for a transistor developed with a high saturation mobility above 50cm2V-1s-1 and ON/OFF ratios of the order of 108. Another success was the development of new multicomponent semiconductor materials for TFT and drivers applications with improved electron mobility and optical transparency and high chemical and physical stability. Several patents have been filed.
Among the potential applications there are 'smart windows' featuring completely transparent computers allowing for interconnectivity; smart labels or implemented chips, for instance to increase cheque security, and far greater resolution for mobile phone screens.

New high-tech materials for smaller, faster, cheaper memories and mobile phones are the focus of **REALISE (Rare Earth Oxide Atomic Layer Deposition for Innovation in Electronics, http://www.tyndall.ie/realise)**. This pan-European research collaboration announced the successful development of a new dielectric material, along with a processing technique that is suitable for semiconductor manufacturing. Two areas of information technology were chosen to test the new material and process – mobile phone components and flash memories – with results that exceed today's best technologies by a factor of three.

Everyone who uses a games console or digital camera is amazed by the greater and greater amounts of data that memory cards and USB flash drives can hold. One of the obstacles to storing more data in flash memory is the interference between adjacent memory cells. Inserting new dielectric materials between adjacent cells can help.

The partners in the REALISE project devised one such material, based on zirconium oxide, with the addition of just enough lanthanum oxide to ensure an atomic structure that responds strongly to electric fields. Nanoscale measurements confirmed the structure and also indicated a three-fold improvement in the relevant dielectric properties over alumina.

The technique has been perfected for laying down the new material in nanometre-thin films with the correct atomic structure. The new material is a great candidate for flash memory cards and USB drives. It is new materials like this that are needed for higher density flash memories, which may now hit the market as soon as 2014.

The second test structure was for mobile phones. Today's mobile phones contain about a dozen chips, connected together with hundreds of more mundane electronic components. Decoupling capacitors are one such component, with over 100 of them hiding inside the typical mobile phone. The size and cost of the phone can be massively reduced by patterning these components onto the chips. The challenge however is to develop a high performance capacitor that can be fabricated as part of the silicon chip.

REALISE developed high purity lanthanum and zirconium. The mixed oxide of these two chemicals was deposited in a thin sandwich between metal layers in order to fabricate high performance decoupling capacitors that are three times smaller than the current record, with the bonus of double the working lifetime. In terms of surface area on the chip, the new capacitors should cost 70% less to produce. Crucially, the project has achieved an atomically controlled deposition process for rare earth oxide layers as an enabling technology for a variety of innovative integrated circuit technologies that will allow for the continued miniaturisation and faster operation of the transistors at the heart of all computers.

Half of the project partners are industrial companies, and they are very involved in the marketing of REALISE's applications, which are highly relevant to the semiconductor industry.

Nanotechnology is always looking to exploit the properties of new materials at the nanoscale. The potential uses of carbon nanotubes in integrated chip technology are at the core of **CARBONCHIP (Carbon Nanotubes technology on Si IC's, http://www.imec.be/carbonchip/)**. Carbon nanotubes have been shown to have extraordinary properties, among which electroconductivity, mechanical and thermal properties stand out.

There is a lot of potential for carbon nanotubes to solve the current need for more power in microelectronics chip design. Copper resistivity (measuring how strongly this material opposes the flow of an electric current) has its limitations. In fact, it increases as scaling is reduced, so there will come a point where a limit is reached and scaling down can no longer continue. This new nanomaterial should allow for another few generations of scaling down within the semiconductor industry, particularly in respect to their potential for allowing transport without scattering.

CARBONCHIP concentrated on the use of carbon nanotubes in interconnects rather than transistors. The project looked to achieve very high density and selected growth of carbon nanotubes. Indeed, it made significant progress in property control of carbon nanotubes and managed to increase the density of this material from around 1010 to 1012 or 1013. CARBONCHIP also produced some very interesting carbon nanotube alignments and integrated them into silicon technology. It also developed a good understanding of the phase diagram such as the temperatures required for single-walled, double-walled or multiple-walled carbon nanotubes. It succeeded in depositing the carbon nanotubes where required and developing a high growth yield as well.

Several patents were filed and there was big industrial participation in the project, whose achievements received a lot of interest from European companies.

Another challenge is to provide a basis for a new set of electronic technology based on the manipulation of this soft electronic matter. COMEPHS (Controlling Mesoscopic Phase Separation, http://www.physics.ntua.gr/comephs/) faced it by setting out to control an array of textured phases in certain compounds, analogous to those in liquid crystals that have the tendency to phase separate into nanoscale domains. CoMePhS aimed to control the electronic structure locally and the properties of those compounds without any need for nanoscale fabrication. By studying several materials and preparation processes the project chose the ones that are most promising for applications (manganites) and most easily manipulated.

Several patents were filed separately by the partners. The main achievement of the project was the proof of concept of the original plan to manipulate the phase separation in certain compounds. During the project, new compounds were prepared, the phase separation in manganites was mapped, the altering of the properties by external perturbations, such as pressure and magnetic field, was proved, and it was also shown that one can manipulate locally the resistivity of a superconductor by X-ray irradiation or light illumination.

Among the most fascinating discoveries over the last few years is the identification of a number of materials, principally belonging to the family of manganites, in which a spectacularly diverse range of exotic magnetic, electronic and crystal structures can coexist at different locations in the same crystal.

The project proved that it is not only feasible, but also surprisingly easy to achieve phase coexistence in chemically homogeneous manganites by using a wide range of parameters. So it is possible to tweak the chemical composition or microstructure of a sample, apply an electric or magnetic field to it or illuminate it with electromagnetic radiation. The coexisting phases may form robust magnetic, electronic and crystallographic textures of 'mesoscopic' length scales – that is in the range between 100 nm and 1 000 nm. By going down this route, COMEPHS could make a revolution in the electronic industry and create nanoscale devices with specific properties by directly manipulating the compounds in a controllable way.

This scenario would strongly impact on electronics consumers and it gives European research an edge. Industry is very keen, and overseas competition also showed a lot of interest in the project's results.

Bioprocesses, rather than materials and compounds, can of course be nanoelectronics' core business too. New approaches to the bio-mediated self-assembly and for the collective manipulation of mesoscale components are the challenges successfully met by **GOLEM (Bio-inspired Assembly Process for Micro- and Nano-Products, http://www.golem-project.eu/)**.

The project showed that DNA can effectively be used to attach beads up to a typical diameter of 10 um. It also demonstrated the functionalisation of various substrates and the attachment of particles in specific locations. The specific bonding force resulting from DNA hybridisation was measured in various situations. The project also investigated new methods for manipulating a large number of components together. Mainly three approaches were studied among which were the use of laser-induced Marangoni flow, dielectrophoresis and electro-wetting where individual droplets are used to carry components. In particular, the use of laser-induced Marangoni flow is particularly innovative, and indeed it was the first time that a laser could be shown to manipulate large-scale components.

The biggest technological achievement of GOLEM has been the implementation of a complete test platform based on mobile microrobots to test micro-assembled components. The originality here has been to propose a flexible, yet ultra-accurate probe station based on advanced stick-and-slip piezo-technologies. A remarkable technological achievement on this aspect is the miniaturisation of a high-voltage power source that is now embedded on the mobile robots.

Several prototypes were tested. The three manipulation principles were demonstrated, showing the collective manipulation of several components. As proof of concept, the project's team attached functionalised beads at specific locations on the same substrate and demonstrated the principle of a bioinspired assembly. The impact on society may still be a few years down the line, when these tools will be applied to assemble meso-scale components without the need for large facilities. This down-scaling of production means it has a potentially direct impact on society as it reduces the footprint of traditional facilities for microsystems assembly as well as their impact on the environment. A GOLEM spin-off company is selling a probe station based on the project's achievements and an industrial partner is marketing a newly developed, new high-frequency / high-voltage amplifier.

AMNA (Addressable Molecular Node Assembly – a Generic Platform of Nano-scale Functionalised Surfaces Based on a 'Digitally Addressable' Molecular Grid) focused on a generic platform of nanoscale functionalised surfaces based on a 'digitally addressable' molecular grid. The main challenge was the possibility of using molecules to build nanotechnology systems from the bottom up instead of from the top down. The project achieved a world first in showing, by using digital recognition strategies based on DNA, that it is possible to build up supramolecular structures that were universally addressed. This was the first time that nanotechnological structures had been built up with sub-nanometre precision instead of using top-down approaches such as lithography. Application areas include not only new electronics, solar energy conversion systems, computational systems and future molecular electronics, but also biotechnology applications such as improved array and binding selective diagnostics and, in a longer perspective, therapeutics for healthcare.

NANOMESH (Nanomesh - Boron Nitride Nanomesh as a Scaffold for Nanocatalysts, Nanomagnets and Functional Surfaces, http://www.nanomesh.ch/) was a fundamental science project aiming to understand the self-assembly processes and determine how the atoms sit within the nanomesh structure and what can be done with it. The nanomesh is a single layer of Boron Nitride formed by self-assembly on to rhodium metal into a very regular nanostructure, which is greater than 350 atoms. The project discovered that the nanomesh can act as a scaffold for metal clusters and molecules.

NANOSPIN (Self-Organised Complex-Spin Magnetic Nanostructures, http://www.nanospin.le.ac.uk/) researched the use of magnetic nanoparticles for single nanoparticle data storage. The project achieved the synthesis of new nanoparticles <5 nm, comprising a core and multiple shells, the so-called nano-onions, with stable magnetisation at room temperature. It also managed to organise them onto a surface in a uniform array and developed a way of reading and writing data into the array, which was achieved at 40 nm resolution, a world record at the time. Additionally, the nanoparticles developed in the project were found to be efficient at generating cancer hyperthermia. The aim is to develop a method for ultra-high–density storage, as existing magnetic storage is likely to reach its limit in the next few years.

SPANS (Single Particle Nanophotonic Switches (bridging electron microscopy and photonics), http://dipc.ehu.es/spans/) studied the underlying physical mechanisms of optical switching based on single-particle phase transitions triggered by light or electron beam excitation and also investigated the feasibility of constructing new types of nanophotonics. The project provides a new paradigm for optical data processing with potential impact in telecommunications and computation technologies by large-scale assembly of such switches in new photonic circuits and will play key roles in other technologies such as intelligent, high-resolution imaging systems and new artificially engineered metamaterials with properties not available in nature. The project also developed new techniques to study nanophotonic structures by combining nanophotonic with electron microscopies. Simple scanning electron imaging providing resolution below the nanometre was combined with other techniques such as cathodeluminescence, equivalently designed as Electron Induced Radiation Emission and electron energy loss spectroscopy, to determine optical properties of photonic and plasmonic structures.

TASNANO (Tools and Technologies for the Synthesis and Analysis of Nanostructures, http://www.medinfo.dist.unige.it/Tasnano/) focused on realising modular parallel scanning proximity probe arrays with integrated piezoresistive readout and their individual and/or modular nanofunctionalisation giving nanotechnologists a new generation of tools for molecular level characterisation and manipulation methods. Industrial applications include sensing, electronics and the life sciences industries, for instance in the field of biomedical sensors, where ideally antibodies might be detected from a drop of blood. A demonstrator has been developed and there is some interest in commercialising the project's results.

ULTRA-1D (Experimental and theoretical investigation of electron transport in ultra-narrow 1-dimensional nanostructures, http://www.jyu.fi/static/fysiikka/id4/) studied the fundamental size limits, when the electron transport in 1D systems can be considered qualitatively similar to macroscopic regime, and explored qualitatively new phenomena appearing below the certain scale. The project focused on fabrication, theoretical and experimental study of electron transport in the state-of-the-art narrow 1D objects, such as normal metals, superconductors, semiconducting heterojunctions and carbon nanotubes and it pushed the limit of 1D object fabrication down to the ~ 10 nm nanoscale.

RECENTLY STARTED PROJECTS

The formation of nanometre-scale structures with novel optical or electrical properties, using metal **or semiconductor nanocrystals and organic molecules is the ambitious goal of FUNMOL (Multiscale Formation of Functional Nanocrystal-Molecule Assemblies and Architectures, http://www.funmol.eu)**. The project brings together an interdisciplinary consortium comprising leading European universities, research institutes and industrial partners.

Key scientific advances achieved within FUNMOL to date include the first demonstration of nanocrystal structures joined by single organic molecules, the development of novel 'anchoring' molecules for stabilising metal nanocrystals (a patent has been filed), the development of new classes of biomolecules for future sensing applications (another patent has been filed), the demonstration of novel light-induced (and electrochemically-induced) properties in nanocrystal molecule network and the development of real-time processes for quantifying formation in solution of molecule-bridged nanostructures with novel optical characteristics.

Three major industry partners play key roles in the project, from assessment of the technological potential of new scientific knowledge generated, through to the co-development of low-cost methods for production and processing of nanomaterials and nano-enabled devices. Key technological targets include three major developments: printable nanocrystal-organic layers for optical and temperature sensors, printable nanomaterials for flexible displays and specific methods for monitoring the electrical properties of assemblies of biomolecule-linked nanocrystals for diagnostic applications.

The scientific and technological innovations within FUNMOL are ultimately focused on improving quality of life and industrial competitiveness in Europe. Their applications would include the production of versatile sensors for medical diagnostics applications, new generations of specialist nanomaterials and new processes for incorporation of nanomaterials into low-cost sensors and electronic devices.

It is critical for European industry to develop new knowledge and low-cost, scaleable processes for assembly and electrical interfacing of these multifunctional materials with conventional contact electrodes in order to produce them into tailored devices and products, in particular on low-cost substrates. The project is on its way to deliver substantial innovations in this field.

Photo-actuating materials expand or contract when illuminated with light of the appropriate wavelength and have the potential to be incorporated into devices. These materials have been explored by **NOMS (Nano-Optical Mechanical Systems, http://www.noms-project.eu)** and carbon nanotube-enriched polymers have been developed, which actuate when laser light is shone on the material.

The project will be bringing this technology to maturity by getting the material to behave according to a set of specifications and then to integrate into a device. NOMS aims to develop a tactile display for the visually impaired by the end of the project period, which may be attached to computers, iPods or mobile phones. The tactile display will be tested on adult volunteers.

Technology for the visually impaired is currently rather archaic with no refreshable media where an image may be felt. To feel an image, a print out using special paper is required. Instead, NOMS's tactile display will allow for the images to be felt across a range of refreshable media. There has recently been enormous growth in consumer devices with touch screens (e.g., iPhone), and tactile displays installed in such devices would also potentially be useful for sighted individuals.

Recent research across the Atlantic investigated tactile displays and found that they reduce sensory overload as vision is not being relied on to the same extent. During the course of the project one of the partners will use the prototype tactile display to conduct fundamental research into how the brain processes tactile information. Additionally, the biocompatible material may have biomedical applications, so another significant benefit is envisaged.

There is a very high industrial involvement within the project, which is expected to have a significant impact due to the societal benefits and the large variety and volume of consumer devices that may eventually incorporate such technology.

Over the last few years, enormous technological achievements have been made in the field of organic electronics and photonics and some applications such as light-emitting diodes, photovoltaics and flexible electronic paper are now in an advanced stage of commercialisation. However, new functional organic materials are still missing to enable the next generation of applications. **ONE-P (Organic Nanomaterials for Electronics and Photonics: Design, Synthesis, Characterization, Processing, Fabrication and Applications, http://www.one-p.eu)** is addressing this challenge face on.

These materials should enable new or enhanced properties in electron transport, conversion of photons into electrons and/or conversion of electrons into photons and being printed in a continuous process. The project aims at developing the missing high performance, low-cost multifunctional materials and their process technology to strengthen industrialisation of the electronics and photonics sector in Europe. It is a big consortium involving 11 European countries and the major players in the field, with a heavy industrial and academic presence. This synergy and the integration of complementary competences on Design, Synthesis, Characterisation, Processing, Fabrication and Applications is driving ONE-P forward.

Through such an integrated approach, the project's partners are developing organic semiconductors, dielectrics and conductors for air-stable circuits based on complementary logic; materials and nanostructures for low-cost photovoltaics and photodetectors, by producing devices with performance that goes beyond the current state-of-the-art; light emitters for organic light-emitting diode architectures and light-emitting field-effects transistors; functional self-assembled monolayers for application in functional opto-electronic interface devices relevant to the other work projects (WPs) and also aimed at the next generation of applications such as rectifiers, switches, ultra-capacitors and sensors.

ONE-P is also processing methods upscalable to large area for continuous fabrication of multilayer functional material stacks and devices with electronic and photonic functionalities. The project aims to develop new materials and formulate methods rather than to achieve specific technological demonstrators. However, at project mid-term three patents have already been submitted. Manufacturing processing for electronic devices on large area plastic substrates has been patented and two sensors have been developed: the first is a new strain sensor, with durable, fast and completely reversible responses and a sensitivity one order of magnitude larger than most commonly used electromechanical sensors, and the second is a gas sensor for detection of NO with a world record in solid state sensing.

By generating new knowledge in the field of organic materials and their process technologies and enabling technologies, the project will develop a knowledge-based industry in Europe and thus create high quality jobs in industries, and also generate new applications with a positive impact on health, security, safety and environment. These include lighting, lasers, optical tags, logic and memory devices, photovoltaic cells, photodetectors and new sensors for medical purposes, security and food safety.

Europe is currently a major player in the organic electronics industry. In order to maintain that position, new functional materials and their process technologies are needed. The industrial involvement in ONE-P is a good indicator of the industrial interest and will provide an efficient exploitation path.

INDUSTRIAL APPLICATIONS

At the sharpest cutting edge of high tech

From nano-patterning to tailorable nanocomposites, nanotechnology's race to etch the future is full on

At the sharpest cutting edge of high-tech applications, these industrial products and processes span across all R&D nanotechnology clusters. A significant sample of them includes anti-biofouling nano-patterning, scanning probes using focused ion beams, multifunctional nanocomposites including the highly versatile, tailorable inorganic-organic kind, nanorobotics for manipulation and assembly techniques, nanocapsules for targeted drug delivery, new nanoscale optical instrumentation and integrated sensors to detect gas, fungi and bacteria for medical and environmental use.

The future is already being etched by a range of techniques called nano-patterning, which involves the way layers of a surface are arranged or designed. It's a completely new, safe way of shaping the very structure of a material for industrial use and of endowing it with extraordinary properties at the same time.

SPOTLIGHT ON...

AMBIO (Advanced nanostructured surfaces for the control of biofouling, http://www.ambio.bham.ac.uk/)

ManMany outstanding benefits are indeed gained when nanotechnology can replace toxic conventional materials with non-toxic smart ones. Biofouling is a case in point. It is the undesirable accumulation of aquatic microorganisms, algae and animals increasing the ship's drag, which can reduce the performance of vessels, make fuel requirements sorely expensive and increase greenhouse gas emissions.

The other big concern about conventional technologies is that some types of currently used biocide-containing coatings have been found to be deleterious to non-target species. Finding suitable alternatives is now a legislative requirement in the EU, due to a more stringent environmental protection regulation.

AMBIO has devised an original way to get round all these problems by building a nanopatterned, environmentally-safe coating to fight biofouling, which can be painted directly on the hull of boats or ships. Biofouling organisms are 'confused' by the nanopatterned surface and they cannot stick strongly to the hull.

A combination of hydrophilic and hydrophobic polymers produces a highly sophisticated amphiphilic surface, meaning that both kinds of surface property can coexist. In fact, the polymers seem to distribute themselves spontaneously into the different patches of the nanopatterned surface. The AMBIO technology allows for these materials to be mixed, at which point they spontaneously start separating into these two different phases at the nanoscale.

The potential beneficial impact of these new coatings on the shipping industry, marine life and human health is enormous. Biofouling carries a fuel penalty ranging from 20% to 80% depending on the degree of fouling. It has been calculated that about 384 million tonnes of CO2 could be saved worldwide by eliminating the extra drag problem caused by biofouling. The nano-patterning technology is also safe, in that there are no nanoparticles inside the paint that could potentially leak into the water because of wear and tear or corrosion. So nano-patterning applied to this field is about providing non-toxic alternatives to current technologies.

The project initially carried out the biological testing by using larvae of barnacles and marine algae. It has been established that a biofilm can add up to 20% drag, and fouling by seaweeds and barnacles over 60%. Environmentally-safe coatings will not only reduce soaring fuel costs and reduce the carbon footprint of the shipping industry, but also minimise the risk of transporting invasive aquatic species and cut down on the input of biocides into the environment.

Among the project's other achievements, fundamental advances have been made in the understanding of how subtle changes in interfacial properties influence fouling organisms. For example, self-assembled monolayers of oligo- and poly-ethylene glycols have clarified the importance of hydration, surface charge, elasticity, conformational degrees of freedom and interfacial characteristics in creating a surface that repels the attachment of marine organisms.

In addition to the amphiphilic nanopatterned coating described above, several other prototype coatings have been successfully tested and AMBIO attracted a high industrial interest, given that the total global market for antifouling coatings for ship and pleasure craft tops EUR 500 million every year.

AMBIO's 31-partner consortium included 15 companies and featured the world's largest manufacturer of marine coatings. The project will commercialise its developments, especially with the strong contribution of SMEs in manufacturing. EU companies are world-leaders in anti-biofouling coating technology with 70% of the global market share, so it sounds fair to say this technology should allow European industry to keep its competitive edge.

Nano-structuring is one of the prime aims of **FIBLYS (Multi-functional Analytical Focussed ion beam tool for nanotechnology, http://www.fiblys.eu)**, together with nano-manipulation and nano-analysis. For this purpose the project is developing, designing and building a single tool combining nanostructures, nano-manipulation, nano-analytic and nanovision capabilities in a hybrid scanning probe (SPM) and dual-beam focussed ion beam (FIB) instrument (including scanning electron microscopy (SEM) capabilities).

The core is composed of a Focused Ion Beam (FIB) and an Electron Beam in a Scanning Electron Microscope (SEM) – combined with a nano-manipulator with Scanning Probe Microscopy (SPM) capabilities.

It combines two microscopes, namely a SEM which enables fast, real-time imaging while the SPM goes to atomic resolution.

This allows for nano-analysis and nano-structuring/ manipulation options that single instruments or sequential use of the techniques are unable to achieve.

In order to improve the analytical capabilities of the core, the project is further developing

- a standard Energy Dispersive X-ray Spectrometer (EDX);
- an Electron Back-Scatter Diffraction (EBSD) option;
- a Time-of-Flight Mass Spectrometer (TOFMS);

nano- Electron Beam Induced Current (EBIC) or nano-cathodeluminescence (CL) capabilities via the integrated SPM.

Thanks to the recent advances in nanotechnology, a growing need has been observed for nano-structuring, nano-manipulation, nano-analytic and nanovision capabilities in one unique 'multi-nano' tool.

FIBLYS will enable users to prepare new structures by FIB milling or EBID/IBID deposition, to view results either by real-time SEM or by SPM with atomic resolution, to analyse samples by EDX, EBSD, TOF, EBIC or CL, and to perform nano-manipulation.

Users will benefit from the option to add or subtract material at the nanoscale while viewing the processes, which provides for the option to get structural and analytical information at the nanoscale and sequentially (3D tomography) on 3D surfaces.

Inorganic-organic nanocomposites are so-called hybrid and they hold enormous potential. They are a new, versatile class of materials with manyfold applications due to their tailorable mechanical, optical and electrical properties. At the same time, there are still major drawbacks obstructing a broader exploitation of electrochromatic technologies, such as high costs, poor colouration efficiency or lacking compatibility with plastic substrates.

NANOEFFECTS ended in 2007 and it is now being followed up by **INNOSHADE (Innovative Switchable Shading Appliances based on Nanomaterials and Hybrid Electrochromic Device Configurations)**, which is aiming to solve these problems by developing new conductive polymer-based nanocomposite materials. The project is also looking into how to equip ophthalmic plastics with transparent conducting oxide films, and how to design and characterise polymer electrolytes and ion storage layers suitable for use in spectacles.

The project has already produced chemical precursors and quality coatings, and it has demonstrated product stability and adjustable colour. This will potentially lead to the development of electrochromic eyewear, anti-static coatings, new conductive polymers and plastic glazings, smart textiles and transparent conductors for plastic substrates. The project has a good industrial involvement.

The impact on different application areas is going to make a difference on European key markets, such as sunglasses and safety goggles manufacturing and production of smart textiles; the automotive industry will also benefit from new automotive glazings. Surface treatment companies and producers of fine chemicals, just like the electronic industry and possibly toy manufacturing, should all be beneficially affected too.

The main scope of **NAIMO (Nanoscale Integrated processing of self-organizing Multifunctional Organic Materials)** is to add ground-breaking multifunctionalities to nanoelectronics materials in cost-effective and environmentally friendly ways. Its distinctiveness lies in transforming a plastic film substrate into a multifunctional composite.

The project aims to make major fundamental advances in material design, synthesis, process techniques and manufacturing tools, and to provide the scientific and technological foundations needed to support the creation of a new industry of thin-film multifunctional materials for better performance of new products. To this effect, multifunctional molecules, oligomers, polymers and clusters have been designed and synthesised to deliver controlled nanostructures (10 nm) by self-organisation.

Nano-fabrication and nanoscale processing of multifunctional materials, such as self-assembling, phase separation, dewetting and printing, were developed as well, together with processes at ambient pressure and temperature that consume little energy and produce no pollution. The project also carried out theory, simulation and modelling of materials processes and systems.

NAIMO strives to simplify fabrication at nanodimensions, so it has integrated self-assembling molecules into functional materials that self-organise into parts of devices. The project also developed nanoscale metrology and tools, such as industrial assessment of technologies developed at lab-scale and standardisation of production.

The project developed prototypes already being exploited by major companies. In particular, it contributed to the development of two major enabling technologies, such as printable metals, in particular gold nanoparticles formulated as inks which can be printed below 200°C and thus enable metal printing on paper and plastics, and molecular junctions, which combines the advantages of small and large-scale electronics in an industrial process.

The project also contributed to the emergence of an important company that has raised over USD 100 million in financing to build a specialised, scalable production facility in Germany and should soon commercialise a new type of e-reader. Another example is the creation of a spin-off from CNR-Bologna focusing on 2D optical tags to replace barcodes with electronic labels that will simplify the tracing of food products and to the commercialisation of a class of organic semiconductors.

NAIMO made a big impact on society by developing smart materials with solution-based additive manufacturing techniques such as printing. Examples include organic electronic integrated circuits and displays, sensors, flexible solar cells and magnetic structures that will directly benefit health (such as a system for better control of medicines), welfare, security and the environment, while improving the competitiveness of the European industry. These applications will minimise use of energy and cut down on raw materials consumption, thereby contributing to the well-being of European citizens.

NAIMO filed more than 350 papers and 15 patent applications, and it trained more than 50 young researchers in the field of organic electronics. A major industrial partner invented the molecular junctions that allow the fabrication of electronic circuits with electrodes separated only by a few nanometres. This could pave the way towards the industrialisation of molecular electronics, which is the use of molecules as ultimate electronic components.

Developing a robotic system suitable for untrained operators for the characterisation and manipulation of nano objects was at the core of **NANORAC (Nano robotics for assembly characterisation)**. The difficulties of handling nano objects result first from the domination of intermolecular and adhesion forces over inertial forces at nanoscale. The dynamic behaviour of the simplest nano objects thus becomes unpredictable and elementary manipulation tasks (grasping and especially releasing) are difficult to perform.

Perception is the second main barrier limiting nano-manipulation. The drastic difference between the nano- and the micro-worlds is the lack of direct imaging. Viewing small nano objects is only possible through non-optical tools like the SEM, which only provides 2D images (insufficient for accurate positioning), and the Atomic Force Microscope (AFM) allowing 3D perception, albeit with scanning delays and a definitive impossibility of performing at the same time as sensing and manipulation.

NANORAC has achieved good results in the modelling and real-time simulation of the dynamic behaviour of nanoscale objects in their environment; the development of micro- and nanogrippers, as well as control strategies for manipulating nanoscale objects; the visual and haptics feedback for the human operator to surpass the unfamiliarity of nanoscale manipulation; the generation of regularly structured nanotube samples for test purposes and the global assessment of the developed hardware and software tools with respect to representative nano-manipulation tasks.

A prototype was built combining a nanohandling station, a set of nanogrippers, a SEM imaging system and a man-machine interface providing haptics and visual feedback based on virtual reality techniques. Developing efficient nano- and micro-manipulation techniques will be a crucial breakthrough in a number of application domains (in RTD departments rather than for production), in particular where Nano- or Micro-Electro Mechanical Systems (NEMS/MEMS) are considered. But the use of SEM imaging, carbon nanotube technology and virtual reality (VR) at nanoscale is also more extended and ranges from education in nanophysics to microbiology.

The project established and maintained good contacts with companies working in SEM imaging, nano- and micro-manipulators, carbon nanotube technology and VR (more precisely, simulation and haptics) at the nanoscale.

The early necessity of nano-patterning was anticipated by **NAPA (Emerging Nanopatterning Methods, http://www.napaip.org/napa/)**, which integrated the new methods into one project and responded to the increasing need for technologies, standards and metrology required to harness the new application-relevant properties of engineered structures on the nanoscale.

NAPA aimed to provide low-cost scalable processes and tools to cover the needs of nano-patterning for a number of applications. To achieve this, it concentrated its work in the field of nano-imprint lithography, soft lithography & self-assembly and MEMS-based nano-patterning.

The project addressed both embryonic and application-oriented research and it developed a nano-imprinting device using Step and Stamp Imprint Lithography (SSIL) for the mass production of solar cells and nanoscale bio-analysis platforms. The nano-imprinting stepper uses a small patterned silicon chip as a stamp, the pattern of which is copied onto a polymer layer by imprinting. The polymer layer can then be used for replicating small sub-100 nm scale geometries onto larger areas.

This technique is faster and less expensive than other techniques and is easily adaptable for printing on new functional materials or using 3D geometries. A printer was also developed combining the new nano-patterning method with gravure printing and flexo techniques in one process run.

The consortium brought together the leading European research and major industrial companies active in the field of nano-patterning.

NANOCAPS (Nanocapsules for Targeted Controlled Delivery of Chemicals) devised new methods for the micro-encapsulation and controlled release of chemicals. Metal plating is an obvious application as paint-containing nanocapsules allowing for better protection against corrosion can bring about a reduction in production costs of European car producers, as current surface treatments make up for about 30% of production costs.

The project developed nanomaterials and nanocomposite coatings for cost-efficient production of nanocapsules, which also found their way into biomedical applications, such as anti-proliferating and anti-allergic agents against mite infestations, as the chemicals can last longer and be more efficient. The other obvious potential application is in targeted drug delivery in cancer treatment.

Basically, the shell was built with a layer-by-layer approach and the prepared capsules can then be loaded and released according to a variety of external stimuli such as a change of pH, temperature and light. Membranes were also used, which allow for larger amounts to be prepared, and a membrane producer was achieved.

Their use in implant manufacturing will be beneficial once the production and manufacturing of the nanocapsules-based coatings starts in Europe. A potential anti-fouling property of coatings containing nanocapsules can also be envisaged.

Although NANOCAPS did not plan to market its achievements, demonstrators are expected within the follow-up MUST project. There have been five patent applications and one patent has now been filed. Industry is very keen on the large number of potential applications, such as corrosion reduction in transport industries.

MIPs are one of the most important technological and scientific challenges in the fields of biotechnology, separation, purification, analytical science, catalysis, biomedical and environmental applications. Particular advantages to be realized by MIPs are the low preparation cost and the potential utility in situations where no recognising biomolecule is available. **NANOIMPRINT (Nanoimprinting technologies for selective recognition and separation, http://lpre.cperi.certh.gr/nanoimprint/)** aimed at novel synthesis routes for the economically feasible production of MIPs, such as nano- and micro-particles and membranes as well as at the investigation of MIPs for selective recognition and separation of biologically active molecules like proteins, peptides, oligosaccharides and as artificial receptors.

The project aimed at developing MIPs for the selective recognition and separation of biological molecules by using reagents and polymerisation techniques for delicate molecules such as oligosaccharides, peptides and for large structures such as proteins. It also used carbohydrate imprinted polymers as enhancers of important bioactive compounds in microbial cultures. NANOIMPRINT developed the use of MIPs as artificial receptors with high substrate selectivity and specificity in analytical techniques such as immunoassays, chromatography, capillary electrophoresis and solid phase extraction.

The project contributed to the understanding of the mechanisms controlling the molecular structure. Experimental and computational tools like molecular stimulations were employed to investigate the molecular function of MIPs, to optimise their performance and to understand interactions between the template molecule and the polymer matrix.

The ultimate goal was the reduction of the cost of fermentation processes by improving the productivity of the desired bioproducts and recovering the biomolecules such as proteins/enzymes or oligosaccharides directly from the fermentation medium, thereby skipping the purification process. Moreover, the development of improved analytical techniques with high selectivity and sensitivity based on the MIPs technology was an additional target.

From an economic point of view, the markets for intelligent materials are continually increasing. The research will provide the pharmaceutical and biomedical industry with novel approaches regarding diagnostic and analytical methods. NANOIMPRINT brought MIPs one step closer to true antibody-mimics enabling the direct use of MIPs in aqueous systems and shed light on the nature and function of the MIPs at a molecular level. In terms of sustainable production and consumption, the developed novel MIP-based bioprocesses benefited from reusability which improves productivity and profit.

NANOIMPRINT had a big industrial involvement, and its SME partners are already benefiting from new market opportunities. The research outcome in MIPs will greatly enhance the competitiveness of the European chemical and biochemical industries and generate new business opportunities in biotechnology and environmental control.

Understanding fat absorption at a molecular level with nanoscale tools can lead to better insights into enzyme function. **BIOSCOPE (Self-reporting biological nanosystems to study and control biomolecular mechanisms on the single molecule level, www.bioscope.fkem1.lu.se)** has provided new knowledge about the biomolecular mechanisms of lipase enzymes relating to the amount of fats absorbed from food.

This outcome may be of interest to the food processing industry and it could also lead to new systems for drug delivery. The project used nanoscale research tools and methodologies that allowed unprecedented insights into biomolecular mechanisms at biological interfaces on the molecular scale. BIOSCOPE considered the biomolecular system itself as a part of the nanoscopic instrument, which in various ways reports to the outside world about its current local state.

This makes it possible to study the local effects on the molecular level when a protein interacts with a biomembrane surface or when a lipase interacts with a lipid surface. The project met the challenge of producing a set of reporter molecules and developing instrumentation and methods for manipulation of enzymes and enzyme activity at the nanoscale by providing insights into the biomolecular mechanisms on a single molecule level. It developed novel forms of integration, at the nanoscale level, of enzymes and non-biological systems such as nanoparticles, artificial membranes, electrical field or force field traps.

It also confined several enzymes to surfaces of nanoparticles or membranes on a less than 10 nm scale in order to achieve a self-organised assembly with a concerted bioaction superior to the simple sum of the same individual enzymes. The function of the nanosystems was optimised for enzymatic action on biosubstrates.

Solid-supported substrates and electrodes were developed, which can be engineered in the form of the nanosensors. A prototype device was achieved by using enzymes connected to gold nanoparticles. The project also developed a prototype assay to monitor lipase activity. The world's largest producer of enzymes was a project partner. They are possibly interested in commercialisation of certain aspects of this technology, such as an assay kit.

Nanoscale microscopy was the main scope of **FORCETOOL (Multipurpose Force Tool for Quantitative Nanoscale Analysis and Manipulation of Biomolecular, Polymeric and Heterogeneous Materials, http://www.imm.cnm.csic.es/ForceTool)**, which took up the challenge to improve the spatial resolution down to 1 nm and the compositional sensitivity of nanoscale microscopy with minimum molecular distortion, so that operation can be carried out in air or liquids.

FORCETOOL demonstrated a new mode of atomic force microscopy (multi-frequency AFM) that can give improved resolution by excitation of the probe at two different frequencies, which also allows for faster microscopy.

A prototype was constructed during the project and the microscope is now commercially available. Such an improvement in optics can help the development of smart nanoscale materials to be used to improve the characterisation of electronics or textiles, and to visualise biological processes occurring in real time with moving rather than static images. It can also assist in the development of ultra fast and optical, chemical, biological sensors for use in medicine, environmental analysis and communications.

A new bioinspiration phenomenon was at the core of **QUORUM (Discovering Quorum Sensing in industrially useful Fungi, a novel approach at molecular level for scaling-up in white biotech)**, which aimed to develop a new scientific approach to the biosynthesis of industrially important products by using quorum sensing in fungi.

These findings will then be used to improve the efficiency of industrial biofermentation processes and to reduce costs. The project identified some of the signalling molecules involved and for this purpose it developed lab-scale processes which are being tested in vitro. In particular, QUORUM focused on the biosynthesis of secondary metabolites and oxidative enzymes such as laccases. In the future it may be possible to lower costs of expensive molecules thanks to this process.

The enhanced properties of carbon nanotubes in the production of gas sensors have been exploited by **SANES (Integrated self-adjusting nano-electronic sensors, http://www.sanes.u-szeged.hu/)**. Commercial gas sensors based on semiconductors are commonly available, but carbon nanotube-based ones are still quite rare. An even more important achievement by the project is an unmatched high gas selectivity, namely the ability to tell a broad range of gases apart, which is usually quite low in gas sensors. This can be of paramount importance for human safety in an industrial environment.

The aim of SANES was to develop self-adjusting sensors with multiplexing ability. The device was programmed to monitor the presence of several different gases simultaneously, but can on request 'zoom in' on a selected number of gases and measure them with much higher precision at the same time. If anything goes wrong, the smart sensor reconfigures itself in order to give the maximum integrated information to controllers.

Fluctuation enhanced sensing (FES) is a method based on the fact that the noise of a sensing system, arising from the adsorption/desorption of the analytes on the sensor surface, carries chemical information about the analyte. By analysing the output data of the sensor with a proper mathematical technique, chemical selectivity can be achieved. The method obviously has to achieve high sensitivity as well. There was a good industrial involvement which successfully delivered a SANES prototype device including a sensor chip, interface electronics and PC software. The smart sensor could hit the market within three years with applications in the automotive industry, environmental protection, healthcare and home use.

A very similar challenge, that of developing new sensors for environmental, healthcare and processing industries, was picked up by **SANTS (Synthesis and Application of Nanostructured Tethered Silicates, http://www.sants-nanosilicates.com/)** via another route, which also opens the prospect to produce new stable and efficient biocatalysts for more environmentally friendly chemical manufacturing.

Silica has a very low cost, with some untapped potential for all sorts of applications. The project focused on the tethering of silica nanoparticles, which can immobilise enzymes and retain practically all of their activity, and seriously looked into the use of tethered silicates for improved sensors and biocatalysis. An industrial involvement in the project confirmed European commercial interest.

BIO-LITHO (Biomineralization for Lithography and Microelectronics, http://www.bio-litho.de) aims to integrate the nature-mimetic biomineralisation/biosilicification processes with micro- and nanofabrication for use in the medium-long term for lithography and microelectronics. The project is focusing on the realisation of patterned, aligned assemblies of silica fibres, in order to use them as insulating layers for prototype transistor devices. Exploiting the unique ability of sponges to form silica under ambient conditions is of huge potential commercial interest for the competitiveness of European industry.

Vastly improved resolution at the nanoscale is the aim of **3D NANOCHEMISCOPE (Combined SIMS-SFM Instrument for the 3-Dimensional Chemical Analysis of Nanostructures, http://www.3dnanochemiscope.eu/)**, which combines a new ToF-SIMS (Time-of-flight secondary ion mass spectrometer) with a new metrological high resolution SFM (Scanning Force Microscope). A 3D Nano-Chemiscope has the potential to reveal the nanoscale surface chemistry and morphology mapping of a sample, which will overcome present limitations by characterising it down to at least 10 nm lateral resolution and 1 nm depth. It will also allow in situ ToF-SIMS and SFM analysis and include a controlled layer-by-layer material removal procedure. It could be a breakthrough in selectivity, sensitivity and resolution and solve real measurement problems. There is a high industrial involvement in the project.

AFM can be used to manipulate water molecules translationally across a surface. This discovery was made by **NANOMAN (Control, manipulation and manufacture on the 1-10nm scale using localised forces and excitations, http://www.nanoman.org)**. This technique could have very interesting applications in nano-assembly and repair. Although this was a fundamental science project, it has extended the application possibilities and power of AFM and it built some specialist pieces of equipment with market potential, as an add-on to existing equipment.

The development of new, ultra-fast smart nanoprobes that will allow investigation and manipulation of materials properties on a nanometre scale was the scope of **ASPRINT (Advanced Scanning Probes for Innovative Nanoscience and Technology, http://www.asprint.science.ru.nl)**. The project also looked at the magnetic and optical interactions and obtained nanomagnetic resolution when the surface was exposed to the atmosphere. The result was the development of functional probes and microwave scanning probes. The industrial partners are already using the technology.

A much needed revolution in scanning probe microscopy will come with the ability to perform scanning tunnelling spectroscopy at the same time as measuring tip-sample interaction forces and energy dissipation on selected atomic or molecular sites. **MDSPM (Equipment and Methodology for Multi-Dimensional Scanning Probe Microscopy, http://www.mdspm.eu/)**. This will allow unprecedented resolution of metallic, semiconducting and insulating surfaces. The aim of this project is to develop, manufacture and commercialise a new ultra-high vacuum (UHV), low-temperature, multi-dimensional scanning probe microscope (MDSPM) capable of impacting heavily on chemical reaction dynamics, nanoscale contacts, local energy dissipation and excitations.

DESYGN-IT (DEsign, SYnthesis and Growth of Nanotubes for Industrial Technology, http://www.tcd.ie/Physics/desygnit/index.php) wanted to help establish Europe as a leader in the design, synthesis, growth and application of nanotubes, nanowires and nanotube arrays for industrial technology. It aimed to create an efficient, clean process to start a cost-effective mass production of high quality and high purity nanotubes accessible to European industry. The industrial partners are among the leading nanotech research groups and spin-off companies have been created.

INDOT (MOCVD technology for production of indium nitride based nanophotonic devices,) developed a MOCVD (Metal-Organic Chemical Vapour Deposition) technology for the industrial production of Indium Nitride (InN) quantum dot-based devices for use in infrared emission and detection, telecommunication applications, high efficiency solar cells and electro-optic modulators. These materials also require non-toxic precursors in contrast to current technology (such as cadmium quantum dots) therefore less damaging to the environment.

Innovative dispersed nanoparticulates are needed. The practical industrial applications of nanotechnology rely on the ability to incorporate nanoparticles into products in a fully dispersed and stable state. Only then can the material express its proper functionality. This challenge was addressed by **PROFORM (Transforming nano-particles into sustainable consumer products through advanced product and process formulation)**. In order to overcome this barrier that is keeping new products from the market, the project, which had a strong industrial involvement, identified new standard methods, protocols and a databank for characterising nanoparticles and nanoparticle dispersions.

RECENTLY STARTED PROJECTS

The automotive industry would greatly benefit from a whole new generation of nanolubricants with improved performance, capable of significantly reducing friction and enhancing machine durability, which would result in substantial energy savings, reduced equipment maintenance and longer machine lifetime. This is the challenge tackled by **ADDNANO (Development and scale-up of innovative nanotechnology-based processes into the value chain of the lubricants market, http://sites.google.com/site/addnanoeu/home)**.

The project also anticipates that these new formulations will assist the durability and performance of exhaust treatment and accordingly reduce harmful emissions. The scientific challenges range from the synthesis of appropriate nanomaterials to the formulation of new lubricants with stable, functional properties and the scale up of all manufacturing processes involved.

So far, several types of novel nanoparticles have been synthesised by four partners and some of the techniques have been standardised. The nanoparticles are being included in intermediate and final product formulations for grease, engine and transmission oil applications. Tools for process design and scale-up are also being developed. One of the partners is in the process of applying for a patent in relation to the synthesis method of the developed nanomaterial. Others are expected as further progress is made.

ADDNANO is on track to provide lubricating solutions for the EU industry well beyond the current status of the art. The project's developments will also potentially lead to reduced energy loss in mechanical systems; improvement of yield, reliability and throughput of the production equipments, reduction and prediction of equipment maintenance, prolonged lifetime of the automotive catalytic converter and the reduction in size and cost due to the reduction of catalyst poisoning associated with the use of existing anti-wear components. This benefit can potentially be expanded to marine lubricants as well. The overall environmental impact would be improved fuel economy and lower CO2 emissions.

Several industrial partners from the automotive production chain across Europe are involved in the project.

The pilot line-scale extraction of proteins derived from natural and recombinant sources through the use of magnetic nanoparticles for pharmaceutical, bio and food applications is the main goal of **MAGPRO2LIFE (Advanced Magnetic nanoparticles deliver smart Processes and products for life, http://magpro2life.eu/)**. While the developments of modern gene technology promise to make an increasing number of sophisticated pharmaceuticals available, their enormous production prices will inevitably place strong pressures upon healthcare systems, even in wealthier countries.

Using smart magnetic adsorbent particles to selectively separate the target product out of a complex product mixture like a fermentation broth or bio-feed stock can drastically reduce costs. By using magnetic separation and extraction technologies to separate the magnetic carrier particles, novel processing ways emerge. This bioprocess intensification is a successful approach where inhibiting products are removed continuously during the fermentation process to increase the production rate. It is crucial to provide highly efficient process equipment, especially for the recovery of the magnetic adsorbent particles. The consortium is focusing on technologies such as continuous magnetic extraction, magnetic field-enhanced centrifugation and magnetic classification.

MAGPRO2LIFE's manufacturing routes are developed to produce magnetic nanocomposites, based on inexpensive magnetic nanofluids and synthetic monomers, with specific chemical and physical properties. Research activities include the fabrication of the magnetic nano- and microparticle assemblies; functionalising using advanced 'self-adapting' polymer materials combined with new highly specific biomolecular recognition systems; and evaluation of produced adsorbents. The patent situation is favourable for fast exploitation. Most of the relevant patents are owned by the industrially-led consortium, which makes for a rapid industrial uptake and exploitation by the company partners, which include a particle manufacturer, equipment manufacturers and users.

If applied to high-value pharmaceutical processes, MAGPRO2LIFE's technology could relieve national healthcare systems of some huge burdens. The range of prices of various industrial protein products vary enormously, but can get to several million euros per kilo for some recombinant high-value products, for example tissue plasminogen activator used for immediate cardiac infarction therapy.

Making the paper industry more sustainable by introducing renewable source materials is the aim of **PLASMANICE (Atmospheric Plasmas for Nanoscale Industrial Surface Processing, http://hlab.ee.tut.fi/plasmanice)**, which is going to develop industrial scale environmentally friendly processes and materials for paper-based packaging.

The processes and materials used in the project have already been developed and prototyped on a lab scale, and the consortium is aiming to increase them to industrial scale. The result is expected to be a reduced impact of paper-based consumer products, which would benefit the environment and society at large.

New insights into thus far inaccessible processes need to be gained if a new knowledge of the molecular biology of living cells is to be achieved. **SMW (Single Molecule Workstation, http://www.till-id.com/smw.html)** aims to combine the most important microscopy techniques into a single, user-friendly workstation.

AFM microscopes require a maximally quiet environment to yield optimal results. A light microscope, on the other hand, has moving parts, such as stage and focus drive, which couple vibrations into a system. By using novel materials and novel concepts for drive control in the light microscope and by combining them with a very 'forgiving' AFM system concept, the project has been able to increase precision and minimise dead-times between measurements.

Speed and precision combined with a lack of vibrations even in the fastest possible mode of the TILL microscope have been successfully combined with an AFM, which allows faster response times than previously possible. The project has developed a prototype combining the Agilent AFM with the TILL iMIC microscope and allowing the control of both from one software.

The impact is potentially huge. Being able to view and manipulate live cells at the same time is a major achievement. So far, light and AFM had been available on their own. Each one of these has certain limitations, in that AFM allows looking at surfaces only, whereas the light microscope is limited in its resolution. However, when used in conjunction, they will enable scientists to put together the best of two worlds within a single instrument. While interesting for basic research right away, it is expected that new application fields will open up in medical diagnostics and drug screening.

According to SMW's plans, the SMEs in the consortium will be able to increase the attractiveness of their products by being able to fully integrate a solution combining two major functionalities.

TEXTILES

Weaving the fabric of the future

Incorporating nanosensors into textiles to monitor earthquakes and switching to biotech, non-toxic dyes can make the environment safer

Whether they are designed to pick up seismic activity or they find their way into antibacterial, MRSA-resistant bandages for medical applications, or fungi is used to replace dangerous colourants, nanotechnology textiles are about high performance. Certain smart nanofabrics can clean themselves by taking full advantage of the lotus effect, or they could be UV blocking, flame retardant or may never wear out. In any case, they are likely to enter the very fabric of our lives, as they could eventually be used for wireless biomonitoring of vital functions at a distance.

Antibacterial textiles with embedded nanoparticles are going to have a major impact in hospitals and care homes, where cross-contamination of bacteria can be dangerous, especially to the elderly and the immune-suppressed. Effective control of bacteria populations in those environments will lead to reduced infection rates.

SPOTLIGHT ON

POLYTECT (Polyfunctional Technical Textiles against Natural Hazards)

Nanosensors embedded into textiles and masonry might pick up small signs of seismic activity in real time and help predict earthquakes. This new concept is called Intelligent Composite Seismic Wallpaper. Embedded informatics is an evolutionary step in the design, construction, maintenance and management of civil infrastructure.

Making these textile fibres more sensitive by embedding special nanoparticles into them is at the core of POLYTECT. The project developed these specially designed sensing nanomaterials, which display strong piezoelectric properties under the application of a mechanical force by producing an electric signal up to 1 V. As an alternative, these nanoparticles could be used to coat the master batch of the fibres.

The project also incorporated nanomaterials into cement composites for the reinforcement of masonry structures. Patenting is under way concerning the fabrication process of the nanoparticles as well as their incorporation into textiles.

POLYTECT's multifunctional textiles are made from sensors, different types of fibres, enhanced coatings and enhanced mortars. When applied to a structure the multifunctional textile becomes integrated with the parent structure and creates an intelligent construction concept.

The project's Intelligent Composite Seismic Wallpaper consists of a textile material with four different directions of fibres embedded in a special mortar. It was developed specifically to reinforce brick buildings in areas prone to earthquakes. The purpose is to stabilise and return to use buildings suffering from seismic damage and problems of static stability. The textile-mortar reinforcement system can also be used, however, as prevention to protect intact buildings. On top of that, it may be employed generally to cover cracks in buildings due, for instance, to subsidence.

POLYTECT's multifunctional textiles are made from sensors, different types of fibres, enhanced coatings and enhanced mortars. When applied to a structure the multifunctional textile becomes integrated with the parent structure and creates an intelligent construction concept. This leads to increased building strength and monitoring. This value translates into increased safety, more optimal structures, more competitive products and a better way of reinforcing and retrofitting masonry and geotechnical structures.

POLYTECT demonstrated this technology in laboratory controlled conditions, where the tests showed that the produced nanoparticles produce an electric current under mechanical stress. This property was successfully transferred into the real industrial production dispersion of such piezo-nanoparticles into organic and inorganic matrices. The cementitious composites, reinforced with the sensor-embedded textiles, were used for the reinforcement of masonry buildings, which were tested under seismic conditions.

Demonstration was given both for the reinforcement of masonry structures subjected to strong earthquakes as well as for geotechnical structures, for instance for the monitoring of sloping soil, railway embankments and settlements in dismissed mining areas with problems of subsidence.

This particular concept answers a need. In particular, the Mediterranean basin countries are rich in cultural heritage structures of which many are unreinforced stone and masonry construction. The same is prevalent in many parts of the world such as China, India, Mexico and Turkey, to name but a few. Each year we read about tens of thousands of lives lost in the collapse of masonry structures. It is not all preventable. It can, however, be greatly reduced. The concept can also be applied to address the problem related to soil movements, subsidence or to the stability of the structure, which could be endangered by seismic actions or heavy rainfalls, providing an alarm in case safety levels are breached.

Extending the life, durability, safety and reliability of infrastructures can lead to massive economic savings, which, indirectly, will stimulate economic growth. The implementation of advanced techniques in the rehabilitation of masonry structures is estimated to reduce the strengthening costs by 30% compared to traditional solutions.

Considering the huge annual bill for repairing and maintenance of the infrastructures, the estimated cost savings would be huge. Extending the durability and, hence, life of structures results in reduced overall cost of the infrastructure, which can lead to massive investment savings. Furthermore, the introduction of advanced materials and new sensor technologies in the structural repair field will lead to the development of more jobs in such industrial sectors.

The consortium had a huge SME presence and filed patents for both the sensing techniques and their application in the reinforcement of dykes. Some new industrial products have already been mar-

The awarded seismic wallpaper concept for the reinforcement and structural monitoring of masonry structures

keted by the project's industrial partners, such as the nanoparticle-enhanced coatings and mortars, and novel sensor-embedded textiles and geotextiles are also ready for sale. The composite system is also being marketed for repair and reconstruction work of damaged buildings.

A completely innovative, successful approach to making the dye industry eco-sustainable was devised by **SOPHIED (Novel sustainable bioprocesses for the European colour, http://www.sophied.net)**, which developed new biomethods by exploiting microorganisms and enzymes capable of synthesising colour compounds in an environmentally friendly way. This achievement paves the way to a reduction not only of environmental problems caused by the colourant industry, but also of treatment costs and the use of water resources.

The start-off idea was the observation that the enzymes of certain mushrooms can be used to biodegrade colourants and decrease their toxicity. Within the lifespan of the project, SOPHIED pulled off a rare feat by synthesising 10 whole new dyes complying with REACH standards of non-toxicity by using immobilised enzymes screened from fungi. To get there, the team initially collected and screened hundreds of strains for dye synthesis and wastewater treatment.

The project set out to implement a three-step plan that included a new bioremediation technology to detoxify dyed industrial waters, the use of enzymes in order to turn existing dye production into a more friendly to the environment and to workers, and the creation of new, less toxic biodyes that can be synthesised in a biological way. It proceeded to isolate 16 mushrooms with potential for discolouration, which made up for up to 90% discolouring and 70% toxicity reduction, and it discovered new enzymes for the synthesis of dyes for potential use in the textile, leather and cosmetic industry.

In its effort to develop new catalytic properties, enhanced stability and activity, SOPHIED obtained nine recombinant enzymes in five host systems. The project developed methods to fully characterise enzymes and scale up their production.

Further screenings led to the selection of 10 precursors and 5 enzymes, as SOPHIED established the mechanisms of ecocolourant biosynthesis by whole cells and enzymatic bioconversions. The 25 most promising dyes were submitted to industrial quality testing for water colour, perspiration and washing fastness, and of course toxicity testing. Out of these, the project selected 10 non-mutagenic dyes with proven low toxicity and improved industrial applicability.

No harsh conditions are created during the synthesis of the dyes, which is beneficial to consumers and the environment. The enzymatic technology of the project is sustainable and could have broad applications in hair dyes and cosmetics as well.

Considering that world production of dyes is estimated to top 600 000 tonnes a year, and that at least 15% of it is flushed out into waterways, it is easy to grasp that the potential environmental benefits of SOPHIED are huge. The industrial benefits clearly are going to go straight to the European colour industry, which was very well represented within the consortium. The project also set up a mentoring system in order to help these traditional companies to go high-tech.

For medical applications **LIDWINE (Multi-functionalised Medical Textiles for wound prevention and improved wound healing)** focused on an integrated system to prevent decubitus and control infection. First, the project developed a contractive polymer for a massage cuff in order to stimulate blood circulation and regenerate the tissues. The project explored chose liquid crystal elastomers, which contract when the temperature is raised above a certain value, and it succeeded in bringing this threshold down to 45°C. The material can contract beyond 20% while carrying more than 100 times its own weight.

Then LIDWINE devised antibacterial nanoparticles with an optimal diameter and connected these particles firmly to the textiles. Ultrasound technology was used to physically bind these particles. By using a different technology the project succeeded in the synthesis of so-called second generation nanoparticles consisting of 1 to 3 silver nanoparticles with a diameter of 1-3 nm embedded in a silica nanoparticle with a diameter around 20 nm. The benefit of those particles is the more controlled slow release of silver ions for antimicrobial action which ensures a longer performance.

A third objective was the development of controlled release systems of antimicrobial agents through encapsulation, activated by an external trigger like water or an enzyme. For both triggers LIDWINE developed a system for release-on-command performance, only when necessary. Our developed enzyme-triggered system may be even upgraded to an on-off release system which has never been demonstrated so far. This possibility would even further upgrade the effectiveness of the releasing agent. The fabrics are made for optimal moisture management, draining wound liquid and releasing antimicrobial agents and for reduced friction.

For all of these three phases LIDWINE entered the product development phase and a patent has been filed for the contractive polymers. Some patents have been secured and prototypes with the silver embedded in silica particles have been produced. The enzyme-controlled release system technology is also secured by a basic patent and a demonstrator for the water-triggered release system has been constructed.

As a spin-off result, a fast operating diagnosis kit for the detection of infection has been developed, which shows a diagnosis after being in operation for 5 minutes and would be very easy for a nurse to handle at a patient's bedside. The potential impact would be widespread. The achievement would make the quality of life for patients much better and cut the huge costs of decubitus treatment. The controlled contractive cuff could also be used in physiotherapy for faster recovery. The project has a big industrial involvement and the market is being tested for the commercialisation of the project's products.

A RECENTLY STARTED PROJECT

Within **SONO (A pilot line of antibacterial and antifungal medical textiles based on a sonochemical process, http://www.fp7-sono.eu)**, which is the follow-up of LIDWINE, attention is being paid to the up-scaling of the required equipment for the production of nanoparticle coated fabrics.

SONO is developing research into the use of ultrasound on chemical processes in both the optimisation of the production process and the evaluation of the antibacterial properties of the textiles being produced. A pilot line is under way for the development of medical antibacterial textiles, which will scale up the production and deposit of antimicrobial nanoparticles on medical textiles like sheets, clothing and bandages that will help to halt the spread of hospital-acquired infections.

Hospital-acquired infections are a major problem in healthcare. The financial impact of these infections counteract medical advances and expensive medical treatments by increasing the length of hospital stay by at least eight days on average per affected patient. Infection control and hygiene measures have been proven to significantly reduce both the number of infections and costs of hospitalisation.

SONO's coated textiles could be used for sheets, uniforms, curtains and other hospital surfaces. The project is in the process of building two machines that will carry out the sonochemical deposition of nanoparticles such as zinc oxide, magnesium oxide and copper oxide. This method strongly embeds the nanoparticles on surfaces such as metal, plastic, paper and polymers (where the nanoparticles penetrated to a depth of around 1 mm) in addition to textiles such as cotton, nylon and polyester. It has the advantage of producing a very strong adhesion with no particle leaks, thereby reducing the environmental impact. The antibacterial properties of these textiles were also tested after sterilisation to ensure they remained intact. Patents have already been filed.

NANOMATERIALS

Mind over matter

Materials change their properties at the nanoscale, which had been impossible to achieve at the macro level

Matter changes its properties at the nanoscale, so nanotechnology's challenge is to find a way to make safe use of the enhanced advantages of carbon-based nanomaterials (such as fullerenes or nanotubes), metal-based materials (such as nanogold, nanosilver or titanium oxide), dendrimers (nanoscale polymers built from branched units) or nanocomposites (combining nanoparticles with larger, conventional-scale materials).

The whole range of R&D clusters in this publication contains vivid examples of application-driven research or fundamental science making significant breakthroughs through the use of nanomaterials or the study of their properties, which had been previously impossible to achieve at the macro or micro level. The recently awarded Nobel Prize for Physics for the discovery of graphene emphasises that nanomaterials can contain a big promise of change inside their atomic structures and behaviour. Obviously, potential safety issues need to be carefully cleared whenever applications are considered.

Self-assembly is a remarkable set of technologies with the potential to complete the nano revolution, by exploiting the interactions between molecules the same way nature does.

SPOTLIGHT ON

NACBO (Novel and improved nanomaterials, chemistries and apparatus for nanobiotechnology)

NACBO was a highly successful project that reached or exceeded its objectives. It managed to design, fabricate and characterise a very broad range of biological and non-biological nanocomposite materials and their hybrids, with uses not just in molecular diagnostics, which had been its original target, but also in drug delivery, forensics, chemistry, process engineering and the quality monitoring of food and the environment.

The project brought together three key European large and small industries, plus several service providers and academic researchers who are experts in the fields of nanoparticles manufacture, characterisation and application, surface activation and modification chemistries, synthetic nucleic acid chemistries, molecular diagnostics methods development, diagnostic kit manufacture and integrated (platform) hardware systems. Its results have excited huge interest and investment from a range of industries.

The project achieved the research, development and commercialisation of discrete but overlapping areas of material science, materials chemistry and supporting hardware systems. In striving to identify what makes materials good, NACBO hit on a key that seemed to unlock a treasure box, namely that certain well made and characterised materials, their surfaces and architectures posses the ability to be used almost universally in a very wide range of applications.

Technologically, the project concentrated on three main themes where market opportunities were open, but where existing approaches, materials or methods were either limiting or non-existent.

NACBO succeeded in making, characterising and comparing nanocomposite materials, based on carbon, magnetite and silica and their combinations. These were multi-walled carbon nanotubes (MWCNTs) and self-assembling macromolecular constructs of their activated forms, nanoporous flat surface materials, nanoparticulate silica-magnetite composites, mesoporous molecular sieves based on silica and nanorods formed from functional organic polymers. The project also developed bio-non bio hybrid materials which are underwriting new strategies in contrast imaging and drug delivery. Another major project achievement was the innovation and improvement of chemistries associated with the immobilisation, activation and marking of surfaces.

In fact NACBO's intention from the start was to generate a 'library' of different but related nanomaterials that could be compared and contrasted in a range of applications, from biopurifications and bioextractions to drug delivery, tissue engineering, forensic genetics and process chemistry.

Among its many other achievements, there are new procedures to fabricate organic and inorganic nanoparticles and nanocapsules from nanoemulsions and by electrostatic polymer-surfactant binding and by the precipitation and coating of ultra small iron oxide particles with silica. New surfaces for use in medical diagnostic mass spectrometry were innovated using carbon nanotubes (CNT)-coated metals and glasses.

Finally, the project also evaluated the toxicology of all materials and chemistries and combinations of them arising from it and their biological and environmental compatibility.

NACBO also contributed to the development of hardware platforms by integrating its newly discovered nanomaterials and chemistries into whole live organisms and diagnostics procedures not only in vitro in the context of biosensors and bioarrays, but also in vivo through magnetic resonance imaging (MRI) and computed tomography (CT) procedures. In the latter context the project demonstrated that very small, specially coated super-paramagnetic nanoparticles can be conveniently encapsulated into human red blood cells to produce a new class of effective, long-lived MRI contrast agents. NACBO also delivered the equipment required to do so, and which is now being used in clinical trials.

Along with many publications, 82 intellectual property rights (IPR)/patent protections also resulted from the project. Materials and processes generated by the consortium, particularly surface activation strategies, materials for use as contrast agents and/or in drug delivery and diagnostic kits, are already being commercially exploited by partners or in later stages of clinical evaluation. Future revenues over the next 5 years are estimated at least around EUR 35 million and projected additional future revenue based on market penetration by project outputs could be in the region of between EUR 100 million to EUR 500 million over the next 5 to 10 years.

Red blood cell loader (courtesy of EryDel Spa)

Two prototypes have so far arisen from the project. One of these is now in commercial production and Phase 3 clinical trials. This particular achievement has been promoted by a collaborative agreement signed between one of the academic partners and a major industrial project partner and has led to the formation of a start-up company with major funding.

Outputs from the project are already positively contributing to the improvement of diagnostics (health and forensics), not only within the European Union but also worldwide. In the context of forensics, improved detection limit sensitivities and better robustness in genetic profiling using materials and procedures developed in the project are already helping to solve criminal cases and increase individuals' security and protection from crime. Finally, the surface activation approaches developed in the project are already making fine chemical manufacturing processes (involved in the production of ultra high quality pharmaceutical grade materials) more robust and reproducible reducing associated cost, time and undesirable environmental consequences.

OTHER STORIES

HY3M (Hydrogen-bond geared Mechanically interlocked Molecular Motors, http://www.catenane.net/hy3m/pubs.html)

It turns out that it is not only feasible but desirable to exploit molecular motion at the macroscopic level, by using key strategic targets. Hy3M sought to create new types of synthetic molecular motors, fuelled by energy in the form of light, heat or electrons, for example, transmitting the effects of mechanical motion from the molecular level all the way through to the macroscopic world. To achieve this, Hy3M developed new methods and mechanisms for controlling sub-molecular translational and rotary motion through manipulation of hydrogen-bonding interactions and also found out how to link such movements to the outside world.

The project had set out to design, synthesise, assemble, characterise and evaluate functional materials that act through mechanical motion at the molecular level. And it managed to produce materials exhibiting various types of macroscopic responses from mechanical motion at the molecular level, such as surface-property change, shape-change, movement of object as well as a synthetic molecular motor coupled to the outside world to do work.

In order to achieve this, both the static and dynamic influences of mechanical interlocking at the molecular level had to be understood, so that the structures must gain the ability to assemble the structures into films or polymers which must be engineered into a useful material. Then, key proximity effects had to be tailored to specific properties.

Hy3M made several important breakthroughs. It developed new synthetic routes towards mechanically interlocked architectures that only require a catalytic quantity of template. It also synthesised several new rotaxane architectures that can be addressed by a variety of external chemical and physical stimuli and it obtained a unique view into the functioning of molecular devices and it developed methods to electrochemically, photochemically, thermally and mechanically switch rotaxane molecules and assemble them on a variety of surfaces.

Importantly, the project demonstrated macroscopic property effects occurring through mechanical motion at the molecular level through fluorinated molecular shuttles that could be driven with light to change the contact angle of liquid droplets. This effect is powerful enough to actually transport the droplets across the surface: this can be described as first example of the transport of a macroscopic object by synthetic molecular machines. The nanomotors can even be used to drive the liquid droplets up a slope: in this instance the synthetic molecular motors, fuelled by light, are doing work against gravity.

This new breakthrough on the use of rotaxanes as molecular machines to displace macroscopic objects is the first ever example of the exploitation of such molecules, and has been successfully used to provide a first proof of feasibility for delivering analytes in a lab-on-chip environment and for performing chemical reactions on a tiny scale without reaction vessels.

The project attracted huge attention and produced prize-winning achievements. Among the patents, the patterning of surfaces by mechanical perturbations applied to a thin film of rotaxanes is being marketed by a spin-off company.

Nano-analysis using finely focused electron beams is a unique, highly specialised field. The creation of a PhD school based in Luxembourg, in collaboration with the University of Luxembourg, aiming at the formation of scientists specialised in the field of nano-analysis is another special, lasting result that came after the successful conclusion of **NANOBEAMS (Nanoanalysis using finely focused ion and electron beams, http://www.nanobeams.org)**, a Network of Excellence (NoE) concentrating on analytical techniques based on focused ion and electron beams in order to develop analytical techniques and instruments matching the requirements of nanomaterials.

This NoE brings together the manufacturers of scientific instruments as well as the leading research laboratories in the field. It focused on the development of efficient instrumentation for the measurement, analysis and manufacture of nano-structured materials at the nanoscale of single atoms or molecules (with a lateral resolution below 10 nm and a depth resolution below 1 nm). Another unique feature was the use of these analytical techniques across some crucial nano-metrology applications, thus greatly contributing to standards.

The Nanobeams NoE led the coordinated effort of instrumentation manufacturers. Its work of dissemination spanned from organising an annual European workshop and two working groups of users in biology and materials science at European level.

The renowned PhD school has aimed at forming scientists, specialised in the field of nano-analysis, with the NANOBEAMS PhD students enjoying the opportunity of attending lectures given by scientists from the different partner laboratories and having the opportunity to perform their research work on the instruments in at least two of these laboratories situated in two different countries. Now a part of the University of Luxembourg, the school continues to attract PhD students in this field of science, according to the specific needs of the community.

Being the only one of its kind in the world, NANOBEAMS made sure from the beginning that the PhD school would focus on complementary techniques, with the purpose to form specialists in the field. The network opened the school to scientists with a degree in physics, biology or material sciences and it provides a complete and up-to-date teaching course on the fundamental, instrumental and application aspects of the topic.

The PhD school is still structured around four 'teaching weeks' and one 'analysis week' spread over two years. During each of the 'teaching weeks', theoretical tutorials are given by leading professors and researchers in the field, whereas practical sessions are held on state-of-the-art instrumentation in small groups. A further 'analysis week' allows students to analyse their own samples of interest.

As a result of the collaborative work within the NANOBEAMS NoE, several publications and advanced training provided by the project contributed to the advancement of knowledge in this highly specialised field. From an industrial point of view, the Network also enabled companies to get a more precise and detailed feedback about the practical use of the instrumentation and the market will benefit from employing its highly trained young scientists.

Nanocoatings are a big sub-cluster of nanomaterials, and a good part of them have been specifically developed for antimicrobial activity. These coatings are generally applied onto implants, surfaces or textiles, so in this respect they differ from antibacterial nano-patterning, which consists of a special etching of a given surface in order to prevent microorganisms from sticking to it. However, the aim is the same, namely to develop a whole new generation of healthcare equipment or consumer goods with the power of preventing disease and fight the spread of the so-called antibiotic-resistant superbugs, and aid the body's healing process in the meantime.

The prevention of post-surgery inflammation and infection in patients who receive prostheses is one of the main purposes of **EMBEK1 (Development and analysis of polymer based multi-functional bactericidal materials, http://www.mpip-mainz.mpg.de/eu-projekte/embek1/)**, which has just finished and whose accomplishments will roll into BACTERIOSAFE (Applying life science principles as models for new nanotechnology-based mechanisms, processes, devices and/or systems) from 2011 onwards.

For this purpose the project has developed 10 new antimicrobial, intelligent biocomposite materials, based on different methods and showing different antimicrobial properties, to be used as coatings for implants and surgical equipment. These are at prototype stage. The project's research also brings the future manufacturing of biologically active devices which might radically change burn treatment a step closer. A whole catalogue of new antimicrobial materials for healthcare use has also been developed.

The behaviour of bacteria on surfaces, namely their different interactions with surfaces, is another crucial issue, which was addressed by EMBEK1. For this purpose the project developed innovative antimicrobial polymeric thin films and materials to improve scientific understanding of these reactions and develop a theoretical model.

The project **BACTERIOSAFE** will validate the processes. These steps are now necessary to prepare for large-scale industrial production. Plasma-assisted methods will be optimised for the immobilisation of nanocapsules onto polymer-based non-wovens. It is envisaged that this will lead to the highly innovative wound dressings that will prove greatly beneficial to European healthcare.

Additionally, BACTERIOSAFE will aim at developing highly selective novel nanocapsules against pathogenic bacteria only, so they will be stable in a 'healthy' biological environment and thus non-cytotoxic. Four different methodologies will be pursued to synthesise the nanocapsules and optimise the properties. The developed nanocapsules will be rated according to their stability, functionality, response and sensitivity towards pathogenic bacteria.

The partners include a diagnostics company and a textile company that are interested in the coatings for their products. By combining life science-based nanoscale phenomena and sophisticated engineering processes, the BacterioSafe project aims at a new class of industrial processes for the manufacture of high added-value products based on nanotechnology-based mechanisms.

Applying appropriate biological properties to the surfaces of medical equipment coming into contact with human tissues requires such surfaces to be modified with nanocoatings. This cross-disciplinary approach was at the core of **PECTICOAT, (Nanobiotechnology for the coating of medical devices, http://www.pecticoat.net/**), which tailored the special biomolecules from a class of complex polysaccharides known to have anti-inflammatory properties and incorporated them into nanocoatings.

The project achieved a prototype of a dental implant by modifying the molecular structure in such a manner as to control the response of mammalian living cells surrounding the coated materials. The molecules were attached covalently to selected biomaterials and the biocompatibility of the modified surface of the medical devices was assessed both in vitro and in vivo. This molecular flexibility and anti-inflammatory property of the nanocoatings could minimise the risk of rejection in a patient. The project presented a good industrial involvement, with the prospect of market applications.

Quite a lot of cutting-edge research on nanomaterials focuses on the mechanisms of self-assembly. **SA-NANO (Self Assembly of Shape Controlled Colloidal Nanocrystals)** is a good example of the way to increase knowledge in this field with a view to applying it to the construction of a new generation of photovoltaics. The project tackled the tough challenge of ordering arrays of odd-shaped nanocrystals by using microfluidics and it succeeded in assembling rod-shaped nanocrystals into well aligned substrates. It also established how nanocrystals interact with each other when they are surrounded by other nanocrystals and it managed to organise the nanocrystals into linear or branch arrays in solution, which is relevant when creating polymers for advanced materials.

Previously, it had been really difficult to achieve control and understanding of shape-controlled colloidal nanocrystals in solution and extracting useful properties such as magnetism or light emission had been problematic.

SANANO patented a strategy to organise nanocrystals in 3D within solution, and the assembly of nanocrystals on substrates starting from an existing anchoring point. Two prototype devices, polarised light-emitting diodes and a solar cell, were built. These achievements demonstrate that by improving self-assembly, the functionality of nanocrystals can be increased through their shape and composition control.

Although this was a fundamental science project, the prospected potential applications have excited the industry's interest. This research could impact on the construction of new plastic solar cells to optimise solar energy conversion. Moreover, it can pave the way to new improved polymers.

Molecular motors, with their self-assembly mechanisms, were at the core of **BIOMACH (Molecular Machines - Design and Nano-Scale Handling of Biological Antetypes and Artificial Mimics, http://www.biomach.org/home.html)**. Again, this was a fundamental science project looking at how molecular building blocks come together and assemble into nano machines. As a first step, the project achieved self-assembly of hybrid bio- and inorganic devices, and then went down to single molecule level: single molecules were visualised by using advanced microscopy and instructed how to self-assemble. Secondly, artificial molecular machines were built 'bottom up' by using relatively simple molecular and atomic 'bricks' and more complex biological motors. BIOMACH achieved a good result when it succeeded in the difficult task of steering the biological molecules into nanostructures.

Although industrial applications are still some way off, nanoscale machines are sure to pave the way to innovative devices and processes capable of revolutionising medicine, or of reducing resource consumption and environmental pollution in manufacturing processes. This would bring enormous benefits in terms of human health and quality of life, as well as greatly enhancing industrial competitiveness.

The self-assembly of natural and artificial nucleic acids into highly organised supramolecular nanoscale structures was accomplished by **NUCAN (Nucleic Acid Based Nanostructures)**. The project made progress in establishing how the growth of such nanoscale structures can be applied to bioanalytics (which is actually quite close), nanoelectronics (about three years away) and pharmaceutical receptor screening in the longer term.

The set of molecules developed for these DNA-based nano devices are still in use and provide a 'toolbox' or set of rules on which further research will build. Two SME companies were partners in the project, which indicates that the future applications are likely to be of great interest to industry.

Metal-organic frameworks (MOFs) are coordination polymers consisting of organic ligands linked together by metal ions. They look very promising, due to the virtually unlimited flexibility in their design, and to their properties as electrochromic, magnetic and storage materials. **SURMOF (Anchoring of metal-organic frameworks, MOFs, to surfaces, http://www.ruhr-uni-bochum.de/pc1/SURMOF/)** found a way to optimise a novel method to attach them to surfaces.

The potential of MOFs in gas storage, catalysis and sensor devices depends, in many cases, on their attachment to surfaces. The project merged coordination chemistry and surface science and shed light on a very new field by developing a new 'layer-by-layer' method to deposit MOFs on solid surfaces. The consortium's efforts in implementing a surface plasmon resonance to monitor the deposition of MOFs on substrates were a success, and so was the loading of the MOFs with metal organic precursors in order to optimise their subsequent conversion into metal nanoparticles. The proof of principle, a novel gas sensor based on surface-anchored MOFs, was achieved.

Although SURMOF was a fundamental science project, potential applications might span from gas storage to catalysis and sensor devices.

These MOFs can display extreme porosity and their function can be tailored during preparation or after they have been functionalised. **MOFCAT (Functional Metal Organic Frameworks as Heterogeneous Catalysts, http://www.sintef.no/Projectweb/MOFCAT/)** used these properties to develop new heterogeneous catalysts and gas adsorbents (adsorption meaning the adhesion of molecules of gas, liquids or dissolved solids to a surface). Catalysts decrease the energy required for chemical reactions and make processes more efficient, economical and green.

This enabled the project to develop new synthesis procedures for known and new MOFs and to understand the interactions governing the stability, self-assembling and adsorption properties by combining experimental and theoretical models. This led to the development of MOF-based hydrodesulphurisation catalysts and to the use of MOFs as gas storage media displaying higher storage capability at increased temperatures, although this needs to be achieved at room temperature too. Future applications are envisaged in the chemical and petrochemical industry.

Indeed, research with nanomaterials can frequently veer into bioinspiration territory. The structures developed by **ARTIC (Nature-inspired micro-fluidic manipulation using artificial cilia)** have cilia, hair-like projections that are used for movement, as their model. For this purpose the project developed microaccuator structures (MEMS) that can be moved by a magnetic field and integrated into microfluidic devices, so that fluid can be moved around with no external intervention. This gives movement within the system much more control and flexibility.

A prototype device has been developed. Although the focus of the project is on the proof of principle, the project has also integrated these structures into devices, with potential future applications as a component of a diagnostics platform. The industrial involvement in the consortium confirms the commercial potential of ARTIC.

As the prospect of nanoimplants grows nearer, **BIOLECTRICSURFACE (Electrically modified bio-**

materials surface, http://www.bioelectricsurface.eu/) has developed a better understanding of the potential biological reactions of the body to a foreign device by developing methods to manipulate surface charge on biomaterials by electrical modification. Innovative nanoscale techniques will enable researchers to obtain a quantitative insight into biological interactions and anticipate a better organised response by the human body. The surface charge is indeed crucial in mediating bio-non bio interactions in vivo.

Although it will go on until the end of 2011, BIOELECTRICSURFACE has already achieved the modification of biomaterials surface charge in dry air. The project has been quite successful with antimicrobial textiles, which might help fight MRSA on hospital equipment. The same has to be accomplished in aqueous solution for the possible applications to range from new stone-free urinary catheters to plaque-reducing cardio stents, which may last much longer with far better results for patients. There is a high industrial participation in the project.

Carbon nanotubes consist of long, thin cylinders of carbon whose diameter is usually only a few nanometres, but whose length can be of the order of a millimetre or more, which gives them a unique length-to-width ratio. Apart from Single-Walled Nanotubes (SWNTs), carbon nanotubes can exist in multiple forms. As Multiple-Walled Nanotubes (MWNTs), looking like cylinders inside other cylinders, they possess extraordinary properties. The safety of carbon nanotubes is hotly debated, but this is thought to depend on their length and purity and on whether they can be embedded into a nanomaterial.

BNC TUBES (Novel, Heteroatomic Boron, Nitrogen and Carbon Nanotubes, http://tfy.tkk.fi/nanomat/bnctubes/) managed to develop single-walled 'doped nanotubes', which is a world first. In 'doped nanotubes' nitrogen and/or boron replace carbon atoms within the structure, and this gives them different characteristics which also depend on the number of layers. The project achieved control of the electrical properties of the BNCs and measured their optical properties as well. It also determined how nitrogen is bonded into the structure.

BNC TUBES produced thin films and some other prototypes, which greatly excited the interest of the carbon nanotube industry. There was a significant industrial involvement in the consortium, as associated developments could enable researchers to produce innovative materials with improved thermal and electrical conductivity with potential applications in electronics, sensors and energy saving, as carbon multi-walled carbon nanotubes can make fuel cells more durable.

CANAPE (Carbon Nanotubes for Applications in Electronics, Catalysis, Composites and Nano-Biology) managed to grow large amounts of nanotubes by Chemical Vapour Deposition (CVD) for applications in areas including electronics, catalysis, composites and nanobiology. It is envisaged that they will be used as metallic interconnects and field effect transistors in future integrated circuits and for field emission-based electron guns for vacuum microwave power amplifiers in satellite base stations. The consortium had a high industrial involvement.

GSOMEN (Growth and Supra-Organization of Transition and Noble Metal Nanoclusters), developed methods for predicting the growth of metal nanoparticles, such as gold, palladium and silver, in various environments, and to test their catalytic, magnetic and optical properties. A system of preparation of nanostructure metal particles by metal vaporisation was delivered at pre-prototype stage, with potential applications in catalysis and materials science, and a patent was filed.

HENIX (Enhanced Nano-Fluid Heat Exchange, http://www.nanohex.eu/) is aiming to up-scale the industrial production of nanofluid coolants to take advantage of their superior thermal performance. The reasons of these properties are still partially unexplained and are also being investigated by the project. Nanocoolants have great potential to reduce energy consumption and costs in data centre cooling and power electronics. The optimisation of nanofluids is also being pursued and the project's team, which is industrially led, is working to build a pilot production line of a few tonnes of nanocoolants.

NANO3D (Precision Chemical Nanoengineering: Integrating Top-Down and Bottom-Up Methodologies for the Fabrication of 3-D Adaptive Nanostructured Architectures, http://www.nano3d.bham.ac.uk/) worked at integrating nanolithography ('top-down') with self-assembly methods to build functional nanostructures, such as building a roof over two nanowalls and creating a nanotunnel which could be used as nanofluidic pumps. There are important investments worldwide into this field of research. Potentially, devices using this technology could be used for implantable drug delivery.

NANOCUES (Nanoscale surface cues to steer cellular biosystems, http://www.nanocues.org/) responded to the challenge of building functional surfaces with materials matching the biological host. The project used nanoscale engineering to recreate biologically functional biointerfaces while allowing for the addition of new artificial functional properties. This way it should be possible to study stem cells in a well defined experimental setting.

PSY-NANO-SI (Nanosilicon-Based Photosynthesis for Chemical and Biomedical Applications) explored a new type of interaction between oxygen and silicon, more precisely silicon in the form of nano-Si and oxygen excited into highly reactive singlet oxygen state. On the basis of the discovery of this new reaction, it also explored the possibility of using nano-Si photo-sensitisers in photo-dynamic cancer therapy and also in environmental protection. A spin-off company was created on the basis of these results.

RECENTLY STARTED PROJECTS

Self-assembly of nanocolloids is the aim of **NANODIRECT (Toolbox for Directed and Controlled Self-Assembly of nano-Colloids, http://nanodirect.eu)** which is focusing on developing different methods to drive it and modulate it. The elements of such a toolbox are the building blocks, such as model particles with varying shape and functionality; the directing tools, such as electric and flow fields, surfaces and interfaces; and the test and development methods, such as experimental platforms adapted at nanoparticle research and simulations methods, capable of dealing with a range of length scales.

So far, the main achievements of the project have been the development of novel set-ups and test methods to study the self-assembly under the effect of external influences, including electric fields, flow fields and the effects of walls and interfaces. NANODIRECT has also produced a range of nanoparticle systems, both metallic and polymeric, with tailored properties that can be used in a toolbox to explore materials design. New characterisation methods have been developed and the development of a new method for synthesising gold nanorods on large scale has been a major achievement.

One method for measuring velocity profiles near walls has already been patented. The impact on society will be in the longer term, when this toolbox will allow designing novel materials rationally, with a range of potential applications in high quality materials and coatings, more efficient electronics and even in the area of cleaner energy. There are several companies, from chemical and polymer manufacturers to consumer care, energy and electronics on the 'users platform' of the project, who are very interested in the developments, for instance in novel emulsions for heat transfer applications and structured nanoparticle coatings.

ENSEMBLE aims at demonstrating the versatility of the eutectic self-organisation mechanisms for the preparation of multi-component, multi-scale structures with controlled physicochemical and structural properties, with geometrical motifs on the submicron/nanoscale, capable of generating novel and controllable electromagnetic functionalities. Such a eutectic mechanism is characterised by the formation of two or more non-mixable crystals from a completely mixable melt. The advantages of eutectic reaction are that micro/nanostructures of various geometries can be obtained, diverse component materials can form a eutectic including metals, oxides, semiconductors, ferroelectrics, ferromagnetics, optically active phases, non-linear phases and others, and structure refinement can be controlled from micro to nanosizes.

ENSEMBLE presents elements of novelty at various levels. Principally the new approach of utilising self-organised eutectic structures for photonics (especially metamaterials), and more precisely: novel materials to be investigated such as metal-dielectric eutectics, new electromagnetic properties accomplished through low-cost procedures, new methodologies in eutectic crystal growth, new modelling tools and new metamaterial applications.

The project will potentially lead to new inexpensive bottom-up solutions in nanotechnology, physics and photonics/optoelectronics. So far, ENSEMBLE developed novel methodologies to manufacture, among others, geometries resembling working metamaterial structures, metallodielectric eutectic structures, bulk isotropic plasmonic material (which is dielectric material doped with silver nanoparticles), eutectics demonstrating high photoactivity and highly anisotropic structural and optical properties.

The project is preparing to file some patents on the materials and the technology to manufacture them. The prospected technological and industrial impact on society is expected to be broad and lasting, going well beyond the state-of-the-art in such fields as communications, security, imaging, lithography, ultra-compact data storage, sensing and biosensing. Another very important aspect will be an impact on society via training and education of young researchers taking part in the project from different European countries. Three European companies already expressed interest in the achievements of ENSEMBLE.

Society as a whole is reliant on mass production of chiral chemicals, in sectors ranging from pharmaceutical companies to computer screens manufacturers, and any process that can improve their preparation is important. Therefore, tonnes of chiral chemicals (made of molecules lacking an internal plane of symmetry, without a superimposable mirror image) are being produced as the industry requires the sustainable resolution of enantiomers (mirror image molecules) on a vast scale.

RESOLVE (Bottom-up Resolution of Functional Enantiomers from Self-Organised Monolayers, http://www.icmab.es/resolve/) works at the very beginning of this chain, where separation of chiral compounds can be complex, and is expected to achieve a more rapid, reliable and environmentally sustainable crystallisation of organic molecules through the discovery of ways to purify them.

The project uses a bottom-up approach, starting from small clumps of molecules upwards, to the separation of mirror image molecules by using a novel separation process involving selective crystallisation. A multidisciplinary team combining synthetic chemists, surface scientists, supramolecular scientists, and involving the tools of nanoscience and technology are working together to reach this goal.

One of the notable achievements so far is the use of attrition-based purification of chiral molecules, which resolves mirror image molecules (enantiomers) by making use of all the material in the preparation of a relevant pharmaceutical product. Also, RESOLVE demonstrated how mirror image molecules can act as mutual inhibitors of the growth of their pure domains in 2D aggregates on the nanometre scale.

This discovery has significant implications, because it could in part explain the preference for mixtures of left and right molecules to crystallise as such, rather than as pure chiral compounds. There are other important milestones in the pipeline, like the resolution of enantiomers in monolayers.

Chiral chemicals are high added-value materials, and the market is estimated to be as much as EUR 500 billion. Helping the industry to isolate them more effectively is a big business opportunity and may lead to a more rapid, reliable and environmentally sustainable crystallisation of organic molecules through the discovery of ways to purify them. RESOLVE involves the application of cutting-edge chemistry, technical know-how and creative experience to a challenging problem which has not been addressed so directly before. Industrial involvement in the consortium is significant and essential.

Cell-directional sensing, consisting in cellular ability to sense environmental cues and respond to them, is at the core of **FINDANDBIND (Mastering sweet cell-instructive biosystems by copycat nano-interaction of cells with natural surfaces for biotechnological applications, http://www.findandbind.eu/)**. Living cells possess an uncanny ability to pick up environmental cues and respond to them by determining the direction and proximity of an extracellular stimulus and converting this information into biochemical signals. So far, the mechanisms of this extremely complex process still need to be explained properly.

Carbohydrates, together with proteins, account for a vast part of the spectrum of these mechanisms, from the most trivial to the most essential to the life of an organism, so FINDANDBIND aims to explore the potential of this class of molecules to mediate specific recognition events and consequently provide the modulation of biological processes at the nanoscale.

By applying the nanoscale mechanisms of cell interactions and their physiological milieu, the project will generate biological design criteria for the development of new nanomaterials and nanodevices, with some very interesting potential developments in the field of regenerative medicine and in biomedical applications.

Combining nano-structured scaffolds from naturally derived polymers and the incorporation of biological signals will provide information and guidance in recreating cell-cell interactions and control tissue formation in vitro and in vivo. Eventually, the project aims to produce 3D cell-instructive materials with the ability to restore and enhance the functions of healthy tissues, a whole new class of biosensors and special surfaces for the selective differentiation of stem cells.

NANOMEDICINE

Diagnostics' Revolutionary Way Forward

New insights into cellular functions and spectacularly accurate imaging pave the way to early detection of diseases

Nanotechnology clearly has the potential of becoming the Holy Grail of diagnostics. By developing small, inexpensive, highly sensitive and possibly portable devices, and by relying on novel nanomaterials and surface modification techniques, it can bring staggering new insights into cellular function in real time, so that diseases could eventually be spotted at the very beginning.

Nanotechnology is building a whole new generation of biosensors. These devices, combining molecules selective for an analyte with detectors known as signal transducers, can be immeasurably improved by the use of nanomaterials. Because of their submicron dimensions, nanosensors, nanoprobes and other nanosystems may allow simple and rapid analysis. Among these nanomaterials, gold nanoparticles, carbon nanotubes (CNTs), magnetic nanoparticles and quantum dots can greatly enhance the sensitivity and specificity of detection. This applies, for instance, to glucose monitoring, early diagnosis of cancer, heart attack or Alzheimer's disease.

Nanotechnology's ultimate goal in this field is to pave the way to personalised medicine. The ambition of point-of-care, in-surgery or even at-a-distance diagnosis and the spectacularly exciting progress in imaging aims to take science over the current 'one-size-fits-all' limitations, with tremendous prospected benefits to society. The clinical diagnostics industry is an expanding market, with annual growth rates of more than 15%.

SPOTLIGHT ON...

CARE-MAN (Healthcare by Biosensor Measurements and networking, http://www.care-man.eu)

The scientific challenge of developing a validated, intelligent, automated diagnostic device to monitor several diseases, such as cardiovascular, coagulation or inflammation disorders was the main objective of CARE-MAN. The project met it by combining biosensor technology and optical transduction principles, biochemical recognition methods and communication capabilities.

The ultimate aim is to develop a point-of-care device which can be used in emergency or intensive care units, or even at general practitioners' surgeries. An ageing society will benefit most from fast, cheap and reliable instrumentation in emergency conditions or health protection.

The scientific challenge was about finding a combination of fast and reliable measurement, with the information technology (IT) component allowing for integration in hospital laboratory information systems and a potential, future remote control use.

Several single and multi-assays were set up by biological recognition elements such as antibodies, aptamer and scaffolds, a combination of which allow for the detection of more than one parameter within a single sample.

Several single and multi-assays have been set up by using the biological recognition elements (BRE) developed within the project, or modified by it, such as antibodies, aptamers and scaffolds. Different immobilisation strategies and assay types, such as sandwich assay and binding inhibition test, transduction enhancement techniques as well as technical components like flow cells and fluidics, blood filter, light sources and detection units have been developed, tested and optimised.

The combination of several biological recognition elements allows for the detection of more than one parameter in parallel within one sample. Different selectivity and sensitivity properties were taken as an advantage to adjust the detection to the clinical relevant concentration ranges of the parameters. The combination of these different kinds of BREs or even different assay types had not been achieved in this way until now.

Within CARE-MAN four devices with different measurement techniques were developed at first, where the consortium focused on optical detection techniques using total internal reflection fluorescence and concentrated on a multi-spot assay. According to the high sensitivity the system using grating coupler, planar waveguides and a CCD camera for fluorescence detection was selected as the primary CARE-MAN device. Like the other systems, especially FABIAN and CAI, both of which are methods using fluorescence detection and excitation via waveguides, it is running automatically and via an interface connected to a database for evaluation purposes.

Prototypes are available for each of the optical detection techniques. Further activities in the project focused on the development and/or modification of special biological recognition elements like antibodies, aptamers and scaffolds, as well as on new fluidic and illumination concepts. Some patents have been filed. Instruments are linked to a database by software, allowing for calibration, validation and reference to other laboratory equipment.

The development of new bio-assay platforms for the detection of biotargets by using nanoparticles extends to the diagnosis of viruses. A different method from current technologies, such as expensive Polymerase Chain Reaction (PCR), has been developed by **NANO-MUBIOP (Enhanced Sensitivity Nanotechnology-based Multiplex Bioassay Platform, http://www.nanomubiop.eu**). Its target is the elusive Human Papilloma Virus (HPV), which is responsible for cervical cancer, the second hardest-hitting cancer among women. The platform developed by the project will target the different HPV genotypes, but it can be applied to any kind of biotarget, such as HIV or genetic modifications.

The project is on its way to deliver a quantitative, highly sensitive, multiplexing bioassay method by using non-biological nanosized particles. Again, this should be fast, cheaper (it is estimated it could reduce by 50% the current diagnostic screening cost, which is about EUR 200), completely automatic (which would make it suitable for use in hospital laboratories) and patient-friendly, as it would need only a small amount of biological material.

This new method would facilitate mass screening and aims to be produced on an industrial scale within a year of the project's completion in 2011, which should expand the market and attract a sizeable number of companies interested in the technology.

So far, the main technological achievements of NANO-MUBIOP include the in silico analysis of the HPV genome and the definition of generic and specific probes able to detect all the HPV types, which amount to more than 100. The project also produced a database of generic and specific HPV DNA probes.

Furthermore, the team developed silica nanoparticles of ideal dimensions, around 100 nm, and functionalised them so that they are now able to covalent link generic probes, and it also produced the functional substrate to link with specific HPV probes. It also developed a deposition system that is capable of dispensing the fluids, including specific probes, on the functional substrate.

Now the prototype of NANO-MUBIOP's optical detection system is able to detect nanoparticles arrayed on the substrate in the presence of the HPV target by using a technique of evanescent wave.

A prototype of the automated device was also developed, with an arm able to dispense fluids and the possibility to incubate reagents at different temperatures. On top of an experimental and theoretical mathematical model of the whole system, the tests have been simulated in vitro. The final prototype is expected to be ready soon for validation. One international patent linked to the technology has been produced by the coordinating partner before the start of the project.

Another major diagnostics challenge for nanotechnology is the early detection of Alzheimer's disease. As the recently published World Alzheimer's report 2010 estimated that the global cost of dementia worldwide this year is set to reach USD 604 billion, including social care, unpaid care by relatives and the medical bills to treat the condition, timely intervention is all the more indispensable.

The report analysed the cost of dementia care and it found that, if it was a country, it would be the world's 18th biggest economy. As if this weren't enough, the number of people with Alzheimer's disease is estimated to rise to 65.7 million by 2030 and to 115.4 million by 2050. An estimated 35.6 million people currently have dementia worldwide, which makes it not just a health issue, but a massive social problem.

According to another source, 5 million people in the EU have dementia, and 3 million of these cases are caused by Alzheimer's.

In order to meet this challenge, the **BIODOT project (Sensing BIOsystems and their Dynamics in fluids with Organic Transistors, http://www.bo.ismn.cnr.it/biodot/)** published the first example of interfacing viable cells on organic semiconductors. This area of research is quite young and for the past three decades it has been dominated by silicon electronics, but these are not so good for cell interfacing. For this purpose the project developed some non-invasive sensors focusing on the properties of highly sensitive organic semiconductors to detect the proteins signalling the onset of neurodegenerative diseases such as Alzheimer's at very low quantities, before the disease becomes advanced, a development which would be especially significant to stem the progress of the disease.

As a successful example of the convergence of organic electronics and biological systems, the project developed new types of transducers which are able to pick up not only any tiny aggregation of the Alzheimer's peptides, but also neural cell signals. The organic semiconductor molecules can indeed be interfaced with biological systems and have an edge over silicon-based electronics in that they can be chemically modified and be made biocompatible and flexible, so that they can ideally be moulded into any shape.

BIODOT developed sensor devices, namely chips containing a number of field effect transistors (FETs), an active layer of organic semiconductor material and a microfluidic cell. The project also succeeded in adapting these semiconductor molecules so that they can now work in water and physiological medium. This is all the more remarkable since organic FETs are normally incompatible with water.

The project finally tested and demonstrated these sensors with living cells or peptides. It also published the first example of interfacing viable cells on organic semiconductors and managed to differentiate stem cells on them. A patent has been filed.

The project's consortium features two leading industrial partners in the field of organic electronics. A second spin-off company is looking to develop the cell interfacing technology.

When trying to meet the crucial challenge of measuring electrical signals in neurons, Alzheimer's is again the big target. The goal of the **VSNS project (Voltage-Sensitive Plasmon resonant Nanoparticles, Novel Nanotransducers of Neuronal Activity)** is to develop a non-invasive method to record the electrical signals in both healthy and diseased neurons.

This should allow medicine to make significant progress in the understanding of the pathology of neurodegenerative diseases, where the electrical behaviour of the affected cells is still unknown and anatomy alone cannot explain it.

This project aims to record, using a non-invasive method, the electrical signals in healthy and diseased neurons.

The project focuses on developing voltage-sensitive nanotransducers (VSNs) suitable for long-term monitoring of neuronal membrane-potential.

The novel concept of electrically tuneable plasmon resonant nanoparticle/nanorods (NPs-NRs), which are nanosensors picking up plasmon resonance shifts induced by the electric fields of neuronal activation, allowed the project to develop these VSNs and to make big strides towards the industrial development of such technology.

VSNS's achievements feature the development of new optical techniques to measure neuronal activity by using Plasmon resonant nanoparticles and nanorods and to record the electrical signals; the project also developed the technology to optimise the signal to noise ratio.

By measuring the electrical properties of both healthy and diseased tissue, new diagnostic and therapeutic treatments may be developed. A patent has been prepared and a prototype now allows scientists to read and record the electrical properties of both healthy and diseased tissue.

A good industrial involvement in the project and its future potential are clear. A spin-off company is already marketing some of the project's achievements.

An early onslaught against bacteria is necessary to prevent infection, so nanotechnology is setting up instruments to detect them before they develop into disease. **BIODIAGNOSTICS (Biological diagnostic tools using microsystems and supersensitive magnetic detection, http://www.eu-biodiagnostics.org)**, targeted in particular Streptococcus sobrinus, a gram-positive bacterium, and Yersinia pestis, which was responsible for the lethal plague epidemics throughout history.

The project proved that these bacteria can now be efficiently spotted by using magnetic nanoparticles as markers for immunoassays. Their feasibility as nanobiosensors was proved by the fact that these assays enable their users not only to save on the time and money required by current technology, but also to end up with a more accurate detection instrument.

The project used transmission electron microscopy to characterise the nanoparticles, which were functionalised with different surface coatings and also magnetically. A database of this information was built and different magnetic-based read-out schemes for the sensors were developed. One prototype sensor from the project has now been successfully commercialised in Sweden, and another has been demonstrated. The accomplishments of BIODIAGNOSTICS were world leading.

Nanotechnology has the potential to improve the stability and electron transfer efficiency, in terms of both sensitivity and power output, of integrated biopowered sensors for use in monitoring and diagnosis. This fundamental research was provided by **BIOMEDNANO (Integrating enzymes, mediators and nanostructures to provide bio-powered bio-electrochemical sensing systems,**

http://www.nuigalway.ie/biomednano/), which probed the role of enzymes, mediators, surfaces and immobilisation strategies, with a view to producing an in vivo self-powered device to detect glucose levels in diabetics.

The project made progress in optimising signal detection and electrical power output, with the aim of developing an implanted feedback system over the next decade, which will use glucose to power the device, which will in turn detect glucose levels for use in diabetics. Currently, a pin-prick blood sample is required. Of course, the issue of the stability of any implanted device must still be addressed.

From an industrial point of view, the biomedical device industry is large and there is a big market for home-testing kits that measure glucose levels at present and industrial interest by big companies is a given.

Biosensors, the major development cutting across nanotechnology clusters, are at the core of **ELISHA (Electronic Immuno-Interfaces and Surface Nanobiotechnology: A Heterodoxical Approach, http://www.immunosensors.com)**, which sought to build an electrochemical biosensor that did not require the use of extra reagents. Radioimmune assaying or ELISA (Enzyme-Linked Immuno Absorbent Assay) had been previously used, but it had disadvantages in that the extra reagents were costly or hazardous to handle (as in the case of radio-isotopes).

Instead, ELISHA looked for proteins relevant to the diagnosis of heart attack, cancer, prostate and ovarian cancer or thyroid dysfunction in one single step 'mix and measure' approach, as well as providing rapid response monitoring of glucose for diabetics on the spot. The biosensor is cheap, would take only 15 to 20 minutes to work and would reduce costs in the healthcare system.

It can measure between 25 and 30 different analytes, including cholesterol, bacteria, antibiotics and viruses, and it developed simple instrumentation allowing the biosensor to be used by unskilled personnel. A spin-off company, ELISHA Systems Ltd., has been formed to market the results of the project. There is also interest in using the technology to monitor heavy metals such as chromate, a carcinogen that can contaminate ground water, so additional opportunities in both remediation and water quality markets are envisaged.

ADONIS (Accurate Diagnosis of prostate cancer using Optoacoustic detection of biologically functionalized gold Nanoparticles - a new Integrated biosensor System, http://www.fp6-adonis.net/) showed that gold nanoparticles can be used to target prostate cancer as nanoscale contrast agents for improving prostate cancer diagnosis. These nanoparticles can be traced by using a new imaging technique based on optoacoustics. An antibody can be attached to the gold nanoparticle by a ligand, and this molecule targets and adheres to the antigens expressed by this cancer. This method costs less than existing imaging techniques and can give better information.

BIOMAGSENS (Ultra sensitive Magnetic Sensors for medical applications,http://biomagsens.free.fr/) focused on developing a new generation of ultra-sensitive, low-noise magnetic sensors based on magnetic tunnel junctions. It aimed to produce magnetic imaging of the human body, mainly targeting the heart and the brain and magnetic-based biochips.

BISNES (Bio-Inspired Self-assembled Nano-Enabled Surfaces), is still ongoing and it is focusing on the precise manipulation and positioning of individual molecules on nanostructures. It aims to develop software products for the representation and quantification of biomolecular surfaces, especially those that self-assemble in long-range nanoaggregates, build nano-structured surfaces replicating biomolecular surfaces and develop novel hybrid biodevices with heightened sensitivity and response time. This could have an impact in the rapid detection of flu. The project has a heavy industrial presence.

CIDNA (Control of assembly and charge transport properties of immobilized DNA, http://www.cidna.de) aimed at establishing the fundamental conditions for developing DNA-based nano-biotechnology. To this effect it delivered a novel spectroscopic approach by applying electrochemical and spectroscopic techniques in parallel and it developed new binding procedures of DNA to metal or semiconductor surfaces. It also provided a high-resolution mapping of the metal-DNA interface and an assessment of the mechanism of electron transport in DNA hybrids.

EXCELL (Exploring Cellular Dynamics at Nanoscale, http://www.excell.nu) aims to develop advanced experimental tools to address fundamental problems in stem cell research. An innovative approach to explore the interaction between biological systems and nanostructures is concentrating on the design of suitable biocompatible nano/bio interfaces to ensure a sustainable cellular environment. These tools could also possibly be used to modulate stem cell differentiation. A first version of the lab-in-a-cell has been developed.

GENSENSOR NANOPARTS (Nano-biotechnical components of an advanced bioanalytical microarray system, http://www.gensensor-nanoparts.uni-bremen.de) used magnetic nanobeads to develop more sensitive and efficient microarray-based gene analytical methods. The magnetic nanobeads containing sequence-specific LNA (locked nucleic acids) need to bind to relevant DNA. They are removed from the sample and put directly on a microarray. Here the sequences fix to the relevant arrays and the nanobeads can be used for sensitive detection.

NABIS (NanoBiotechnology with Self-Organising Structures, http://www.nabis.kth.se) singled out new technologies to produce high performance biochips for future medical applications in accelerated drug discovery, diagnostics and personalised medicine. The project explored novel polymers for bio-probe arrays, externally applied surface acoustic waves and novel magnetic bio nanowires on a platform of magnetic nanodots. The use of these technologies could provide unique possibilities to increase ligand density and enhance the kinetics, resulting in improved sensitivity and faster assay performance.

NAS-SAP (Nano Arrayed Systems based on Self Assembling Proteins, http://odevie.ubs.u-bordeaux.fr/nas-sap) addressed the challenge of manipulating the surface of bacteria for application to vaccines or diagnostics and it achieved the self-assembly of individual proteins at the nanoscale. It also provided single molecule studies on individual proteins and filed two patents.

RECEPTRONICS (Label Free Biomolecular Detectors: at the Convergence of Bioengineered Receptors and Microelectronics, http://www.receptronics.com) aimed at developing low-cost, label-free biomolecular detectors for biomedical applications by integrating concepts and methods from bionanotechnology and microelectronics. Among its achievements there is a single ion channel recording, which consists in a complete structure made of several spots, with one ion channel in each one of them, to detect and record single molecules in real time. This reduced time to study ion channels could have an impact on drug discovery, predictive and personalised medicine. The project also bioengineered a high quality receptor with respect to signals. These receptors are working well in nature. The challenge is to obtain quantitative detection of target molecules by using single molecule signalling.

SNIP2CHIP (Development of a complete integrated SNP analysis system, http://www.tyndall.ie/projects/snip2chip/) addressed the huge challenge of developing a single-platform, 100% accurate, point-of-care genetic analysis of a blood sample. The project strived to accomplish this by testing the integrated system, consisting of a portable instrument and a disposable cartridge. The blood sample would be initially applied to the chip, where magnetic beads are used to capture and purify the DNA from the white blood cells. The genes of interest are then amplified on the chip within nanodroplets by using PCR. Identification of mutations is then performed using an array of magnetic and optical sensors to identify which mutations are present in the sample. The project managed to extract DNA successfully from 250 nl of blood and amplification was also obtained by using a tiny 64 nl sample. One patent was filed for the optical detection system and another US/EU filed patent for the magnetic sensing system.

TAMIRUT (A new bio-sensor concept for medical diagnosis: targeted micro-bubbles and remote ultrasound transduction), focused on an innovative biosensor for advanced medical diagnosis of cancer, in which the biological material is carried by targeted microbubbles injected inside the body and the transducer is remote. Such a transducer operates on the basis of the ultrasound response of such microbubbles, which are gathered and processed by an improved version of an ultrasound medical scanner (UMS). The project, whose aim was to quantify nanomolar concentration of the analyte inside an organ and to generate a contrast-enhanced ultrasound image at the same time, concentrated especially on prostate cancer. There was a substantial industrial involvement and a prototype has been developed.

RECENTLY STARTED PROJECTS

While nanotechnology in regenerative medicine is concentrating on restoring some of the functions of human senses, nanodiagnostics is mimicking some olfactory properties to detect certain compounds. This is the primary aim of **BOND (Bioelectronic Olfactory Neuron Device, http://bondproject.org)**. Current electronic nose devices can detect and identify odourants in different kinds of environments, but these still have significant limitations concerning sensitivity, reliability and selectivity. This project relies on a new concept, validated in the FP5 project SPOT-NOSED, which imitates the olfactory system of the mammalian nose by using olfactory receptors (OR, proteins located at the plasma membrane of olfactory neurons) as the sensing part of the electronic nose.

The system is capable of detecting odourants at concentrations imperceptible to humans. The project will build upon this achievement to develop a point-of-care, lab-on-a-chip device for analysis and detection of cancers or organ failure from urine, blood or pus. The main challenge is to scale down this new biotechnology and combine it with nano and IT for integration into a single artificial device. To do this, the project has developed an original strategy. The OR will be displayed in nanometric lipidic vesicles (nanosomes) that can be coupled to nanoelectrodes to conform the basic unit of the device, the nanobiosensor. An array of these will be capable of detecting specific odourant patterns or fingerprints. Finally, this array will be interfaced with an electronic and highly-miniaturised apparatus, which will give the proposed system several considerable advantages over existing chemical sensors: portability, low cost, user friendliness and online monitoring.

While the use of OR in electronic noses is being explored by other research teams outside the EU, the approach of the BOND project is unique and has already led to the development of new technologies, such as new procedures enabling the identification of specific ORs for a given odourant and the production of OR-containing nanosomes, and new protocols to anchor them onto the surface of the electrodes. New tools to characterise the sensors at the nanoscale have also been designed, as well as an adapted electronic circuitry. Several patent applications will be submitted for the prototypes of the smart biosensors and the entire nanobioplatform, as well as for some specific tools (AFM probes) that will be developed for the biosensor characterisation.

The technology developed within BOND will lead to the design and construction of new molecular devices that will directly provide benefits for public health and security. For example, the project will lead to the development of new non-invasive diagnostic tools that will reduce the number of false positives and healthcare costs by analysing the released volatile gases in blood or urine. They could also be used to detect harmful chemicals, explosives, narcotics and pathogens cheaply and easily by using odour as the control parameter. Although at this stage the development of the project is focusing on the healthcare industry and the agrifood sector, the clinical diagnostic industry is its ultimate aim.

The diagnosis of cancer is the prime concern of **CAMINEMS (Integrated Micro-Nano-Opto Fluidic systems for high-content diagnosis and studies of rare cancer cells, http://www.caminems.eu)**. The project is aiming to develop a clinical instrument to detect and analyse circulating tumour cells in the blood before they lead to metastasis. The concentration of these cells can be as low as 1 cell per 1 billion red blood cells, which makes them difficult to detect. As nanotechnology can go smaller than a red blood cell, it can potentially detect secondary cancers earlier and establish their molecular characteristics. At that point the risk to the patient and the best treatment strategy could be established and contained.

Secondary cancers are responsible for 90% of all cancer deaths. Current methods to detect these cells have a low cell capture efficiency, which this project aims to improve greatly. In many cases metastatic cells are not detected but patients subsequently develop secondary cancers. This may happen either because the cells are not continually present in the blood or because the tools are not good enough to detect them. CAMINEMS combines the microfluidics techniques and the self-assembly of magnetic nanoparticles to detect these cells and develop a whole new tool and it has already provided proof of concept for this type of detection.

If cancers could be detected earlier and the molecular characteristics of the cell consequently determined, then clinicians would be able to use this knowledge to decide on the best course of treatment available, which would be a big step towards personalised medicine. An industrial partner of the project specialises in lab-on-a-chip technology and it is envisaged that a future tool could also be used to screen cells and develop new drugs for specific cell types, with a direct impact on the drug development.

Establishing a nanocarrier-based technology for the drastic improvement of cancer treatment and diagnosis is the aim of **NANOTHER (Integration of Novel Nanoparticle based Technology for Therapeutics and Diagnosis of different types of Cancer, http://www.nanother.eu)**. One of the biggest challenges in chemotherapy is to reduce secondary effects, and the project wants to achieve precisely that without affecting the efficacy of the treatment. So far, the team has selected a number of nanoparticles suitable to achieve the project's goals in terms of non-toxicity, drug-loading capacity and imaging of nanoparticles in mice. At this point the project will focus on tracing the nanoparticles across the body and checking the effectiveness of the drug-loaded nanocarrier compared to current chemotherapies.

The project looks at lung, breast and colorectal cancer. Magnetic nanoparticles are being used for diagnosis by labelling with specific receptors and therapy by hyperthermia effect, and polymer nanoparticles by specific site drug delivery. Furthermore, NANOTHER will explore all relevant data regarding the in vitro and in vivo toxicity of the nanoparticles, in order to determine the applicability of new nanoparticle systems. Drug encapsulation into nanoparticles could improve drug delivery and reduce the dose; external or non-invasive imaging analysing systems would lead to a whole new system of diagnosis and therapy monitoring.

So far, NANOTHER filed a patent on a system and method for the imaging of nanoparticles and it expects to obtain several more and for a nanoparticle-based system that will be capable of treating and diagnosing several types of cancer. The potential impact on society might be huge. At the moment, many non-tumoural cells die because of chemotherapy and as the secondary effects are so damaging to the whole body that treatment may have to be stopped.

Using nanocarriers should allow clinicians to concentrate the dose of the drug used in the immediate surroundings of the tumour, thereby greatly diminishing the death of non-tumoural dividing cells, and also avoiding hair loss, sterility and other major problems.

The potential industrial impact would go hand-in-hand with the impact on society, as it would be greatly beneficial to the well-being of patients. Several pharmaceutical companies are involved in the project, as drug nanoencapsulation is clearly a good route to improve the activity of their compounds. Also, nanoparticle synthesis companies will have another clear market ahead of them.

The onset of diabetes could be detected in a routine screening years before the clinical symptoms of the disease become manifest. This very early stage diagnosis method is the aim of **VIBRANT (In Vivo Imaging of Beta cell Receptors by Applied Nano Technology, http://www.fp7-vibrant.eu)**, which is creating nanoscale probes for specific imaging of pancreatic beta cells with readout for functional beta cell mass (BCM). The project strives to develop a novel MRI technology, combining the high sensitivity of specifically labelled iron oxide nanoparticles with reagents providing superior spatial resolution. Therapies for the regeneration of the pancreas could also be developed and monitored.

Beta cells are located in the human pancreas and produce insulin, which regulates blood glucose levels. The non-invasive quantification of functional BCM is of paramount interest for the diagnosis and eventually the therapy of diabetes, a devastating disease, from which currently about 30 million citizens of the EU are suffering. Imaging of BCM is an unsolved problem, because a tiny cell mass of 1-2 g, irregularly dispersed in a small organ of about 100 g, which is embedded in a human organism of about 75 kg, has to be specifically labelled with a contrast agent.

This could be used as a tool for the early prediction of diabetes as beta cell depletion occurs up to seven years before any symptoms become apparent, so that some changes in diet and exercise might help the patient in good time. This imaging tool may also be used in the development of new therapies for diabetes. There is a peptide marketed as Byetta, which was isolated from the gila monster lizard. It has been suggested that this peptide can stop the decay and promote regrowth of beta cells but this cannot be confirmed without a tool for identifying the cells.

This project aims to develop this tool through to pre-clinical stages.

Tiny polymer capsules smaller than the 10 000th part of a millimetre were prepared, containing a payload of superparamagnetic iron oxide, a fluorous phase and/or fluorescent semiconductor crystals. These materials show properties superior to currently used materials. Also, special carbohydrate structures were prepared. After being attached to the surface of the capsule, these should direct and anchor the capsule to the beta cells. VIBRANT filed a patent regarding the carbohydrate structures.

Industrial involvement is strong. Very recently, the project's associated industrial advisory board, representing renowned members of the pharmaceutical industry together with a global charitable diabetes advocate organisation, convened in order to advise on potential scenarios leading to a clinical development.

The goal of **3DNANOBIODEVICE (Three-dimensional Nanobiostructure-based self-contained devices for Biomedical applications, http://www.mah.se/3dnanobiodevice)** is to construct self-contained, wireless and potentially implantable 3D-nanobiostructures–based biodevices for glucose or oxygen monitoring. These sensors will be powered by biofuel cells and should be efficiently working in a variety of bodily fluids such as plasma, blood, saliva or sweat. This project builds on results obtained by the aforementioned project, BioMedNano.

By developing a better understanding of the fundamental principles for controlling electron transfer reactions between 3D nanomaterials and different redox enzymes, the project is working on several self-contained prototypes of a biofuel cell producing electrical power from biological molecules such as glucose and oxygen, a wireless transmitting device to send the information to a medical database/computer and a biosensor for detecting glucose or oxygen. An integrated microchip will be used to control the sensor and collect data. It will include a unit to transform the voltage from that of the biofuel cell (0.5 V) to that of the electronics (>2 V). A data transmission system is also being developed. Although the prototypes will be potentially implantable, this project will not be going into clinical trials.

Innovative, self-contained, wireless biosensors could be highly useful for monitoring and treating diabetes, and in the longer term they could be used in simulations for the treatment of a whole range of health conditions. Within the project, industrial involvement is focused on two companies, respectively producing enzymes for biotechnology applications, and an SME producing unique wireless devices, which will have to be miniaturised significantly.

Alzheimer's early diagnosis and treatment are again the main challenge for **NAD (Nanoparticles for Therapy and Diagnosis of Alzheimer's Disease, http://www.nadproject.eu)**. One of the symptoms of this illness is the accumulation of protein fibres within the brain, so the project aims to develop targeted nanoparticles that can cross the blood-brain-barrier (BBB) in order to image and block the formation of these fibres, or destroy them, at the same time.

A synthesis of the nanoparticles for drug delivery and the development of an Alzheimer's model have been successfully carried out. Since current therapies cannot halt the progression of the disease, there is great hope in a treatment that, if successful, could reverse the formation of these fibre aggregates. There is a strong industrial involvement in the project, with some definite market potential prospects.

Nanotechnology can develop the tools to provide the reading of our DNA mapping, with all its possible clues about our predisposition to certain illnesses and ways to prevent or cure them. A major effort is going on in this field worldwide, and **NANODNASEQUENCING (Nanotube-Junction for High Throughput DNA Sequencing, http://www.nanodnasequencing.org/index.htm)** is part of it. It is hoped that this work could lead to a huge breakthrough in modern medicine and potentially save countless lives. Crucial genetic information would be used to detect, diagnose and treat patients on the basis of the individual's unique genetic make-up.

In general, the major hurdle that this whole scientific effort has to overcome is that the accuracy threshold needs to be very high. The project is preparing a number of patents and has made major progress in developing proof of concept so far. A breakthrough would have a global social impact once completed, as diseases could be prevented and cured if research could provide proper notice and treatment before the very onset of illness. This is a classic example of nanotechnology propelling science forward towards the manipulation of the building blocks of life. The final tests of the project will start in 2011 and will be rolling into 2012 and beyond.

The project's industrial involvement is very aware of the industry's keenness and the importance of protecting the patents that are being generated.

For the first time, **NANODIARA** combines a nanoparticle approach to a generic platform for the diagnosis of inflammatory and degenerative diseases, especially rheumatoid arthritis and osteoarthritis. The project uses modified superparamagnetic nanoparticles as a tool to develop new bioassays and imaging aimed to detect molecular and cellular processes with high sensitivity and specificity, thereby addressing key requisites for modern therapy.

The multidisciplinary consortium, which has a good industrial presence including one multinational company and four smaller companies, will protect and exploit these new technologies. The project is taking great care of any ethical and legal issues concerning nanoparticle development. The potential social impact of NANODIARA is clear, considering that treatment and disability costs resulting from musculoskeletal diseases like rheumatoid arthritis and osteoarthritis represent a very heavy economic burden to healthcare services. Despite considerable advances in the treatment of rheumatoid arthritis, a significant proportion of these patients continue to have active disease, while no disease-modifying treatment exists for osteoarthritis.

Clinical interventions and successful outcomes usually depend on the early identification of arthritis and an effective therapy to protect against skeletal damage. However, key progress in treatment precisely depends on developing new tools for early diagnosis, identifying the speed of disease progression and providing short-term readouts of treatment efficacy.

NANOMEDICINE

Crossing Cell Barriers to Deliver Drugs

Nanovectors could be guided to a specific site in the body and release therapeutic agents on site with the utmost precision

A brand new generation of carriers able to interact with biological matter at sub-cellular scale could potentially solve the problem of poor specificity and efficiency of drug delivery and uptake. Nanoparticles are considered suitable vehicles for drugs as they are of the same size as many biological entities. They could reduce the risk of adverse reactions and increase therapeutic efficiency. Encapsulation of reformulated drugs or DNA into nanovectors could cross hitherto insurmountable obstacles such as the BBB and the gastrointestinal (GI) tract barrier, but the issues of body clearance and safety are of paramount importance.

Some of the main developments include targeting cancer on site by the use of magnetised nanoparticles in combination with hyperthermia, or by carbon nanotubes for gene transfection; oral delivery of insulin could make early treatment of diabetes much more effective. The use of polymeric nanoparticles, liposomes, inorganic nanoparticles and carbon nanotubes are being actively investigated.

The benefits offered by nanovectors in terms of high stability, drug-carrying capacity and ability for controlled release are opening up a whole new frontier for therapy. Just to give an example, systems could be activated by a range of external inputs, such as targeted ultrasound, light or magnetic field.

SPOTLIGHT ON...

NINIVE (NON INVASIVE NANOTRANSDUCER FOR IN VIVO GENE THERAPY, http://www.ninive-project.org)

The NINIVE project demonstrated gene transfection in vivo by using ultra-pure carbon nanotubes (CNTs) in combination with electromagnetic fields for the first time. If the safety of carbon nanotubes, which would seem to depend to a large extent on their purity and dimensions, could be proven for this particular variety, this breakthrough could help to phase out the need for viruses as carriers in gene therapy.

This discovery points to potential new therapeutic possibilities for the treatment of cancer, including breast and pancreatic cancer, and brain glioblastoma. It could also have a significant impact on the next generation of gene therapy, drug therapy and electrostimulation for cardiac, neuromuscular and visceral myopathy disorders.

There are several safety issues linked to carbon nanotubes, which are better described in the Nanosafety Cluster. However, in the specific case of the NINIVE research, carbon nanotubes were injected in a mouse's cerebral cortex without causing degeneration of the surrounding neurons. These rolled up, seamless cylinders of graphene sheets have a particular combination of electric, optical and chemical properties. One day, provided that properly functionalised carbon nanotubes were cleared by environment, health and safety (EHS) studies into human safety, these nanovectors could potentially help to overcome the problems in the targeted delivery and uptake of molecules including DNA – which are normally impermeable to the cell membrane – to specific diseased tissues.

Regarding their electromagnetic properties, NINIVE discovered that ultra-pure carbon nanotubes can act like an efficient thin-wire dipole receiver antenna when irradiated with an electromagnetic field (EMF) in the microwave range. This phenomenon of detecting and amplifying an EMF induces 'enhanced cell permeabilisation', meaning that the cell membrane allowed the passage of therapeutic molecules into the relatively impermeable cells. In particular, the project's team showed the capability of carbon nanotubes to transfer gene material into neural cells of the central nervous system (CNS), which is a particularly challenging case study.

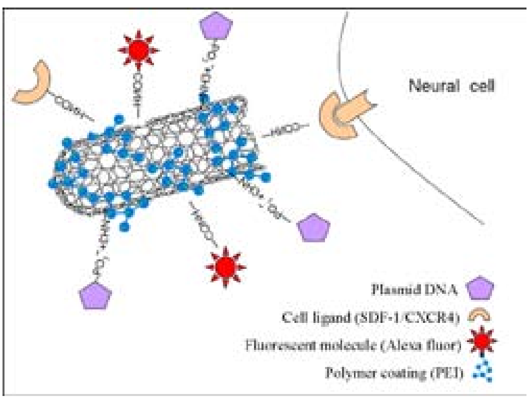
Carbon nanotubes were functionalised by allowing the attachment of: 1) nucleic acids (e.g., a plasmid encoding the reporting green fluorescence protein (GFP); 2) fluorescent moieties for nanotube tracking; and 3) a cell ligand specific for neuronal targeting.

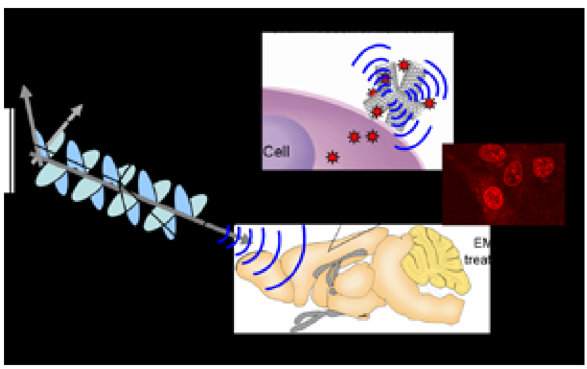
Finite element modeling (FEM) clarified the mechanism of carbon nanotubes-mediated permeabilisation. Specifically, these ultra-pure carbon nanotubes work as an efficient thin-wire dipole receiver antenna when irradiated with an EMF. The EMF could penetrate the cranial bones of a mouse and concentrate in the brain where – in presence of carbon nanotubes – it reached high values and was able to alter the natural trans-membrane potential of CNS cells, thereby allowing cell uptake of the therapeutic molecules. It seems likely that, by giving energy to the cell, pores open up within the fluidic mosaic of the membrane, a phenomenon otherwise known as electroporation, a transitory phenomenon lasting only a few milliseconds. Pores can let the drugs or DNA inside the cells with no adverse biological or behavioural effects on the mice.

The NINIVE experiments pointed out two main findings. First, the presence of carbon nanotubes coupled to the EMFs induce a strong increase of nuclear localisation of an anticancer drug (doxorubicin) which is a crucial consideration for the cytotoxic action of drugs which interact directly with

Figure 1. We developed a strategy of functionalisation which allows the attachment on the surface of the nanotubes of: i) nucleic acids, ii) fluorescent moieties (for nanotube tracking) and iii) a cell ligand specific for neuronal targeting (chemokine CXCL12 (namely SDF-1) which binds its receptor CXCR4).

Figure 2. The "antenna" properties of MWCNTs induce cell permeabilization in mouse brain which allows for intracellular delivery of therapeutics impermeable to cell membrane. Results demonstrate that the stereotactic injection of MWCNTs in the cerebral motor cortex of mice facilitate genes/drugs to enter the cells when exposed to a RF field in the microwave range.





the nuclear DNA. Second, carbon nanotubes' antenna-like properties can be used to transfer genetic material in a mouse brain when exposed to EMF in the microwave range. This was proven by using an anti-apoptotic gene, Bcl-2, in view of potential applications in human CNS disease, such as cerebrovascular stroke.

The NINIVE team patented the process of cell permeabilisation mediated by nanoantennas and/or EMF, and the partner responsible for nanotube production has developed new commercial products, such as ultra-pure (99%), pure (98.5%) and vertically aligned multi-walled carbon nanotubes (MWCNTs). There is a clear interest from pharmaceutical multinational companies in the project's achievements.

NANOBIOPHARMACEUTICS (http://www.nanobiopharmaceutcs.org) aimed at delivering protein/peptide drugs across different physiological barriers by using nanoparticle systems as carriers both in vitro and in vivo. It achieved a real breakthrough in its effort to overcome the notorious difficulties in the oral delivery of insulin, by way of a system potentially capable of crossing the GI barrier and eliminating the need for insulin injections. The potential social benefits of insulin tablets would be enormous.

The project's team showed that in the animal model they could reach a sufficiently high bioavailability of insulin in the GI tract by oral administration. Although it could take another four to five years to get to therapy, NANOBIOPHARMACEUTICS demonstrated that the insulin eventually goes into the bloodstream where it is meant to go, like it happens with injected insulin; from there it reaches all different types of cells. The criteria for body clearance were also satisfied, since the project showed that orally-taken insulin is eliminated in the same way as the injected one: to some extent it is excreted through the kidneys, and in some ways it is metabolised. The polymer nanoparticles releasing the insulin remain in the GI tract and are not absorbed, so there are no systemic side-effects. The vectors protect the insulin from degradation in the GI tract and are then excreted.

Since it takes an average of five years from when patients get the first indication they have diabetes to the moment they come to terms with the fact they have to inject insulin for the rest of their lives, by which time their condition has become worse, insulin tablets would bring huge potential benefits in the early treatment of diabetes. A patent for the oral delivery of insulin was filed, that could result in much higher patient compliance with diabetes therapy from its very early stages.

On top of the oral delivery of insulin, NANOBIOPHARMACEUTICS pursued another hot challenge, by developing nanocarriers for the treatment of neurodegenerative diseases such as Alzheimer's or Parkinson's disease. This was met by the development of a very promising range of nanocarriers potentially capable of transporting drugs across the BBB in a very targeted, functionalised way.

Crossing the BBB safely is one of the crucial issues of nanotechnology applications in medicine. Many EHS studies have focused on it with keen concern, since it appears to be just about the most delicate issue in this field. It is well known that one of the major challenges of the pharmaceutical industry is to transport drugs of high molecular size across it, since the body designed it to protect the brain from unwanted and potentially harmful substances. Obviously, nanotechnology scientists are striving to prevent any unintended crossing of the BBB. However, it looks as if for the treatment of neurodegenerative diseases such as Alzheimer's or Parkinson's the drugs would have to go through the BBB and access the brain in order to be efficient.

The project created a nanoparticle library and developed and implemented an agreed standardised protocol for toxicological testing of nanoparticles, which is of utmost importance in medical research. It also developed and tested very promising systems for oral or nasal delivery for crossing the BBB. All this is of great interest to the pharmaceutical industry.

On another front, **SONODRUGS (Image-controlled Ultrasound-induced Drug Delivery,http://www.sonodrugs.eu/)** is developing drug-containing capsules for image-guided controlled release to fight cancer and cardiovascular disease. Most conventional drug treatments for these diseases are administered orally or by injection; however, once they enter the body it is very difficult to control where they end up and often, as in the case of chemotherapy, there is a very small therapeutic window where the treatment is effective with acceptable side effects.

The SONODRUGS capsules will also be distributed throughout the body but, by using imaging techniques their arrival at the target area can be monitored. Then a stimulus, such as a focused ultrasound pulse, can be applied to induce the capsules to release their drug only at this specific location. So far, the partners have primarily focused on the development of new materials for the capsules and on research studies on the co-administration of drugs, or dyes, in combination with microbubbles.

The partners are currently working on the development of new nanocarriers, and the final goal of the project is to produce two different capsule candidates for image-guided drug delivery. The project is also developing new therapy protocols for the use of imaging techniques. Some key issues to personalised treatment of two major diseases are addressed here: early detection, localisation through imaging as well as local treatments. The project has produced and tested the first nanoparticle prototypes and has implemented a magnetic resonance high-intensity focused ultrasound (MR-HIFU) system for image-guided drug delivery. It is also developing new protocols for the use of imaging techniques.

The project presents a strong industrial involvement, also at multinational level. Philips Healthcare, Nanobiotix and Lipoid are all part of the consortium. They aim to bring the technology to a certain maturity, then each of the partners can decide if they wish to commercialise certain aspects of the technology.

Molecular motors set a substantially different perspective in nanomedicine. They are the concept behind **ACTIVE BIOMICS (Active Biomimetic Systems, http://www.active-biomics.org)**, a project standing at the crossroads between drug delivery and regenerative medicine. Biomimetic systems imitate or are inspired by biological systems. They involve two types of biomolecular nanomachines, growing filaments and stepping motors, which are able to generate force in the nanodomain.

Active processes within cells are driven by energy. The filaments resemble long, thin rods with two ends: on one side they are built and on the other end destroyed. The molecular motors (proteins such as chryozine or myozine) walk along the filaments and transport cargo such as vesicles fuelled by an energy compound, such as ATP. After less than 100 steps the motors detach from the filament. The myozine protein is responsible for the movement of muscles. In this instance one of the project partners managed to develop nanomuscles by putting together an active filament with myozine and ATP to contract and relax muscles.

This fundamental science project delved into a deeper understanding of the molecular mechanism underlying this force generation and explored new possibilities for the integration of molecular machines into nano- and microsystems. In the future, active biomimetic systems are likely to be applied to drug delivery systems, molecular sorting devices, diagnostic tools for cell screening, or scaffolds for tissue engineering. This might lead to the ultimate construction of nanorobots, which could perform either useful diagnostics on single cell level, or drug delivery tasks in getting to specific target cells, or even non-invasive surgery.

Self-assembly mechanisms of membrane proteins over nanoporous substrates underlie the approach of **ASMENA (Functional assays for membrane protein on nanostructured supports, http://www.asmena.ethz.ch)** to drug delivery. The project addresses the need for the pharmaceutical industry to have a more reliable and efficient screening of membrane proteins as drug targets. These new products and methodologies will allow standard profiling and screening against membrane protein targets, shorten time and cost in drug lead development by increased predictability as well as contribute to fundamental understanding of structure-function relationship of membrane proteins.

Since more than 50% of all interesting drug targets are membrane proteins, the impact of new technologies addressing specific problems of drug screening on membrane proteins is obviously huge. It can be expected that new research tools making it possible to screen function of membrane drug targets will open up new venues for original drug development. As a result, the public will benefit from potentially more rapid and cheaper drug development. This is also very relevant for the wider study and understanding of viral susceptibility or neurodegenerative diseases.

ASMENA developed a number of key technologies and scientific insights, such as a new parallel method to fabricate well ordered nanostructures, for electrochemical or plasmonic sensors using self-assembly. This is a patterning technique that can be scaled up to arbitrary size and applied to all size ranges at low cost. The project also developed a new method to form supported lipid bilayers over surfaces including nanostructures by driving them over surfaces in microfluidic devices. This allows precise control of positioning of membranes and great flexibility in their composition.

Assembly of supported lipid membrane over nanopore structures can be achieved by several other new methods, ranging in their complexity from methods suitable for high-end research needs to robotic mass production, the latter by combining microfabricated sensor chips with spray coating of polymer membranes on top of which lipid membranes then can be assembled. For these systems the advantages, in terms of long-term stability and sensitive recording of peptide channels in membranes, have been demonstrated. Stability and ease of assembly of sensor structure are key elements for industrial implementation.

A new model for studying how membrane toxins or antimicrobial peptides interact with artificial cell membranes assembled on waveguide sensors has been developed. This approach allows studying the detailed mechanism which depends on such things as rearrangement of lipids within the membrane and could be studied by combining the new methodology with technologies from several of the industrial partners. This has not only led to scientific progress, but already also to launch of integrated technological platforms between some of the consortium partners.

ASMENA has produced scientific results at the forefront of nanoscale molecular and particle assembly, nanoscale sensing and membrane sensing. Two different prototypes for sensor fabrication, sensor functionalisation, membrane protein localisation, as well as read-out are being developed with a big industrial partner. There are several patents in the area of surface functionalisation of sensors for specific readout and guiding molecules to sensor structures, and several more have been filed. The interest of European industry is assured and the consortium has a very high industrial participation.

GANANO (New Generation of GaN-based sensor arrays for nano- and pico-fluidic systems for fast and reliable biomedical testing, http://www.ganano.eu.org) developed a novel Gallium Nitride (Gann)-based integrated system for fast physical, chemical and biological analysis of metabolites, drugs, proteins and pathogens in aqueous particle- and pico-droplets for hospital and lab needs.

MEDITRANS (Targeted delivery of nanomedicine, http://www.meditrans-ip.net) is developing drug-carrier systems including lipids, polymers or carbon nanotubes and aimed at optimising the targeted imaging agents for use with MRI probes. A set of nanodrugs has been developed, among which anti-inflammatory nanomedicines for chronic inflammatory diseases such as Multiple Sclerosis (MS), Crohn's disease and rheumatoid arthritis.

RECENTLY STARTED PROJECTS

Magnetic nanocontainers to be injected into the bloodstream for combined hyperthermia and controlled drug release are one of nanotechnology's most interesting top developments. Ovarian cancer, women's fourth worst killer, is considered to be a highly significant tumour model by MAGNIFYCO (Magnetic nanocontainers for combined hyperthermia and controlled drug release, http://www.magnifyco.eu) because it can be reached by a local injection.

The magnetic containers are attracted by a specific magnetic force (such as an alternated magnetic field or a radiofrequency) and produce heat locally; whenever this force is absent they behave as if their magnetic memory was simply not there. This very important property is crucial when it comes to concentrating the magnetic containers in a specific region of the body for carrying out hyperthermia. Tumour cells are more sensitive to heat and therefore a hyperthermic effect will kill them. The local heat also triggers the controlled release of the drug by 'overcooking' the nanocontainer.

So far there has been a very strong interaction within the project between the partners developing the nanoparticles and the groups working on the drugs and on the techniques designed to attach human antibody fragments to the surface of the functionalised nanocontainers to be delivered selectively to ovarian cancer cells. Several types of these nanocontainers are being tested and developed. Among these, some new iron oxide-based magnetic nanoparticles will be associated to self-assembled peptides and engineered tobacco mosaicovirus. Some are more hydrophobic and some more hydrophilic; indeed, the drugs are calibrated on the different nanocontainer types and their surfaces.

A year into the project, no immunogenic response or other adverse effects have been recorded. This raises the expectation that much tinier quantities of drugs will be required. There is a clear industrial involvement in the project: a partner, Magforce, aims to bring the scientific achievements onto the market.

Hyperthermia, again in combination with localised nanoparticles, is also at the core of **NANO3T (Biofunctionalized Metal and Magnetic Nanoparticles for Targeted Tumour Therapy, https://projects.imec.be/nano3t/)**. Both optical (laser) and varying-magnetic field energy sources are used to heat the particles. Whereas a large amount of passive particles is typically injected into the tumour cell tissue and heated, the project aims to achieve a selective targeting of tumour cells by using active particles. This is obtained by functionalisation of the surface of the particles. Specifically, the project selected two tumours with appropriate mouse model, such as pancreas and prostate cancer, to demonstrate this proof of principle in vivo.

Both of them express specific membrane proteins in large amounts in the cancer cell. NANO3T tested many ligands and selected two of them, an antibody (recombinant) and a peptide (artificial) to direct the particles to pancreas and prostate cancer cells. After the particles localise the cancer, they tether to the cancer cell membrane by molecular recognition and key-lock principle. Heating is obtained by magnetic and optical heating. The project demonstrated this principle in all aspects in vitro and is now ready to test it in vivo.

The project already developed and patented a novel star particle with the stabilising chemistry and the biochemistry to covalently bond cancer-targeting peptides to it. The team also developed the biochemistry to covalently bond antibodies to PAA coated magnetic particles for pancreas cancer. There are three prototype magnet set-ups as well as a laser, and the project patented partial aspects of the whole procedure. A small company is involved in developing their equipment according to the project's needs.

A completely different approach to tackling chronic inflammation such as rheumatoid arthritis comes from **NANOFOL (Folate-based nanobiodevices for integrated diagnosis/therapy targeting chronic inflammatory diseases, http://www.nanofol.eu/)**.

The new theranostic perspective uses folate-based nanobiodevices (FBNs), which should be able to provide a new type of cost-efficient, low side effects treatment. FBSs are designed, developed and produced to target effector cells directly. The project provided proof of concept in vitro and in vivo of a folate-based nanodevice in chronic inflammation and designed models helping to minimise animal testing and ensure high human safety.

NANOFOL has adopted a gradual risk-containment strategy to attain objectives with a step-by-step approach allowing to improve specificity, stability, side effects efficacy from the lower to the higher risk solutions. It combines expertise in nanotechnologies, biology, chemistry, materials science, biotechnology, engineering, risk analysis, medical and pharmaceutical fields. Rheumatoid arthritis affects around 1% of the world's population. Good industrial involvement of two large and two small technological spin-off companies adds value to the project.

NANOMEDICINE

Towards the body's self-repair

Nanomaterials lead the way in mimicking vital functions, making cells work more efficiently and restoring life's building blocks

Tissue engineering is becoming an increasingly realistic prospect thanks to the unique properties of engineered nanomaterials, which can make cell interactions much more efficient than conventional materials. In fact, the building blocks of tissues themselves are nano-structured, so that the right choice of non-toxic nanomaterials can meet the necessary requirements to regenerate them.

This regeneration can take place the same way nature does, by the power of so-called bioinspiration, thanks to the development of biomimetic nanomaterials; or the nanoparticles can be wholly artificial and multifunctional instead. Nanotechnology can develop scaffolds for either neural, retinal or corneal implants, or for the replacement of bone and cartilage; or else, it can be used to coat artificial implants. In order to avoid rejection, scientists are cultivating cells inside the materials themselves.

A chapter to itself is the staggering advance of the so-called 'converging technologies' combining biological, cognitive and robotic sciences, propelling nanotechnology firmly into the future together with a range of related ELSA (ethical, legal and social aspects) issues that needs to be carefully explored. Neural interfaces and implants fall into this category.

SPOTLIGHT ON...

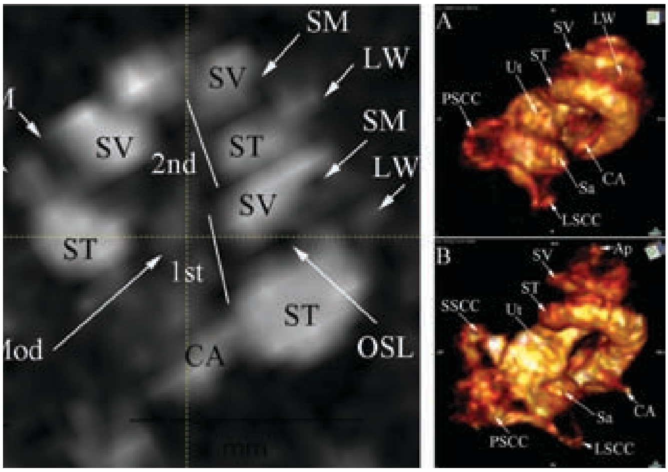
NANOEAR (3g-Nanotechnology based targeted drug delivery using the inner ear as a model target organ, http://www.nanoear.org)

Patients suffering from the majority of hearing disorders, ranging from total deafness to age-related hearing loss, can hope to have their hearing restored through the immission of eight safe multifunctional nanoparticles into the inner ear. Eventually, a nanohearing implant will also be developed within the next 10 years.

NANOEAR made a real breakthough by obtaining a most innovative 3D imaging of the functioning human cochlea, or inner ear, by furnishing the nanoparticles with MRI visible (and EMEA-accepted) contrast agents, such as SPION and Gadolinium chelate. This allows the project's team to see where the nanoparticles target, accumulate and are secreted, in order to deliver corticosteroids, peptides, genes, siRNA and shRNA through the same route. The MRI of nanoparticles, thanks to its new properties, can also provide safer and more detailed imaging than the one obtained with traditional contrast agents.

The process works like this: the multifunctional nanoparticles target specific, selected regions in the inner ear. They are imaged through MRI and tracked up to the point when they deliver a payload of drugs, proteins or genes.

The project's team also demonstrated that the best access to the inner ear and balance organ is not through the round window membrane as it had been believed until now, but the most efficient drug delivery route is through the ligament around the small ossicule in the oval window. By visualising



fine structures of the mouse cochlear in Gd-DOTA enhanced MRI

the functioning cochlea in 3D, it is also possible for scientists to visualise hearing disorders that were previously unidentifiable.

Among NANOEAR's technological achievements in drug delivery, key peptides were recently identified, which help the nanoparticles to escape the endosome storage system, where most of them are placed and dysfunctionalised by the cells for safety reasons. By escaping this system the nanoparticles can deliver the therapeutic agents that are aimed to work either in the cytoplasm or in the nucleus. The nanoparticles can also carry hydrophilic or hydrophobic drugs, growth factors, genes and mimetics, which are small drugs working as larger proteins.

A 'stealth cover' allows the nanoparticles to pass the cell membranes, unrecognised by the immune system. The project team recently saw that the nanoparticles can be traced from the ear up to the entry of the CNS, as they prefer to pass along the nerves. Now the system should be fine-tuned by developing more advanced targeting moieties and organising trials with commercial mimetics. The delivery of proteins, drugs and genes has been achieved in animal models.

Imaging and drug delivery are not the only remarkable achievements of the project. NANOEAR's third frontier is a radically new generation of cochlear implants, which is still under development and can be expected within the next 10 years. The principles of this new type of hearing aid and nerve stimulator based on nanotechnology, or 'nano-hearing aid', have been worked out. It would be a major breakthrough. In fact, conventional technology is still not quite within the 'nano-range'; in particular, the electronics and the coils are currently in the 'micro-technology' class.

The cochlea implants can be coated with drugs with novel plasma-coating technology providing 10-20 um layer consisting of nanoparticle carrier. The drug from the nanoparticle is dispersed by a slow-release mechanism. The other innovation is the incorporation of nanogels into a tiny storage space within the cochlear implant electrode. From this storage the drug diffuses to fight surgical trauma and revitalise the inner ear. Notably, the electrode is as flexible and smooth as non-drug–containing electrodes.

The largest cochlear implant company in Europe is a project partner and they have an interest as this work could lead to a completely new generation of cochlear implants and hearing aids.

NANOEAR holds several patents, mainly in electrode technology and drug incorporation, and is aiming to produce prototypes for human use. It is in the process of establishing joint ventures with the pharmaceutical industry to commercialise the nanodelivery items and provide a much needed carrier system for the regenerative medicine industry.

Neural interfaces are another most ambitious frontier which the nanotechnology revolution can bring ever closer to our doorstep. In the case of **SMARTHAND (The Smart Bio-adaptive Hand Prosthesis, http://www.elmat.lth.se/~smarthand)**, the term refers to a particular application in neuroprosthetics, that of a robotic hand giving back sensation to amputees. Neuroprosthetics connect the brain, or nervous system, to a device in order to transform an intention to move into actual movement (the other development encompassed by the definition of neural interface, namely the Brain-Computer interface, is not the case here).

SMARTHAND holds proof of concept that you can use an ultrathin, highly stretchable 'cuff electrode' (which is built on a very thin layer of polymer, like a film, and then mounted on a silicone sheet) wrapped around the peripheral nerve bundle to control a hand prosthesis. This was attained by acute implantation on an animal so far. This particular application would involve an implant and be connected by wireless technology to the prosthesis. It is longer term, invasive and it would suit the most serious amputees, who lost a limb above the elbow. One of the scientific challenges in the future will be about making the implant biocompatible while maintaining the ability to record the small nerve signals.

The other very important achievement of this multidisciplinary project, which was successfully experimented on some amputees and is already on the market for research purposes only, is a non-invasive cyber-hand prosthesis constructed with sensory substitution connected to the amputees' sensory 'phantom hand' map. It has been shown that by pushing the skin on certain locations of an amputee's forearm, the amputee feels as if this pressure occurs on some of the phantom fingers in a proportional way. This results from a cortical reorganisation of the sensory map of the forearm.

Both the invasive and non-invasive SMARTHAND options will potentially increase disabled people's quality of life by restoring functionality through sensation and control. This would lead to increased acceptance of the prosthesis, as if it belonged to the body, and it would reduce 'phantom pains', which are still actually felt by amputees. With amputation along the forearm there are a lot more muscles remaining so the already existing non-invasive option can work very well, whereas in patients with an above-the-elbow amputation scientists there may be a couple of functioning muscle groups in the upper arm, so sensations and movements are much more impaired and a neural interface implant would be the best solution.

The robotic hand is already providing intuitive sensory feedback. It is 'intrinsic', meaning that all motors are integrated in the hand and controlled by way of a 16 channel EMG recognition system. A sophisticated network of sensors picks up external sensation and triggers a sensory feedback mechanism that, via a range of actuators placed on the forearm, is used to control the robotic hand. There are actually over 40 sensors inside the fingers, regulating position, force and contact. The hand has a universal wrist that can be attached to a traditional socket. This gives the amputee an 'artificial sensitivity' and a high capability to control daily activities and very subtle movements, like holding a cup without breaking it or dropping it. The currently available prosthesis does not involve the use of the 'cuff electrode' and suits amputees below the elbow best.

In time, the carbon-fibre socket will also be able to contain a receiver for 'cuff electrode', namely the soft neural interface option that will be implanted in the patient's arm. By pre-stretching the silicone before the electrode is glued to it, the device curls by itself and becomes like a tube, which can be opened and wrapped harmlessly around the selected nerve bundle in the upper arm.

All the project's groups are continuing with their research and development of concepts and subsystem for the prosthesis. For instance, work is still continuing on the sensory feedback system in order to make it generic, so it should be possible to use it on all types of extremity prosthesis in order to provide sensation for amputees. There is indeed potential for the technology to be used on leg amputees as well.

A completely new approach to bone and ligament substitution comes from **TEM-PLANT (New Bioceramisation processes applied to vegetable hierarchical structures)**, whose aim is to apply breakthrough processes as to transform high quality raw materials from plants and wood into carbon templates for bone and ligament regeneration.

While this project can rebuild bones out of red oakwood, paradoxically it also showcases bioinspiration at its simplest. The transformation wood into a ceramic that is identical to hydroxyapatite, the mineral part of bone which makes up 80% of it, is indeed 'natural' from top to bottom, in the sense that no synthetic or hazardous by-products are created at any stage. It fully belongs to the nanotechnology domain, since it takes place at molecular level and it has been successfully tested on sheep.

The TEM-PLANT technology particularly suits the regeneration of long bones, such as a tibia. It could help with the regeneration of bones that have been shattered by a tumour, a trauma or the ageing process.

After undergoing a five-step chemical transformation sequence lasting about a week, a piece of red oakwood goes into a machine and it comes out as hydroxyapatite, which is the most important part of the bone. This ceramic material can be inserted into the gap of a fractured bone and stimulate the cells to wrap themselves around it and incorporate it, thereby forming new, healthy bone tissue.

Nothing in the morphology of the substance is changed along the way. First, the red oakwood is inserted into an oven and it comes out as black graphite. The pyrolisis takes place in the absence of oxygen.

This carbon is then put into another oven, yet again in absence of oxygen, inside a calcium vapour current where it becomes a Templant (structure) of calcium monocarbide (CaC).

This is turned into calcium oxide (CaO) inside an oxygen vapour current.

The fourth phase is the most critical, since the resulting compound must not be turned into calcium hydroxide (CaOHOH), as this can make the bone degenerate very quickly even in humid conditions. So the calcium oxide is put into yet another machine inside a CO2 current, where it is transformed into calcium carbonate (CaCO3).

Here the fifth phase, namely phosphatisation, occurs and the product comes out as a hydroxyapatite, which is the mineral phase of the human bone (the remaining 20% is collagen). This material is the most important part of the human bone, as cells can make up for the lack of collagen by themselves whereas they cannot regenerate any bone if hydroxyapatite isn't there. Collagen is obviously a facilitator and the nourishing element, but it is not the differentiating stimulus.

The mineral phase is the one that gives the undifferentiated cells the message that allows them to become bone tissue. Indeed, it has been shown that if collagen alone is put into a bone gap, it generates fibrous tissue, whereas only hydroxyapatite induces bone formation. This happens because of cell 'tensegrity', whereby bone cells mechanically 'feel' the 3D organised space of the tissue around them and produce organised, 'mature' bone morphology.

In the case of the TEM-PLANT material, which is a very well organised structure, cells organise the tissue around it because they 'recognise' it as if it were an autologous bone. So this material gets completely incorporated and remoulded by the bone, to which it acts as a scaffold. Hence the need to keep control of a hierarchical organisation of structures that goes from nano, through micro, to macro.

Two prototypes have been developed and tested: a silicon carbide external shell mimicking the cortical bone filled with apatite and collagen composite, like a biologically inspired internal core, and the graded porosity hydroxyapatite prototype developed from wood transformation.

As a growing number of old people are subject to bone and cartilage loss, bioinspired scaffolds obtained from natural materials for bone and tissue regeneration are becoming of great interest. This was also the main approach of **HIPPOCRATES (A Hybrid Approach for Bone and Cartilage Tissue Engineering using Natural Origin Scaffolds, Progenitor Cell and Growth Factors, http://www.hippocratesproject.org/)**.

The project developed a ceramic scaffold out of red algae and a polymeric one which is mainly based on chitin/chitosan, starch and protein-based polymers. The main aim was to provide new tissue engineering technologies for therapeutic treatment/regeneration of osteochondral defects and for this purpose the team developed advanced functional materials.

A wide range of techniques to develop these scaffolds to be used on cartilage, bone and osteochondral tissue engineering was developed. One of the main innovations was the production of specific software packages for designing patient-specific scaffolds. The scaffolds were also loaded with a range of growth factors that have been shown to have some ostheogenic potential. Primary cells and progenitor cells obtained from animals and later on from human patients were used to develop the tissue-engineered products. In vivo functionality assessment experiments were also carried out.

The surface characteristics of the scaffolds were optimised in order to enhance cell adhesion and proliferation and control the cell differentiation. Red algae culturing techniques were developed, which allow for their growth and mineralisation in order to produce synthesised hydroxyapatite and tri-calcium phosphate scaffolds. The materials biodegrade at the same time as the bone regrows.

The project, that presented a strong industrial involvement, also developed a technology allowing for the combination of these ceramic and polymeric structures in order to produce specific matrices for the regeneration of osteochondral defects. Among its achievements there is a starch-based fibre mesh coated with a ceramic material to regenerate the bone and a soft and smooth hydrogel to support the cartilage. The material has been proved to be working effectively in both small and large animal studies and the project also achieved a rapid prototyping system. A spin-off company was set up to commercialise the project outcomes.

On an altogether different front, that of the merging of nanotechnology and cellular engineering, **CELLPROM (Cell Programming by Nanoscaled Devices, http://www.cellprom.net)** develop methods for a more reliable and efficient differentiation of stem cells and took big steps towards the development of an industrial process that can be used for regenerative medicine and autologous cell therapy.

The project developed nanopatterned surfaces (NanoScapes) that can influence stem cell growth and differentiation. To this effect it produced two prototype automated systems for use with two different types of cell culture: an approach focused on use with suspended cells and another used adherently on growing cells. Both of these systems had to be developed in context as the requirements could not be fully met by either on its own. Also, novel surface structures were created and the projects filed some patents.

There was a big industrial presence within the consortium and pharmaceutical companies are definitely interested in this technology for screening.

The conventional approach to neural tissue repair had always been fraught with all sorts of intractable issues. But **NEURONANO (Towards new generations of neuro-implantable devices: engineering NEUROns/carbon NANOtubes integrated functional units, http://www.neuronano.net)** rose to the challenge by discovering that neurons actually love carbon nanotubes, so that carbon nanotubes could be potentially engineered to 'teach' neurons which way to go in order to reconnect.

This means that, eventually, carbon nanotubes might be used like 'intelligent' 3D scaffolds 'feeling' neuronal language to help neurons recover their functions and lost connections not only in neurodegenerative diseases such as Alzheimer's, but also by helping to bridge up partial spinal lesions where the neuronal links are missing.

The project demonstrated that neurons, explanted from the brain, re-grow in vitro and survive for weeks in excellent health conditions on a cell-culture substrate made of ultra-pure carbon nanotubes. NEURONANO's achievement was to develop a carbon nantotube substrate that could be integrated with neurons, and to manipulate the functioning of the neural network by interfacing this with carbon nanotubes. To this effect the team managed to integrate carbon nanotubes with multi-electrode array (MEA) technology to develop a new generation of biochips capable of helping to repair damaged CNS tissues.

Similar to brain circuits, neurons in vitro reorganise into microcircuits and networks, elongating and branching their neurites and establishing functional connections among themselves by synapses. This implies that carbon nanotubes emulate the extracellular environment neurons they are surrounded by under physiological conditions, and thus support the formation of the circuits that underlie neural elaboration of information.

Because carbon nanotubes are also electrically conductive, like metals, and neurons transfer and process information by electrical impulses, the project showed that carbon nanotubes can support and boost the exchange of information among neurons. This is one of the most exciting nanotechnology developments, which might open up completely new perspectives in neuroengineering and neuroprosthetics. When the neurons integrate with carbon nantotube substrates, it is as if they were using the carbon nantotube material to their advantage. It means that neurons co-opt carbon nanotubes to their service in the emission of electrical signals.

The project made great progress in understanding the way conductive nanosubstrates can organise the components underlying CNS electrical activity. As NEURONANO discovered that carbon nanotubes have the ability to re-engineer neuronal integrative properties at the single cell level and to stimulate the synapsis between neurons, it is now clear that carbon nanotubes can be exploited to reengineer network connectivity endogenously.

The project developed a number of techniques to produce new MEAs functionalised with carbon nanotubes. The interactions between neural tissues and electronic devices provide very interesting new tools for investigating the connectivity and the dynamic properties of neurons.

Although the project's research did not deal with clinical applications, the discovery has significant potential for the treatment of neurodegenerative diseases and carries great promise for the progress towards a neuro-implantable device for neural repair. The challenge is to see whether carbon nanotubes might potentially solve the problem of immuno-rejection of neural implants and greatly improve the transfer of information between the neurons and the electrodes themselves.

There are two possible application areas towards which this research might be developed. The first concerns Deep Brain Stimulation electrodes, which are already being successfully used for Parkinson's; the second one is about Brain-Machine Interfaces.

Nano-scaffolds are of the utmost interest in eyesight regeneration as well. **CORNEA ENGINEERING (Three-dimensional reconstruction of human corneas by tissue engineering)**, opens up the possibility of reconstructing and grafting corneas made from patients' own cells in order to overcome rejection risks. The engineered corneas could be used in partial or full corneal transplants.

The project actually managed to reconstruct a human cornea by using human cells and a scaffold made from corneal proteins (mainly collagen). Corneas are highly organised in order to allow high transparency and mechanical function. CORNEA ENGINEERING was able to replicate this organisation by using a magnetic field to orient the protein fibres in the correct way. This process has been patented.

An in vitro test to replace the use of animal corneas has been developed and is in use by one of the companies involved in the project. Existing tests only use the upper layer, or epithelial cells; however, this one also uses cells from the lower layers to give a better model of the cornea.

These achievements can also be used as an in vitro alternative to animal testing, particularly the Draize test, which uses rabbit corneas to test sensitivity to drugs and cosmetic products.

The reconstructed corneas have been tested in human clinical trials to repair damaged epithelium. When considered that epithelial damage, either from burns, genetic disorders or trauma, affects tens of thousands of Europeans and 25 000 corneal grafts are carried out every year, the impact of these achievements can be potentially huge. It is well known that cornea grafts carry several disadvantages. Above all, there is a shortage of donors, the patient is at risk of contracting diseases and transplant rejection is a distinct possibility. Also, laser eye surgery can change corneas to the extent that they cannot be used in grafts. By using corneas grown from the patients' own cells all these problems can be overcome.

Nanodiamonds are **DREAMS' choice material for retinal regeneration (Diamond to Retina Artificial Micro-interface Structures)**, whose great potential for neuron cell interfacing applications was demonstrated here. The project succeeded in building several prototypes of retinal implants as well as MEA systems.

The real challenge for the team was to gain the ability to process nanocystalline diamonds as a 'dream' semiconductor material, which the project successfully met by creating some highly advanced biointerfacing. Diamond, much like silicon, is a semiconductor but it is also very biocompatible, so that its surface is able to send electric signals to the optic nerve.

DREAMS actually demonstrated that cells can be in close contact with nanodiamonds, thus enabling better interfacing and reduced stimulation currents in order to reduce pixel size, improve resolution and provide the patient with far better vision. What makes nanodiamonds so attractive is that the number of image pixels within the same area of the retinal implant can be increased. The project proved the unique properties of this material by managing to pass on signals from cells to diamonds.

An eventual DREAMS implant might have the added advantage that no studs would be needed to peg the implant on top of the retina (as in the epiretinal mode) into the corpus vitreum, since the implant would lay behind the retina (in sub-retinal mode) and stay in place by itself. The implants have holes so that the retina can tolerate the interface better.

A variety of implant shapes have been tested. One project prototype, looking rather like a ping pong racket, is namely a thin polymer film 'encrusted' with nanodiamonds where the contacts, or pixels, are deposited in strips on its surface, forming a MEA. For the project the crucial point was not just a matter of increasing the number of pixels; in order to achieve this, the pixels needed to be made smaller and stimulation currents had to be reduced, since high currents cause loss of resolution.

The goal is to achieve at least 600 pixels in a retinal implant, which would allow patients to recover the function of reading. DREAMS's scope was not to produce an actual medical implant but to demonstrate the viability of nanodiamonds implants, so they can be a good alternative to the existing implants. One of the project's partners, the Vision Institute in Paris, won the Altran Prize in 2007 for research on an artificial retina incorporating the nanodiamond interface.

It is expected that industrial development for retinal implants will follow up the three patents filed by the project and an industrial partner has been identified. If successful, diamond-based implants for retinal stimulation could take up to five years to be developed, and the impact might be potentially huge.

In the field of bioinspiration, mimicking and restoring the functions of human senses extends to tact. Although it was not specifically aimed at neuroprosthetics, **NANOBIOTACT (Nano-engineering biomimetic tactile sensors/Nano-resolved multi-scale investigations of human tactile sensations and tissue engineered nanobiosensors, http://www.nanobiotact.org/)** managed the feat of building a biomimetic tactile sensor suitable for incorporating into the fingerpad of an artificial finger capable of 'feeling' the properties of complex surfaces. By connecting the sensor to a computer, the project focused on explaining the operational characteristics of the human mechanoreceptors and the human neural coding of tact.

As a result, the artificial finger may one day keep patients and doctors literally 'in touch' across different countries. This could ultimately lead to a breakthrough whereby long-distance diagnosing and even surgery may be made possible. In such an instance, clinicians might become able to carry out a 'hand' examination and treatment of a patient's body through communicating computers.

Small silicon devices (MEMS or microelectromechanical systems) mimic the nerve endings (mechanoreceptors) in the finger by converting tactile forces to electrical signals; the computer connected to the sensor interprets the signals from the finger and by behaving very much like the human brain. The artificial brain processes hundreds of complex signals from the finger very quickly to interpret the information about what the finger is feeling. And it does that in a learning mode, by using new information from experience. So the computer is using its networks in the same way the brain's neural network operates.

However, for the time being the information obtained by the artificial finger can be extracted and recognised, but not relayed yet. It might take another 10 years before science develops some displays systems making contact with a person at the other end. The sensor application might help develop robots requiring more sophisticated feedback. In the longer term, the artificial finger could also be applied to prosthetics technology for people to regain their sense of touch. In the medium term, it could be coupled with the work that is going on around the world in the field of neural interfaces; in the shorter term, it may be used as an industrial application for quality control along the production line, for faster and cheaper screening of textiles or personal care items.

The prototypes of NANOBIOTACT have been developed and the NANOBIOTOUCH project will build upon them. A large industrial company is involved and there is a lot of commercial interest about the sensor.

Nanomaterials inspired to natural biological fibres for use in devices is the main scientific challenge addressed by **BENATURAL (Bioengineered Nanomaterials for Research and Applications, http://www.materials.uoc.gr/~BeNatural/)**, which specifically aims to develop a novel class of peptide nanostructures as tools for bio-nanotechnology and biosensing. The long-term scientific and technological perspective of the project is to arrive at a well-understood, well-documented organic counterpart to carbon nanotubes and inorganic nanowires.

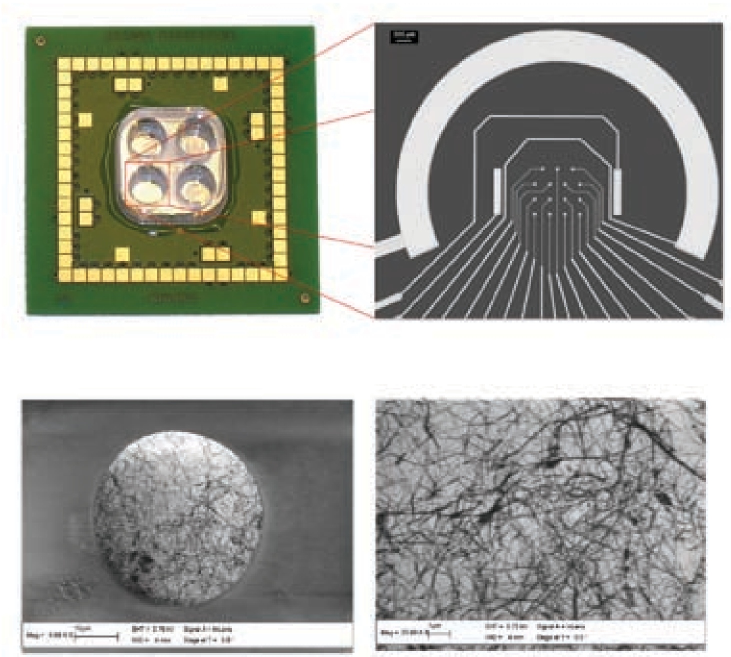
Nano-bioassemblies offer several advantages over inorganic nanowires, such as chemical versatility, easier functionalisation, and less costly fabrication and more environmentally friendly production conditions.

The project succeeded in designing, characterising and producing biological nanofibres acting as templates for the fabrication of metal nanowires and tubes. Techniques for nano-manipulation of the peptide nanotubes have been developed, leading to their controlled positioning between electrodes. Subsequently, the nanowires and tubes have been successfully integrated on biochips and MEAs. Furthermore, several encouraging results were obtained on optic nerve regeneration using peptide 3D scaffolds.

The advantages compared to existing, non-biology–based technologies could lead to the development of smaller, more sensitive and versatile biosensors with a broad range of applications in environmental, personal safety and homeland security. Furthermore, the use of self-assembling scaffolds is envisaged for nerve regeneration applications.

Although most of the research carried out by BENATURAL is fundamental, the project made such fundamental progress in the knowledge biological self-assembling materials as to pave the way to the development of biology-inspired future generations of nanodevices, as it holds proof of concept of the potential integration of nano-bioassemblies into devices. The technology is in the process of being developed and a joint patent has been filed.

An industrial partner whose core business is microfabrication, biosensors and cell-based biochips, especially those based on electrochemical detection techniques, is demonstrating the potential applications of this research in the biosensor area, with a high market potential in the area of life sciences. The bio-nanoassembly approaches developed are on the forefront of nanotechnology research, combining a readily customisable platform for assembling a potentially unlimited range of nanostructures onto microsystems, with a high flexibility in tailoring the component to the application. This could provide EU-based companies with a technology for the integration of nanocomponents with microsystems.



Left: Special Microelectrode array (MEA60) biochip with 4 wells and gold electrodes. (Ayanda Biosystems S.A.)

Bottom left: Scanning electron microscopy (SEM) picture of MEA electrode covered with self-assembled peptide fibrils. Bottom right: Enlarged view of the fibrillar network.

SINGLEMOTOR-FLIN (Long-Period Observation (LPO) of Single (Bio)-Molecular Motors by Novel Minimal-Invasive Fluorescence Lifetime Imaging Nanoscopy), aimed to improve the sensitivity and resolution of FLIN (fluorescence lifetime imaging nanoscopy) to examine four types of single molecular motors (which are involved in Alzheimer's disease, Werner syndrome and infectious diseases among others). The research focused on how these motors operate and break down in disease, and it successfully developed a microscopy prototype, to be used in biological/artificial interfaces.

RECENTLY STARTED PROJECTS

Treatment of autoimmune diseases is an enormous challenge and so far only non-selective immunosuppressants with many side effects are available. More than 80 such diseases have been identified; prominent examples include type 1 diabetes and Crohn's disease.

In a healthy condition the human immune system is highly efficient at eliminating pathogens. Specific immune cells recognise surface markers of the pathogen and trigger a complex immune response. Other cell types are important in controlling the appropriateness of this response to avoid an overreaction, such as regulatory T-cells (Tregs), which may also play a crucial role in many autoimmune and inflammatory diseases. In these disorders the immune system is misguided and may attack specific body cells or tissues.

NANOII (Nanoscopically-guided induction and expansion of regulatory hematopoietic cells to treat autoimmune and inflammatory processes) is using novel nanotechnologies to try to produce artificial but biofunctional interfaces that should help to convert non-specific precursor cells from a patient into highly specific Tregs outside the body. The transfusion of the Tregs into the patient could then help to bring the immune system back on track. The basis for this approach is the observation that the interaction of immune cells with their native environment happens at well-specified interfaces with other cells or proteins. To mimic such surfaces researchers must be able to position molecules with great spatial precision, ideally with nanometre accuracy.

The approach of using Treg cells in order to control the immune response by its own highly specialised means is obvious but difficult. The main challenge is to generate a therapeutically significant number of highly specific regulatory T-cells.

Materials scientists in NANOII are developing this expertise using a nanolithography method, which should allow building a training field for Tregs with extremely high precision. The technique should be simple, not very costly and suitable for large-scale production and the establishment of chips for high-throughput screens.

In collaboration with immunologists and clinicians these chips will be tested for their ability to direct the differentiation, proliferation and tissue-tropism of Tregs focusing on Crohn's disease and type 1 diabetes with the final aim of taking a first step towards T-cells–based therapy.

The issue whether the features of nanoscale structures are playing a role in neuroscience is at the core of **NANOSCALE (Understanding interactions between cells and nanopatterned surfaces, http://www.nanoscale-fp7.eu/)**. The project is investigating the interactions at the nanoscale between neurons and surfaces with specific nanopatterns, which appear to control several major biological processes, such as cell proliferation and differentiation.

When neurons are growing or retracting, a dimension in the nanoscale cannot be seen with ordinary microscopes. By using an AFM, the project's team singled out holes or fragments in the growth cones.

The project's team expects that the use of nanostructures can be used to influence the rate of stem cell proliferation and differentiation and drive the stem cells to make neurons and neuronal networks. NANOSCALE is aiming to produce and develop a whole range of nanodevices for growing, guiding and manipulating cells, neurons and neuronal cultures. Although this is a fundamental science project, it could have a long-term impact on neuromedicine as it aims to establish a new cellular and molecular basis for the development of a third generation of biomaterials to be used in designing substrates for tissue engineering. There is a clear involvement of small companies in the project, indicating an interest in the marketing of future outcomes.

SECURITY

A quantum leap in security

Nanosystems for the unintrusive monitoring of public places and a rapid biosensor for water supply safety can make a real difference

Nanotechnology can give a vital contribution to civil security through innovative detection, protection and identification methods. Detection systems include selective imaging of objects and biosensor monitoring of bacterial and viral contamination, for instance of drinking water supplies.

SPOTLIGHT ON

TERAEYE

Active security, passive nanosystem: **TERAEYE (A low cost and fully passive Terahertz inspection system based on nano-technology for security application, http://www.teraeye.com/)** could be the much needed breakthrough in terrorism prevention that can guarantee security and protection of individual privacy at the same time. Its objective is to develop an innovative range of inspecting passive systems, based on nano-fabricated semiconductor quantum dot sensors. Under laboratory conditions, an experimental device working at sub-K temperature able of converting a single terahertz (THz) photon into 10 million electrons has been developed, thereby demonstrating the exceptional high gain of the sensor.

The absolute novelty is that TERAEYE will constitute the basis for the introduction of totally new passive and unintrusive detection and scanning systems for security applications, which would open up new market perspectives for a new set of products and services based on passive THz detection, and thereby supporting a radical transformation in the security sector.

Indeed, if this application became widespread, it would provide a welcome alternative to some other security technologies currently worrying the public because of their disliked intrusiveness and especially with the persisting doubts about their effects on human health.

Even if the THz radiation has been demonstrated to be safe for human health, the approach followed by the TERAEYE consortium was to develop a complete passive system, which will have the capability of analysing the radiation spontaneously emitted by any object, including the human body. The security procedure will receive a complete new impulse from a technology such as this and in particular the perception of an intrusive system will slowly disappear from public opinion.

Some other security applications of the THz frequency band have attracted controversy about the violation of individual privacy because, if targeted in a certain way, the frequency can allow security agents to 'see' a person through their clothes. This is not the case of TERAEYE at all, as this system works only to detect harmful substances carried by people. Today, with the danger of terrorists determined to conceal liquid bombs or other agents, such as biochemical, on their person, this need for establishing a whole predetermined range of dangerous substances that need to be quickly identified within a crowd becomes imperative.

The system works as a 'traffic light' by spotting these harmful substances that may be hidden on the human body without further imaging of body parts. A given substance emits waves within a THz band. By exciting the frequency bands of the nanosensor, a given substance produces absorption 'peaks'. The sensor picks up single photons and it calculates them. This calculation produces the wave shape of that substance. The spectrum is compared with a database. Such passive THz information, processed by dedicated alarm management software, will just flag up the dangerous substance as a highlighted area on the normal image of the scanned person.

Such a technology could prove to be the ideal answer to many outstanding security questions. In conjunction with CCTV surveillance, TERAEYE could allow the real-time, thorough monitoring of any crowded space that needs protection from terrorist attacks, such as airports, metro stations, railway stations and shopping malls, as it would spot the dangerous individuals and secretly alert the CCTV surveillance system about their movements, so that security would have a chance to intervene and prevent an attack. It's not a visually invasive system at all, because it sees what the CCTVs see, but it discriminates danger. It will have to be coordinated with the pre-existing video surveillance system of the area for any suspects to be picked up.

The system does not emit any kind of radiation, so it is completely safe to be used anywhere. The box containing the system would have to be installed at a secret checkpoint, for instance in an entrance hall. It does not need a portal such as a metal detector, but it would keep a keen eye on a whole public area, in search for explosives, weapons and any other ingredients that can be used to assemble a bomb.

Currently, two prototypes have been assembled in two separate European laboratories. They contain different solutions aiming to demonstrate the complete functioning of the system. The advanced prototype has a complete new approach in electronics and cooling system. The sensor under testing is the same for both laboratories.

TERAEYE will contribute to enhance the introduction of new technologies, pioneered at laboratory level, within industrial sectors such as security, electronics and aerospace sectors. European industry shows a deep interest in the project's applications, especially the airport security network, with the prospect of a potential future collaboration with some major airports in Europe for the field test of the complete system in a real public environment.

In order to protect the population from the risk of biochemical attack, the monitoring of drinking water supplies is critical. A system that is capable of rapid detection of bioterrorism agents at very low concentrations will increase public security. **DINAMICS (Diagnostic Nanotech and Microtech Sensors, http://www.dinamics-project.eu/)** is doing just that by developing an integrated, automated and highly sensitive measurement device to simultaneously monitor the presence of several bioterrorism agents in the supply network.

The two major scientific challenges tackled by the project are the reduction of the sample volume by a factor of more than 1 million (from 1 000 litres to 1 millilitre) and the integration of several technologies such as nanotechnology, microfluidics, microelectronics and molecular biology.

Large sample volumes are necessary to guarantee the highest security level for the population while small volumes are required for optimal detection by a system based on microfluidics and nanotechnology.

So far, the project developed a first version of an 'in-line separator' that reduces the sample volume by a factor of about 10E4. For an automated macro-microfluidic interface, this enrichment factor is quite high, especially when considering the large starting volume of over 1 000 L.

The integrated, cost-effective nanobiological sensor for detection of bioterrorism and environmental assays will be a portable lab-on-a-chip device for detection of pathogens in water using on-the-spot recognition and detection based on the nanotechnological assembly of unlabelled DNA. DINAMICS is integrating DNA hybridisation sensors with microfluidics and signal conditioning and processing both on silicon and polymer substrates.

A highly sensitive and robust detection module has shown an excellent detection limit of 1 000 E. Coli bacteria. The microelectronics is able to read out 32 photodiodes in parallel at fA currents. Many other viruses and bacteria are quickly detected by the device.

The project completed a multi-scale modeling toolkit allowing for coupled molecular and macro-scale modeling tools to be applied to practical geometries as well as a meta-model for DNA transport-enabling simulation of the movement of DNA in microfluidic channels in a more precise way.

A prototype of the detection system and the multi-scale modeling toolkit is expected at the end of the project in 2011. A patent application is being sought for the detection device.

Some results of DINAMICS, such as detection system, software and simulation toolkit, will enter the market most likely within 18 months of the project's completion. The quality of the results has already attracted the interest of industry outside the consortium. Partners who offer engineering consultancy services have broadened or deepened their expertise and hence become more competitive. At first, the results will be applied in the healthcare, pharmaceutical and food industries.

The fastest and most sensitive single photon optical detector was built by **SINPHONIA (http://www.sinphonia.org)** and it is based on a new nano-structured superconductor for optimum performance at telecom wavelengths. Quantum cryptography allows for the secure communication of information by banks, the security services and was first demonstrated by communicating the outcome of elections in a Swiss canton. Moreover, the detectors can be used as ultrasensitive optical detectors for R&D.

The project achieved the deposition of very thin films and patterning of nanostructures. New architectures provide new functionalities and improved performance, which was a very big challenge. The team demonstrated the system's implementation into real applications such as quantum cryptography, long-distance optical communications, remote sensing and diagnostics and testing.

The project managed to achieve photon resolving number function, which is the ability to measure the number of photons in the pulse. The project also improved the speed of the pulse from 100 MHz to 1 GHz and demonstrated the technology in quantum cryptography at record distances.

The two-channel, fibre-coupled single-photon detection system operates at 3 K. Fibre coupling technology is a must, but this requirement has also been met by the project.

SINPHONIA's technology involves a full system of fibre coupling, packaging and the detector. This can be transported and used as required with no previous notice.

Such a system represents an invaluable tool in the fields of quantum communication (the project indeed reported a successful application for quantum key distribution over a 200 km distance), near-infrared spectroscopy and quantum optics, and any other application requiring ultimate sensitivity and temporal resolution.

A full system prototype will soon be on the market. An earlier prototype was commercialised by a spin-off company of one of the project partners, who is also likely to market the more advanced prototypes that have been developed with the project. At present, the optical detector is mostly being used for scientific research.

CARING FOR THE SAFETY OF HEALTH AND ENVIRONMENT (EHS)

Highly focused research into engineered nanomaterials aims to make nanotechnology secure and sustainable for environmental and human safety (EHS)

Engineered nanomaterials (ENs) present tremendous opportunities for industrial growth and development, and hold great promise for the enrichment of the lives of citizens, in medicine, electronics and numerous other areas. However, there are considerable gaps in our knowledge concerning the potential hazardous effects of ENs on human health and the environment.

The nanoscale offers a massive increase in the surface area available for reactions with other molecules. Some materials, virtually inert in their everyday bulk form, display novel but potentially toxic properties at different nanoscales.

For scientists to be able to carry out effective nanosafety research, they need to know that they are working on precisely the same nanomaterial or particle. However, nanosafety is such a new area that many scientific descriptions and definitions still have to be agreed upon and, at the nanoscale, tiny differences can make all the difference.

As human health and environmental safety are of paramount importance, every single R&D project funded by the European Commission needs to have a specific safety work package.

The effects of engineered nanoparticle and nanomaterials are being thoroughly investigated. With a better understanding of nanoparticle toxicology the potential hazards can be minimised for consumers, workers and the environment and proper protocols can be adopted. This research will be useful for public and occupational health as well as for the successfulness and sustainability of the nanotechnology industry.

SPOTLIGHT ON...

NANOIMPACTNET

A very effective coordination action bringing together Europe's top experts in nanotoxicology, nanoecotoxicology and nano-risk assessment, whether they are from university research laboratories, regulatory agencies or industry comes from **NANOIMPACTNET (European Network on the Health and Environmental Impact of Nanomaterials, http://www.nanoimpactnet.eu)**.This transparent, multidisciplinary project facilitates collaboration and communication between all stakeholders.

NANOIMPACTNET promotes the coordination of testing strategies and methods, screening tools, risk assessment tools and methodologies to over 800 members of the research community, via its website, newsletter and physical events. It also reaches out to over 1 000 companies developing or using nanomaterials, and numerous non-governmental organisations (NGOs) and government departments.

Sharing and discussing existing knowledge aids these stakeholders to identify knowledge gaps and define strategies for addressing them. The project's events have not only trained dozens of PhD students and post-doctoral researchers in the latest techniques, but have also produced valuable consensus reports on these issues.

To enable scientists to effectively replicate experimental conditions, a database of nanosafety research protocols (precise, detailed descriptions of scientific methods) is an important ongoing work. All this work goes towards the goal of helping to implement the EU's Action Plan for Nanotechnology.

Especially as nanomaterials become ubiquitous, NANOIMPACTNET takes the view that we are all stakeholders in a healthy future enhanced by nanotechnology. Ideally, manufacturers would be able to guarantee no adverse effects of nanotech on health or the environment. It is neither in civil society's interests, nor in industry's, to see a battle like the one surrounding genetically modified organisms (GMOs). Most importantly, the project is actively engaged in helping to give a scientific basis to future legislation to protect all stakeholders.

The project offers nanotechnology industries a platform to exchange research ideas with Europe's most renowned experts in nanosafety, to contribute to reports, and to learn state-of-the art thinking at workshops and training schools. As with the scientific media, positive results are far more interesting than negative ones. Unproven dangers are less interesting to the media than the latest nano-enhanced product or the possibilities that a new nanoproperty may bring in the future.

Alhough this is a European network, NANOIMPACTNET has attracted a lot of interest from other countries dedicated to developing their nanotechnology industries responsibly.

NANOINTERACT (Development of a platform and toolkit for understanding interactions between nanoparticles and the living world, http://www.nanointeract.net) seeks to understand how engineered nanoparticles interact with living systems, from the moment of first contact, through uptake and localisation, and finally to the onset of functional and signalling impacts induced by the presence of the nanoparticles. For this purpose the project correlated nanoparticles as they exist in a biological fluid (for instance cell culture media where they acquire a protein corona) with their interaction with living systems, looking at a series of end-points such as uptake, sub-cell localisation, cytotoxicity, genotoxicity, apoptosis in cells, and mortality of daphnia magna and growth inhibition of algae.
The emphasis in all aspects was on quantitative reproducibility, which started with understanding the applied nanoparticle dose (related to the particle size distribution in the assay media), and ensuring that identical responses were observed across operators, across instruments, and across laboratories.

The workflow of NanoInteract

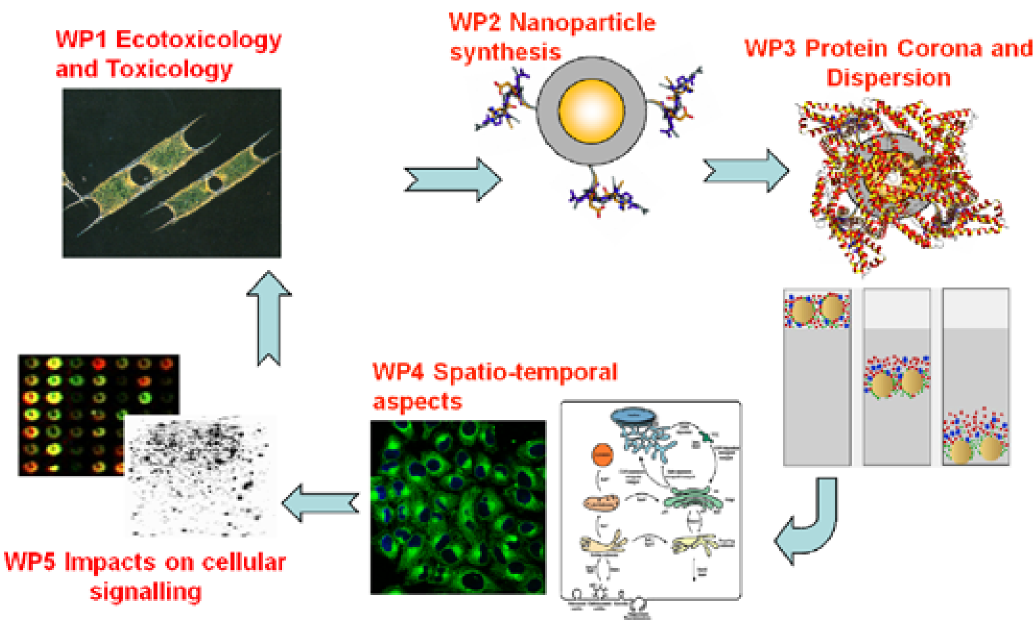
Among its main achievements, NANOINTERACT described the nanoparticle-protein corona as the biological entity that interacts with living systems and cellular machinery. It also showed first evidence of nanoparticles modulating the rate of protein fibrillation in solution: in fact, depending on the nanoparticle-protein pair, the presence of the nanoparticles can accelerate or inhibit the rate of protein fibrillation in solution.

The project demonstrated how nanoparticle uptake and localisation can be made quantitatively reproducible, and that polystyrene and silica nanoparticles localise in lysosomes, without any evidence of exit pathways. Cells continue to divide normally and the load of nanoparticles is split equally among the daughter cells. NANOINTERACT also showed that silica nanoparticles can inhibit stem cell differentiation, suggesting that further investigation of potential impacts of nanoparticles on developmental toxicity is needed.

Another significant result is that chronic toxicity of cerium dioxide nanoparticles in crustaceans, Daphnia magna and Thamnocephalus platyurus, was found to increase with decreasing nominal particle diameter and the difference in toxicity could be explained by the difference in surface area. The project established and tested protocols for all aspects of nanoparticle purification, dispersion, characterisation, presentation to cells, uptake and localisation studies, high content analysis and end-point assessment, such as genotoxicity, apoptosis and ecotoxicology.

The project's main impact was to show that assessment of nanoparticle interactions with living systems can be made into a quantitative science via an interlaboratory Comet assay for genotoxicity, rather than simply testing and reporting observations. The concept of the nanoparticle protein (bio-molecule) corona as the biological entity that interacts with living systems, and which determines fate and behaviour is now increasingly accepted in the community, and has been adopted into many subsequent research programmes internationally. It also introduced the science of bio-nanointeractions as the underpinning science for nanosafety and nanomedicine.

The outcome was to add clarity and structure to the question of nanosafety assessment and to resolve some of the issues contributing to uncertainty and unease among industry and other stakeholders regarding the potential hazards presented by nanomaterials. NanoInteract has been successful to a large degree in this respect, and the coordinating team is now trusted by industry and other stakeholders, such as regulatory agencies and NGOs for their transparent approaches to addressing complex issues.



NANOSAFE2 (Safe production and use of nanomaterials, http://www.nanosafe.org) concentrated its efforts on a small number of engineered nanoparticles for their safe industrial production. The project took off from the paradigm of risk assessment and risk management and it chose to address exposure during manufacturing processes and nanomaterial exposure in the environment.

Screening techniques were developed for carbon nanotubes, zinc oxide, carbon black, crystalline silica of a size around 50 nm and no larger than 200 nm.

The project's risk assessments aimed to estimate, and if necessary quantify, how much damage or injury can be expected from exposures to a given risk agent, and to assist in determining whether these effects are significant enough to require action. NANOSAFE2 aimed to develop innovative detection, traceability and characterisation techniques for engineered nanoparticles in both air and liquid media will be investigated.

NANOSAFE2 created a database on toxicology related to nanoparticles in order to collect and organise all the available knowledge from the most differet sources worldwide, from existing literature all the way to companies, who were asked to share data or support toxicological tests for specific nanoparticles. The project also focused on the development of advanced technologies to limit both exposition to nanoparticles in factories and leaks into the environment by designing safe production equipment, handling automation, dynamic confinement, individual protection devices and filtration.

NANOSH (Inflammatory and genotoxic effects of engineered nanomaterials, http://www.ttl.fi/partner/nanosh) focused its research on the toxic effects of nanoparticles that are relevant to the occupational environment.

This was an experimental and field study. The experimental part with animals and cell systems explores genotoxic and immunotoxic effects of titanium dioxide and carbon nanotubes in these systems. In the field studies, assessment of exposure mainly to titanium dioxide nanoparticles is carried out in 20 different workplaces in Germany, the Netherlands, Poland and the UK by using state-of-the-art methods. A database on the results of the exposure assessment has been prepared. Also, a strategy for sample collection of nanomaterials in such studies has been developed. Further, 35 different nanomaterials have been carefully characterised and published in a NANOATLAS book. An important part has also been the research of the titanium dioxide and other nanoparticles on circulation, especially microcirculation, in animals.

Genotoxicity studies have provided evidence that both titanium dioxide nanoparticles and carbon nanotubes have the potential to induce genotoxicity both in in vivo and in vitro systems. These are important and partially novel observations already published in open literature. Immunotoxicology studies have shown that titanium dioxide nanoparticles induce pulmonary inflammation both in in vitro and in vivo systems, especially when titanium dioxide nanoparticles have been coated with amorphous silica (silicon dioxide) indicating that the surface properties of nanomaterials have an important contribution on the effects. For field study effects, the exposure levels in all workplaces to which we had access were low no matter which metrics were used (such as number concentrations and surface area). The particles had an impairing effect on microcirculation in experimental animals.

The project produced important information to be used in the risk assessment of nanomaterials and already being used; e.g., in assessing of risks of cosmetic products containing titanium dioxide nanomaterials, for instance sunblock creams. These assessments are carried out by, for example, the Directorate-General for Health and Consumers (DG SANCO) Scientific Committee on Consumer Safety (SCCS). The project results will also most likely have an impact on nanosafety policies in Finland and other EU Member States and Commission policies as a part of the common database.

The results of the field studies are important for the production industry and also industry sectors using the nanoparticles in terms of providing guidance how to carry out the assessment of exposure to these materials.

CELLNANOTOX (Cellular Interaction and Toxicology with Engineered Nanoparticles, http://www.fp6-cellnanotox.net) focused on the primary interaction of lung and intestine with nanoparticles, while liver, kidney and the immunological system were selected as the secondary major sites of interaction, following the penetration of nanoparticles into the blood circulation.

The project explored the mechanistic aspects of interaction, uptake and recycling of selected nanoparticles by the different cellular systems, some toxicity mechanisms that emerged following the interaction of nanoparticles with the different in vitro cell models, certain nanoparticle-induced metabolic changes using precision-cut liver, kidney and lung slices an the nanoparticle-induced activation and inflammatory response of the immune system. It appears that different tissues have different sensitivities to nanoparticles.

A unique data-mining methodology was used to validate, transform and compare safety data.

DIPNA (Development of an Integrated Platform for Nanoparticle Analysis to verify their possible toxicity and eco-toxicity) provided novel information on in vitro assays for the detection of NP effects on human cells, instruments and methods for environmental nanoparticle detection, and recommendations for nanotoxicologists and researchers. The project aimed at creating and validating new instruments and assays to assess the possible toxicity of nanoparticles and to detect nanopollution at occupational sites, in order to promote safe nanoparticle manufacturing and handling. The impact of cobalt, gold, cerium, and iron oxide nanoparticles in liquid suspension and in dry state on different types of human defence cells was investigated in vitro to identify biomarkers of nanotoxicity and design assays. Upon acute exposure most of the nanoparticles tested did not cause any relevant toxic effect nor could affect selected inflammatory parameters in human leukocytes, and lung or gut mucosal epithelial cells. Cell growth inhibition and production of reactive oxygen species was observed only for cobalt nanoparticles.

In its final review, **ENRHES (Engineered Nanoparticles: Review of Health and Environmental Safety)** presented a comprehensive and critical scientific review of the health and environmental safety of four classes of nanomaterials: fullerenes, carbon nanotubes, metals and metal oxides. The report considers sources, pathways of exposure, the health and environmental outcomes of concern, followed by a risk assessment based upon this information. The report includes an illustration of the state-of-the-art as well as ongoing work, while identifying knowledge gaps in the field and priority recommendations. The findings strongly support the further development of thorough characterisation (including proper considerations of agglomeration/aggregation) of the nanoparticles in exposure media and data generation.

RECENTLY STARTED PROJECTS

ENPRA (Risk assessment of engineered nanoparticles, http://www.enpra.eu) develops a novel risk assessment approach, integrated with uncertainty analysis, for engineered nanoparticles. In vitro and in silico animal and human models of exposure-dose-response relationships for five target organs (pulmonary, hepatic, renal, cardiovascular and developmental) and five endpoints (oxidative stress, inflammation, immuno-toxicity, fibrogenecity and genotoxicity) will be used for the hazard assessment and considered for high-throughput screening tests. The project will also develop in vivo models for the hazard assessment of nanoparticles to complement the REACH (Registration, Evaluation, Authorisation and Restriction of Chemical substances) and OECD (Organisation for Economic Co-operation and Development) guidelines.

Among its further targets, ENPRA aims to obtain a bank of commercial engineered nanoparticles (ENPs) with contrasting physicochemical characteristics in order to measure them, to construct mathematical models to extrapolate the exposure-dose-response relationship from in vitro to in vivo and to humans, and to implement a risk assessment of ENPs using the weight-of-evidence approach. It will also disseminate its findings to potential stakeholders.

Among the particles being studied, there are TiO2 nanoparticles (rutile, positive and negatively charged) of different size distribution, ZnO nanoparticles (coated and uncoated), silver nanoparticles and multi-walled carbon nanotubes (short and long). The results can be used for future modifications of nanoparticle physicochemical characteristics.

This project, and risk assessment studies of nanoparticles in general, could have a major impact on society.

It has become necessary to study the activity of nanoparticles within a range of biological models of increasing complexity and organisation. **ENSSATOX (Engineered Nanoparticle Impact on Aquatic Environments: Structure, Activity and Toxicology, http://www.ennsatox.eu)** concentrated its efforts on the behaviour of nanoparticles in environmentally relevant aquatic systems. The project will examine whether the environment alters the chemical or structural nature of these particles. The project starts off from the hypothesis that the biological activity and environmental impact of nanoparticles is directly dependent on their structure and functionality. By evaluating these relationships predictive models can be produced, which can be deployed for statutory controls of nanoparticle use.

ENSSATOX will perform toxicity assays by using in vitro models of cell and tissue culture and in vivo models of several different aquatic species of key indicator organisms. All the procedures for toxicity testing are selectively developed and optimised for nanoparticles. This means that streamlined protocols for nanoparticle toxicity testing will be formulated which can later be exploited as routine tests for nanomaterials.

The biological membrane and its dependent mechanisms play important roles in nanoparticle toxicity for two reasons. Firstly, the biological membrane forms the boundary of the living cell that nanoparticles will need to cross and, secondly, the biological membrane hosts many of the physiological processes such as respiration and nerve conduction and any disruption in its structure will lead to a disruption in the function of the incumbent processes. The effect of nanoparticles on biological membrane structure is entirely unknown, and so is the cell membranes' permeability to nanoparticles.

The project will look at the environmental impact of nanotechnology, particularly metal oxide nanoparticles, on model organisms, and how they are transported by waterways and rivers. This is why it is relevant to industrial waste discharge.

HINAMOX (Health Impact of Engineered Metal and Metal Oxide Nanoparticles: Response, Bioimaging and Distribution at Cellular and Body Level, http://www.hinamox.eu) focuses on the hypothesis that metal and metal oxide nanoparticles might be potentially dangerous to biological organisms. Metal oxide and metal nanoparticles are widely used in various industrial processes and common products. Some examples of these are TiO2 and ZnO as catalysts and UV protectors, CuO in anti-fouling paints, Al2O3 as a surface protector, CeO2 in polishing, indium-tin oxides forming anti-electrostatic coatings and various rare earth oxides in electronics manufacturing

The project wants to investigate the safety of metal and metal oxide nanoparticles for two reasons: it is thought they may possess increased catalytic activity due to nanoscale structure or chemical modification of their surface, which might interfere with numerous intracellular biochemical processes; and the decomposition of nanoparticles and subsequent ion leakage may result in a continuous formation of free radicals and metal ions, which might interfere with the intracellular free metal ion homeostasis in cell metabolism.

The project will look at a number of aspects including physiochemical characterisation of nanoparticles, studies on the effects and distribution at a cellular level, cytotoxicity, particularly inflammation, and general risk assessment. HINAMOX hopes to establish protocols for nanosafety testing. The research will have a significant impact on both workers and consumers and, like the others, it is needed to increase public confidence in nanotechnology.

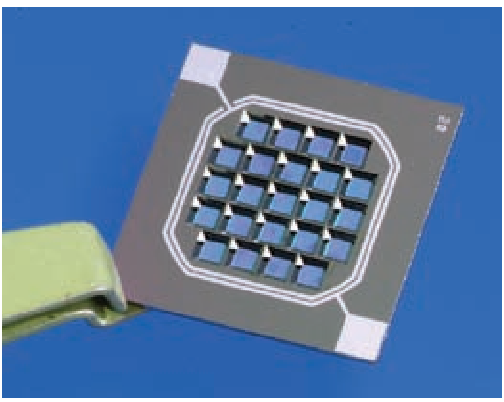
INLIVETOX (Intestinal, Liver and Endothelial Nanoparticle Toxicity Development and evaluation of a novel tool for high-throughput data generation, http://www.inlivetox.eu) develops a novel modular microfluidics-based in vitro test system modelling the response of cells and tissues to the ingestion of nanoparticles (gold, silver and TiO2).

Cell culture models of target tissues such as the gastrointestinal (GI) tract, the liver and the endothelium will be interconnected via a microfluidics system so that knock-on and cross-talk effects between organs and tissues can be monitored.

The project aims to answer some key questions, such as how these tissues individually respond to nanoparticles, how the interactions between the different tissues modulate their responses. Another two important issues are whether gut inflammation may affect the toxicity of nanoparticles and their ability to cross the intestinal barrier and which physical and chemical features of nanoparticles may influence their uptake by intestinal epithelial cells and their subsequent interactions with endothelial and liver cells.

The InLiveTox system will be validated by an in vivo study of nanoparticle toxicity in rats carried out in parallel. The microfluidics system will be flexible and modular so that the complexity of the system can be increased stepwise to include additional cell types, more complex 3D models of tissues, and more sophisticated tests of cellular responses to the presence of nanoparticles.

The project, which is designed for the industry, takes the view that in order to understand the potential behaviour and responses of the body, and to manage the resulting risks, it is essential to investigate the hazard (toxicology) of the large number of engineered nanoparticles in different formulations and at different points in their life-cycle (from production to disposal), in relation to different routes of exposure and different target organs and tissues. The number of experiments required to address all of these issues is enormous and so for INLIVETOX it is essential to develop rapid and reliable non-animal models to assess potential nanoparticle hazards. This is very important in order to reduce animal testing and comply with existing safety legislation.



Single chip support for the model intestinal epithelium: These support chips include a microporous membrane for the epithelial cells to grow on and which divides the fluidics system into two circuits: one representing the intestine and one representing the bloodstream.

NANODEVICE (Novel Concepts, Methods, and Technologies for the Production of Portable, Easy-to-Use Devices for the Measurement and Analysis of Airborne Engineered Nanoparticles in Workplace Air, http://www.ttl.fi/partner/nanodevice/) addresses the paucity of knowledge of the health effects of engineered nanoparticles in workplace air, and on the shortage of real time, cost-effective ways for the reliable assessment of exposure levels.

Due to their unique properties, engineered nanoparticles are used for a lot of novel applications, and many more are to come, with great technological and business importance. However, some of these properties, especially their surface reactivity, have raised health concerns, which have prompted scientists, regulators and industry to seek consensus protocols for the safe production and use of nanoparticles.

Apart from establishing the metrics of airborne nanoparticles and analysing industrial processes, the project paves the way to create nanoparticle air-monitoring devices by using living cells to assess the biological significance and level of a given exposure. Such devices should be affordable and easy to use. NANODEVICE will improve workplace safety and make exposure limits easier to implement.

NANOMMUNE (Comprehensive Assessment of Hazardous Effects of Engineered Nanomaterials on the Immune System, http://www.nanommune.eu) is focusing on the immune system, which has the capacity to respond to invasion by pathogens and foreign particles. The core concept underpinning the project is that the recognition versus non-recognition of engineered nanomaterials by immune-competent cells will determine the distribution as well as the toxic potential of these novel materials. Moreover, NANOMMUNE will assess whether ENs interfere with key functions of the immune system in vitro and in vivo. Through a multidisciplinary approach, the project aims to establish an array of read-out systems for the determination of toxicity not only of currently existing ENs, but also for the prediction of hazardous effects of new ENs that are being developed, thus enabling a sustainable growth of the nanotechnology-based industries.

Moreover, NANOMMUNE is striving to harmonise safety testing and risk assessment efforts between Europe and the US through international cooperation and data sharing. Carbon nanotubes, particularly single-walled carbon nanotubes (SWCNTs), have found numerous applications in different fields of industry due to their excellent strength and high electrical conductivity; moreover, functionalised (surface-modified) carbon nanotubes are emerging as novel components in nanoformulations for delivery of therapeutic molecules.

The spread and distribution of carbon nanotubes in the body is dependent, to a large extent, on their specific interactions with cells of the immune system. Systematic study of the therapeutic efficacy of carbon nanotubes is anticipated in the near future; however, detailed investigations of potentially hazardous effects on cells of the immune system remain to be performed, and are of paramount importance for the successful application of carbon nanotubes in nanomedicine. Moreover, there is a pressing need for careful consideration of the hazardous effects of carbon nanotubes for industrial workers.

In response to concerns that they may be persistent in the body, several members of the NANOMMUNE consortium have recently demonstrated a novel route of biodegradation through enzymatic catalysis. The latter studies, which show for the first time that cells of the immune system can break down carbon nanotubes, were jointly funded by the European Commission and the National Institutes of Health (NIH). Biodegradation thus occurred in primary human neutrophils, key players in the innate immune system, and to a lesser extent in macrophages. Biodegradation of single-walled carbon nanotubes was enhanced when nanotubes were pre-coated with immunoglobulin (IgG) to promote neutrophil internalisation of single-walled carbon nanotubes through Fc receptors. Furthermore, using an established mouse model of pharyngeal aspiration of single-walled carbon nanotubes, it was shown that biodegradation attenuated the characteristic inflammatory responses to carbon nanotubes. These findings strongly indicate that novel biomedical applications of carbon nanotubes may be achievable under conditions of carefully controlled biodegradation.

This project will directly benefit not only public health and researchers, but also the industry, because NANOMMUNE plans to incorporate its characterisation protocols and risk assessment guidelines into a Quality Handbook. Its consortium has a strong international dimension as it is comprised of several leading European and US institutes.

NANORETOX (The reactivity and toxicity of engineered nanoparticles: risks to the environment and human health, http://www.nanoretox.eu) is developing novel and robust protocols for the safety testing of nanomaterials.

NanoReTox is approaching the challenge in a detailed, systematic and interdisciplinary manner, with material scientists, chemists, toxicologists and biologists working closely together, thus generating robust and reproducible data involving a variety of toxicity indicators. Among the other nanoparticles, the project is specifically looking at metals, metal oxides and metal sulphides. It intends to examine the molecular and cellular reactivity of well-characterised nanoparticles.

As it is still unclear which engineerd nanoparticles may induce cellular reactivity, how and where, NanoReTox will comprehensively address all physicochemical properties of industrially important metal-based nanoparticles with a potential to induce toxicity (particle size, size distribution, shape, agglomeration state, crystal phase, chemical composition, surface area, surface chemistry and surface charge).

NANORETOX takes the view that society, particularly in Europe, needs to regain its confidence in nanotechnology and this can be achieved by discovering more about comprehensive, detailed studies of the safety of nanomaterials, with a more systematic approach to evaluate the processes that may determine a hazard.

This project has indeed a dedicated public understanding component. European nanotechnology will benefit from the project by gaining insights into particular physical and chemical properties of nanoparticles that may be linked to toxicity, to allow the design of safer materials in the future.

NEPHH (Nanomaterials Related Environmental Pollution and Health Hazard Throughout their Life Cycle, http://www.nephh-fp7.eu) looks at human health and the environmental implications of nanotechnology-based materials from a holistic life-cycle perspective. The aim of this project is to identify and rate important forms of nanotechnology-related environmental pollution and health hazards that could result from activities involved in nanostructures throughout their life-cycle, and to suggest means that might reduce or eliminate these impacts.

The nanomaterials selected by the project are polymer composites reinforced with silicon- based laboratory and industrial nanoparticles. On the one hand, silicon-based nanoparticles including (nano)silica (SiO2), layered silicates (MMT), glass (nano)fibres and foam-glass-crystal materials have been selected. On the other hand, three polymeric matrixes have been selected (polyamides and polypropylenes as bulk materials and polyurethanes as foamed polymeric materials). According to this selection, 12 polymer composites will be produced on the basis of the combinations of all nanomaterials and polymeric matrixes.

The novelty is that NEPHH is looking at models of 'real-products' that will be used to simulate physical processing during a product's life-cycle including crash testing and accelerated ageing under environmental conditions. A set of characterised complex samples including nanoparticles, engineering matrixes and mixtures of both –corresponding to the actually released (nano)dust from real nanomaterials currently on the market – will be produced and analysed from the human health and environmental impacts evaluation perspective.

Workers may be exposed to nanoparticles during the research, development, manufacture, packaging, handling and transport of nanotech products. Exposure may also occur in cleaning and maintaining research, production and handling facilities. NEPHH wants to increase the understanding of the mechanisms of toxicity of nanosize dust generated during cutting, fracture, breakage or cracks of nanoreinforced end-use products.

The project also aims to determine acceptable exposure limits. Ways for monitoring workplace exposure to nanoparticles will be determined in research and manufacturing stages. According to results obtained, a safety protocol for exposed workers will be developed. Working conditions will be improved as protection methods for occupational exposure will be evaluated, and NEPHH will provide Europe with evidence for the appropriate regulation regarding the prevention of exposure of the general population and nanotech manufacturers and handlers, as to ensure the successful and sustainable introduction of nanotechnology into the market.

The project is bringing in experienced scientists from different research areas: toxicology, ecotoxicology and polymer-chemistry. The environmentally efficient production processes that contribute to industrial costs savings and nanotech products will be marketed in a more effective and sustainable way.

NEURONANO (Do nanoparticles induce neurodegenerative diseases? Understanding the origin of reactive oxidative species and protein aggregation and mis-folding phenomena in the presence of nanoparticles, http://www.neuronano.eu) brings together a unique team, several of whom have pioneered the preliminary results in this field, and supplements them with the necessary skills and facilities required to address these questions. It is a knowledge-based approach, for it probes the questions in the deepest manner, by isolating each separate element of the nanoparticles physicochemical qualities that control fibrillation and oxidative stress and access to the brain, determining their consequences separately.

The project wants to address the questions whether nanoparticles measuring less than 40 nm could potentially enter the brain by passing through the BBB, and whether some nanoparticles may induce oxidative stress in living systems. Oxidative stress from ambient or combustion particles contribute to cell damage, including DNA damage.

Also, the large surface area of nanoparticles means that they can modulate the fate of protein fibrillation in solution, but it remains to be seen whether this may have any significance in vivo.

Oxidative stress and protein fibrillation are both associated with neurodegeneration, but it remains to be seen whether these issues, separately and in combination, mean that nanoparticles may have a role in neurodegenerative diseases at all.

NEURONANO aims to establish a simple screening and risk assessment matrix for nanoparticles in neurodegenerative diseases. Significant progress is being made in all areas of the project in terms of clarifying all of the issues, and to date, no clear hazards from the nanoscale have emerged.

ADDRESSING UNCERTAINTIES ETHICALLY (ELSA)

A good look at the Ethical, Legal and Social Aspects (ELSA) of nanotechnology needs to anticipate their impact on our lives

Because nanotechnology is so novel and complex, there may be real difficulties to single out, quantify and manage the potential risks that might be involved, especially the long-term ones. As for all nanotechnology applications, the main key concerns are centered around the potential health and environmental hazards of nanoparticles and nanomaterials and the corresponding ELSA issues.

While the most topical ethical questions may currently regard a lack of knowledge about many nano-applications, it is more than likely that the widespread use of nano products in the medium term will raise the issues of data protection and privacy. Finally, although some nanotechnology scientists think that the very controversial human enhancement scenarios are very far off, appropriate and responsible questions need to be seriously asked.

In 2007, the European Group on Ethics in Science and New Technologies (EGE), an advisory body to the EC President, published an opinion document on nanomedicine recognising its potential and placing an emphasis on conducting research both into its safety and its ethical, legal and societal aspects.

SPOTLIGHT ON

NANOMEDROUNDTABLE

The very promising nanomedicine developments are bound to add new, complex dimensions to many ethical, social and economic issues. **NANOMEDROUNDTABLE (Nanomedicine ethical, regulatory, social and economic environment, http://www.nanomedroundtable.org)**. The project emphasised that for these promises to achieve the maximum innovation benefit for everyone, the way has to be paved for a safe, integrated and responsible approach. This will also be a necessary condition for the sustainable competitiveness of nanomedical R&D in Europe and for its healthcare industry, so all possible impacts and consequences need to be understood in advance.

The main purpose of NANOMEDROUNDTABLE was to raise awareness and provide European stakeholders with a set of recommendations to support decision making regarding nanomedical innovations, based on a thorough analysis of existing documents, multi-stakeholder debate and construction of scenarios about the possible consequences. Five Working Groups brought together experts selected for their expertise and representation from each specific field to address the issues relating to patient needs, ethics and societal impact, economic impact, regulation and communication and respectively prepare detailed, state-of-the-art reports.

Regarding patients' needs, the project emphasises that the EC, national governments, trade and research associations must play a key role in the dialogue with them. ELSA aspects need to be better defined along with the purposes of nanomedicine. Predictions on the economic impact need to rely on solid data on healthcare costs, benefits and prospective market growth. A proactive regulatory system requires better coordination and harmonisation and needs to ensure that dialogue with stakeholders is carried out early on and promptly. Balanced communication and information must facilitate public understanding.

This project, encompassing a variety of nanomedicine aspects, informed both policymakers and the public. It shed light on nanomedicine as arguably the best case study for changing business models in order to move from a curative to a preventative approach, which also needs to encompass economics, supply chain and insurance. The convergence of these disciplines will surely affect the impact of nanomedicine.

A final conference was organised at the European Parliament in June 2010, hosted by STOA (Science and Technology Options Assessment).

NANOMEDROUNDTABLE also published recommendations for policymakers in its final report and it is expected to make an extensive impact.

A key cooperation between European trade union organisations, environmental NGOs and universities, which got together to formulate balanced position statements on nanotechnologies, came from **NANOCAP (European trade union and environmental NGO positions in the debate on nanotechnologies, http://www.nanocap.eu)**. The project deepened the understanding of environmental, occupational health, potential safety risks and ethical aspects of nanotechnology.

As a result, five European NGOs adopted a position on the responsible development of nanotechnology and the European Trade Union Confederation adopted a resolution representing 60 million workers in Europe. This joint effort was pressingly required by the rapid growth of many nanotechnological disciplines, the introduction of nano products onto the market, and the far-reaching effects that these developments may have on our society. This way NANOCAP gained a recognised position in the European debate.

One of the main concerns of civil society organisations was the obligatory notification of the nanoparticle content of nano products, which should not be brought onto the market if they introduce new or uncertain risks to health or the environment while any self-proclaimed benefits cannot be substantiated. Taking this precautionary approach seriously is a delicate task, as policy instruments must be used to balance economic value (such as potential benefits, replacement of scarce raw materials, stakeholder interests, new job creation) against 'acceptable' risks (such as hazard and exposure assessment, risk behaviour and uncertainties).

Accepting precautionary measures might be problematic for many companies. However, trade unions and NGOs believe these voluntary systems cannot replace binding legislation. The public debate was well represented at NANOCAP's final conference, which involved the presentation of the civil society positions, through the establishment of a relationship with the European Parliament and STOA. Among the project's recommendations, there was a call on the EC to fund research in order to eliminate further knowledge gaps on environmental and human health impacts.

The trade unions calld for transparent and independent risk assessment is to ensure a safe workplace for all working with nanotechnologies and nanomaterials, while at the same time preserving the potential for creating new jobs. For environmental NGOs, the responsible governance of nanotechnology applications is crucial and it implies the adoption of a strict regulatory framework, which will ensure the maintenance of environmental and human health while following the principle of sustainability. NGOs also demand that the precautionary principle should be employed for nanomaterials until there is an adequate EU regulatory framework, and the safety of current products should be assessed.

Calls were made for a precautionary approach also to include exposure registration for workplaces and for a transparent communication involving a public consultation on nanotechnologies and nanomaterials. NANOCAP called for a EU-wide public debate to set clearer parameters for the current uses and future developments of nanotechnology.

Such a public dialogue took a step forward with **NANOBIORAISE (Nanobiotechnology: Responsible Action on Issues in Society and Ethics, http://nanobio-raise.org/)**, which focused on a specific set of nanotechnology applications and pinpointed the areas where the debate is expected to take different roles in social acceptance or rejection. This might be the case, for instance, of nanomedicine compared to nanofood applications.

NANOBIORAISE brought together nano-biotechnologists and ethics and communication specialists to anticipate the societal and ethical issues that are likely to arise as nano-biotechnologies develop and plan the response to some probable public concerns. The project's activities included building an Expert Working Group on human enhancement. It also organised three Horizon Scanning Workshops on key topics such as human enhancement, nanomedicine and nanofood, a series of convergence seminars to assess public perceptions across Europe, the publication of a set of briefing papers for various audiences and the organisation of several courses on applied ethics and public communication for nanotechnologists.

The project resulted in a range of new insights into the wider impacts of nanotechnological developments, leading to several academic publications as well as a set of documents aimed to inform policymakers, nanoscientists and broader audiences about the ethical and societal dimensions surrounding nanotechnological developments, which may become more important as further innovations enter the market. The project also raised awareness with nanoscientists of the possible social and ethical dimensions of their research through the workshops and courses.

A key target of NANOBIORAISE was the provision of information to its target groups. More importantly perhaps, it enhanced awareness with nanoscientists that the consideration of social and ethical aspects in the early phases of their research facilitates the alignment of new technological innovations with public values and concerns.

The project highlighted the growing awareness that a successful innovation system requires the integration of broader social considerations in the early phase of research. The EC's Science in Society Work Programme 2007 aims to 'encourage actors in their own disciplines and fields to participate in developing Science in Society perspectives from the very beginning of the conception of their activities'. NANOBIORAISE ventured into such 'socio-technical integration' by building interdisciplinary collaborations between social and natural scientists in the area of nanotechnology. The results have encouraged nanoscientists, policymakers and the general public to consider the broader social and ethical aspects very early on.

The phenomenon of technological convergence concerns the coming together of Nano-, Bio-, Information technologies, and the Cognitive sciences (NBIC-convergence), which was at the core of **CONTECS (Converging Technologies and their impact on the Social sciences and humanities, http://www.contecs.fraunhofer.de)**. The project shed light on the expectation that major scientific breakthroughs will originate from the overlap of two or more of these technology fields. There is a strong connection to the notion that the interplay will lead to the enhancement of human capabilities, especially of cognitive capabilities, a vision headlined as 'brain enhancement'. However, technology convergence has many more aspects, ranging from the organisation of interdisciplinary research to the question whether or not an overarching concept is needed for basic scientific advances at all.

CONTECS combined a bibliometrical approach with expert interviewing. It called two expert workshops to discuss the findings. The bibliometrical research allowed the project to identify eight application areas where technology convergence is required. A vision assessment approach was provided to analyse the impact of research policy on the conduct and directions of leading researchers.

The project formulated a research agenda for the Social Sciences and Humantities (SSH) about how to deal with the phenomenon and hot topics to address in the future. The main points of this agenda include tracing the origins of the convergence debate and predicting impacts on R&D, defining the role of cognitive science, addressing the interdisciplinary approach as the common denominator of CT, addressing ethical questions, questioning the emerging deterministic models of humans whereby natural sciences may take over SSH domains and deciphering the potential role of enhancement.

CONTECS proposed a strong engagement of a broad variety of SSH in the debate, analysis and shaping of actual processes of R&D convergence, as they can dispel any naïve conceptions of these pro¬cesses. It also found out that, although some products would indeed qualify for being 'convergent' in the NBIC sense, researchers in firms and universities are mostly not aware of the concept.

A pilot initiative of a network of 11 high-profile female scientists, acting as 'ambassadors for women and science', led to **WOMEN IN NANO (Strengthening the role of women scientists in Nano-Science, http://www.womeninnano.de/)**. The project provided role models for girls and young women with a view to encouraging them to consider studies and pursue careers in nanomaterials and nanotechnologies R&D. It also stressed the importance of strengthening the role of women scientists already working in nanoscience and of establishing a networking of female nanoscientists at national, regional and European levels.

WOMEN IN NANO addressed the fact that women are still underrepresented in scientific institutions, especially in key positions, and called for female scientists to participate in EU programmes. It attained the goal of mobilising stakeholders in favour of gender equality in scientific research and of facilitating a healthy dialogue between science and society.

After reviewing the particular situation of women working in nanoscience and mapped their competences at national, regional and European levels, a media campaign was organised involving participation in open and public events, lab visits, regional workshops and the setting up of summer and winter schools. The project made contact with decision makers in research, politics and industry at national and European levels to develop 'best practice' policies in the recruiting and employment of scientists and to highlight the intellectual potential and contributions of female scientists in advanced research.

The project's public outreach activities also helped to bring nanoscience closer to the public. These outcomes fully met the European Commission's promotion of equality between women and men in research, which is an essential condition for an optimum development of European research.

In order to encourage public engagement in the debate about nanotechnologies, DECIDE (Deliberative Citizens Debates in European science centres and museums,) developed an online game. The first trial took place in the science centres and museums before being extended to schools, public libraries, shopping centres and retirement homes across five continents. The website provides all the materials required for the game and the results of the group discussions can be uploaded for a comparison between countries.

The game provided insights into the differences between countries. The format has been used by teachers, government agencies and other interested parties. Specific audiences also featured it for training scientists in ethical, legal and social issues associated with controversial scientific developments. The International Conference of Rare Diseases used it to train and empower patients suffering from such conditions to lobby at European level.

MESSENGER (Media, governance and engagement in Europe, http://www.sirc.org/messenger/intro.html) wanted to give a true European perspective to the existing Guidelines on Science and Health Communication, a European provenance. So the project set up a Europe-wide consultation with representatives within the science, technology and health communities, the media and civil society.

A media analysis of science, technology and health issues across Europe was implemented in order to assess the different cultures and roles of the media in communicating science. The consultation involved nearly 200 stakeholders across Europe, seeking their advice with a view to developing a whole range of original Guidelines on Science and Health Communication, which the project disseminated to leading European scientific institutions, the media and NGOs.

DEEPEN (Deepening Ethical Engagement and Participation in Emerging Nanotechnologies, http://www.geography.dur.ac.uk/projects/deepen) focused on developing integrated social and ethical implications of emerging nanotechnologies by using insights from philosophy, ethics and the social sciences. It especially looked at applications in nanosensors and nano-biotech and addressed the potential unwanted consequences of some nanotechnology developments and the risk of increasing social inequalities.

NANO ROAD SME (Development of Advanced Technology Roadmaps in Nanomaterial Sciences and Industrial Adaptation to Small and Medium sized Enterprises, http://www.nanoroad.net/) developed a roadmap model for the SME industry, detailing scientific breakthroughs and assessing the new properties of nanomaterials in the context of market drivers. The project surveyed a number of SMEs, from those companies developing their own materials and looking for information on fundamental science breakthroughs, to producers looking for nanomaterials in the development and testing phase, to companies seeking materials that are on the market.

PRIME (Policies for Research and Innovation in the Move towards the European Research Area, http://cournot.u-strasbg.fr/users/beta/prime.htm) was a NoE that addressed the three major challenges and policies for research and innovation in Europe: the changing dynamics of knowledge production, the relationship between science and society with the concerns and public debates about priorities and research practices, and the growing importance of both regional and European public authorities.

ETHICSCHOOL (Ethics of Emerging Technologies) aimed to set an education standard in the ethics of nanotechnology and converging technologies. The project recognised the need for scientists to communicate with society outside the research community, where they are likely to be asked questions about issues, risks and ethics that they would not necessarily encounter in their professional life. The project also aimed at disseminating the EC's Code of Conduct for nanotechnology research.

PATH (Participatory Approaches in Science and Technology, http://www.macaulay.ac.uk/socio-economics/research/path/index.html) focused on establishing a network bringing together academics, practitioners, policymakers and stakeholders to exchange knowledge and develop future directions for the involvement of society in the deliberation of science policy issues. The project examined best practices for public participation in science and technology (S&T) issues, by widening the scope of participation to debate by stakeholders to a national scale, and looked into a better way of bringing underrepresented voices in society to the fore.

RISKBRIDGE (Building robust, integrative interdisciplinary governance models for emerging and existing risks, http://www.riskbridge.eu/) identified six different risk fields (nanotechnology, stem cells, sedimentation, climate change, nuclear waste and electromagnetic radiation) and looked at the way they handle the associated risks and try to learn from each other about best practices for risk governance.

EUROINDIANET (Bridging the Gap between Europe and India's Nanotechnology Knowledge Bases towards an understanding of Innovative Support Structures, Training Programmes and Policies, http://www2.spi.pt/euroindianet/) provided an important contribution towards strengthening the collaboration between the EU and India in nanotechnology R&D. The project built important networking opportunities for prestigious scientific European and Indian institutions and assisted in the development of joint research activities by providing a database of organisations and infrastructures, information on policies, training programmes and the latest opportunities for research funding.

KNOWLEDGE NBIC (Knowledge Politics and New Converging Technologies; A Social Science Perspective, http://www.converging-technologies.org/project.html) focused on putting together all information about the development of the notion of converging technologies. It also examined the broad perspective of the knowledge politics surrounding the issue and sought to involve social sciences, philosophy and humanities by providing expert interviews, forums and international conferences where research could be discussed. The project contributed to the debate on the implementation of the EU nano Code of Conduct.

TOWARDS A COMPETITIVE, KNOWLEDGE-BASED ECONOMY (CSA)

Nanotechnology is crucial for the improvement of the quality of life of Europe's citizens, while respecting society and environment

Coordination and Support Actions (CSAs) are EC-funded projects aimed at coordinating or supporting EU research activities and policies about nanotechnology. They may include NoEs, conferences, transnational access to research infrastructures and exchanges, actions aimed at implementing the Framework Programmes and at developing synergies with other policies.

CSAs and NoEs are known as 'structured actions'.

The participation of SMEs, industries and civil society organisations is actively stimulated and encouraged.

SPOTLIGHT ON

EURONANOFORUM 2009 **(http://www.euronanoforum2011.eu/past-events)** EC nanotechnology events on such a scale are held only once every two years. The EURONANOFORUM 2009 (ENF 2009) conference was launched by the Czech Presidency as a milestone in the history of nanotechnology communication. It was the fourth of a series of top-level, biannual international nanotechnology conferences organised by the rotating national Presidencies of the European Union. It was held in Prague at the beginning of June 2009 under the auspices of the Czech Ministry for Education, Youth and Sports with the support of the Industrial Technologies Programme of the European Commission.

Focusing on 'Nanotechnology for a sustainable economy', ENF 2009 reflected the state-of-the-art in European nanotechnologies and nanosciences. It highlighted the latest advances in fundamental research, as well as a whole range of cutting-edge developments relevant to a wide range of industrial and societal needs. It addressed several crucial issues, such as the need for a dramatic reduction in carbon emissions and fossil fuel dependence, a substantial increase in energy and material efficiency, pollution control, clean water management and a sustainable quality of life for European citizens through a whole range of nanotechnology applications.

Nanotechnologies hold great promise for sustainable development. The aim of ENF 2009 was to formulate future priorities of European research in the nanotechnologies and nanosciences. The excellence in singling out the priorities was based on the best knowledge made available by world-leading experts.

These priorities are being included in the forthcoming EU plans about nanotechnology R&D. The issues of Europe's competitiveness depending on its potential for innovation and acceptance of nanotechnology by society and the necessity of a broad-based dialogue about it were also addressed at the top level during the conference.

As well as examining the contribution nanotechnologies are making to the transformation of European industry and society, the conference also considered the questions of governance, regulation and standardisation as being crucial to ensure a sustainable future for the technologies themselves. As nanotechnology is emerging as crucial for Europe's development as a knowledge-based economy and for the quality of life of its citizens, it is offering a major set of solutions to find a way out of the present global crisis, and its potential contributions in areas such as electronics, photonics and smart materials, as well as in health and pollution monitoring, could be of the highest importance.

Among the many cutting-edge applications that nanotechnology can make towards the creation of a sustainable economy and improved quality of life, ENF 2009 featured new nanomaterials in the construction industry to improve the energy storage performance of buildings and their efficient refurbishment, nanotechnology for the production of a new generation of fuel cells and organic photovoltaics, environmental pollution monitoring and remediation such as water purification and wastewater treatment.

The conference's main topics also included the use of nanotechnologies in diagnostics , drug delivery and regenerative medicine, or aimed at the new frontier of molecular electronics, all the way to the use of new nanomaterials in the construction industry to improve the energy storage performance of buildings and their efficient refurbishment, to increase the eco-efficient industrial production in the transportation industry and also to give manufacturing industry an advantage by the introduction of nanolayer coatings and nanoparticles into materials for boosted performance.

ENF 2009 also attracted young people, students and the general public by organising a road-show exhibition of the highly successful 'nano truck' by demonstrating various nanotechnology applications and their potential for the future. During the 3-day conference the 'nano truck' was seen by over 3 000 visitors.

Like most large-scale NoEs of this kind, **NANO2LIFE (A network for bringing nanotechnologies to life, http://www.nano2life.org/)** was relying for its highly efficient governance on boards and working parties. The project's major outcome is the building of a nano-biotech and nanomedicine community.

NANO2LIFE achieved this by initiating over 35 R&D projects with the participation of the industry, by producing a wide range of deliverables such as technological roadmaps and foresight studies, by shaping the ethical issues related to nano-biotechnology thanks to the creation of the first ever ELSA Committee on Nanobiotechnologies. It initiated a huge, friendly and still lively network across Europe and beyond, supported by a dedicated human resources management scheme, including a gender action plan and a mentoring programme. It also shaped and delivered the recommended higher education in nano-biotechnology curriculum.

The project's major outcome is that it built the existing nano-biotech and nanomedicine community, and it addressed the development of nanotechnologies for biology and healthcare. It remains the largest international network on nano-biotechnology, with 450 scientists coming from over 50 public and private partners. This is a true landmark aiming to make Europe a leader in nano-biotech.

Although Nano2Life was a scientific and technological NoE, its work is going to have a lasting impact on society, which is proportional to the growing importance of nano-biotechnology. More than 35 industrial partners, ranging from high-tech SMEs to large international groups, participated in the activities proposed by the project. They have been more significantly involved in R&D collaborative projects as well as in foresight activities.

Due to its novelty and to the great media interest in nano-biotechnology and nanomedicine, Nano2Life had very good media coverage.

OBSERVATORY NANO (European observatory for science-based and economic expert analysis of nanotechnologies, cognisant of barriers and risks, to engage with relevant stakeholders regarding benefits and opportunities, http://www.observatorynano.eu/project/) aims to present reliable, complete and responsible science-based and economic expert analysis, across technology sectors, to European decision and policymakers regarding the benefits and opportunities of nanotechnology developments, balanced against barriers and risks, allowing them to take action to ensure that scientific and technological developments are realised as socioeconomic benefits for an innovation-driven Europe.

The project collates and analyses data regarding S&T trends (including peer-reviewed publications, patents, roadmaps, and published company data) and on economic realities and expectations (including market analysis and economic performance, public and private funding strategies). The S&T and economic analysis is further supported by assessment of ethical and societal aspects, impacts on environment, health and safety, as well as developments in regulation and standardisation.

The project regularly produces concise 'factsheets' outlining the most exciting nanotechnology developments, four-page briefings providing wide-ranging scientific, economic, societal and risk analysis on topics of particular interest, and substantial 'general sector reports' providing more detailed S&T analysis for each of the 10 technology sectors and market reports. A company survey activity has commenced, which will map the activities of companies involved in nanotechnologies throughout Europe, thereby supporting the European Commission innovation strategy.

The project's impact consists in providing decision and policymakers with balanced and responsible science-based analysis for the safe and responsible development of nanosciences and nanotechnologies. The business tools are also used by companies to address the Corporate Social Responsibility (CSR) issues which are vital for public acceptance and market success. The project is aimed at the European decision and policymaker or those within national governments rather than the general public. However, the annual report for the public is highly accessible.

ObservatoryNANO has established relationships with international organisations including the EPO (European Patent Organisation), OECD and ISO (International Organization for Standardization), and will establish links to relevant European Technology Platforms (ETPs), ERA-NETs (European Research Area networks), and other relevant EU-funded projects to develop accurate indicators of the socioeconomic impact of nanosciences and nanotechnology RTD.

To see how the different clusters and nanotechnology applications can be transferred to the market, **NANO2MARKET (Best practices for IPR and technology transfer in Nanotechnology developments, http://www.nano2market.eu/)** established their respective value chains. The project also aimed at establishing good practice criteria in successful intellectual property (IP) protection and their transfer to market.

NANO2MARKET looked at crucial variables such as the best time to market, market size and growth and different commercialisation methods, also by drawing information from case studies of how some nanotechnology applications have been successfully transferred to the market. The project had an intensive dissemination plan addressing a broad range of stakeholders from policymakers to individual SMEs, which was aimed at reducing the time gap for bringing nanotechnology research to the market.

It also provided expert opinion on the importance of patenting. The project was a true 'first' within the high number of market-focused projects in recent EU calls.

The hot issue of how to measure nanotechnology manufacturing products, for which conventional metrology has become inadequate, is being tackled by **CO-NANOMET (Coordination of nanometrology in Europe, http://www.co-nanomet.eu/)**. This is an essential issue that needs to be developed at the same time as nanotechnology itself in order to support its industry and business potential. The project was motivated by the fact that there was lots of activity in nanometrology but no coordination.

The project combines assessment of the current situation with foresight review aimed at potential future strategies. This nanometrology work is going to become very important in the future. The project set up action groups ready to tackle key technical needs and reviewed specific skills and training in nanometrology. It is also reviewing current strategies in this emerging, crucial field worldwide.

Arguably, a new, consistent nanometrology will be part and parcel of any new nanotechnology regulations, whose foundations CO-NANOMET is also contributing to shape.

Another NoE, this time focused on the cross-over between life sciences and nanotechnology, was at the core of **FRONTIERS (Research and facilities directed at instrumentation for manufacturing and analysis of single molecules and individual nanoclusters, targeted at life sciences, http://www.frontiers-eu.org/)**, which aimed to establish leadership in research and innovation on behalf of life sciences-related nanotechnology. The network represented 12 nanotechnology institutes all over Europe. Jointly, about 200 researchers bring a considerable European knowledge pool together.

The project's primary aims were to establish an integrated and lasting network of excellent researchers, and, in particular, to provide a platform for young researchers to communicate and establish their own networks. Many of these partners continue to collaborate and cooperate well after the formal end of the project. A large number of joint projects were initiated leading to joint presentations and publications, leading to the application of four joint patents. In addition, a virtual nanoscience laboratory was established.

FRONTIERS was involved in helping to spin-off three companies from partner institutions, and was involved in technology transfer to a company developing medical systems for point-of-care diagnostics. The project primarily succeeded in establishing a network of excellent researchers.

NANOSCI-E+ (Transnational call for collaborative proposals in basic nanoscience research) is the direct outcome of the work initiated within NanoSci-ERA, a consortium created with the objective of promoting the integration of the national research communities in nanoscience throughout the ERA. This had achieved the launch of a first transnational call for collaborative proposals in nanoscience, whereas the objective of NanoSci-E+ is the implementation and follow-up of a second call.

The call organised by NanoSci-E+ was open to 'frontier research projects that address the issue of interfacing functional nano-objects or nano-materials'. The projects expected to fit within the scope of the call span over many disciplines of nanoscience, which makes it accessible to the researchers of all 13 participating countries.

The project intends to support the generation of fundamental knowledge, which is not necessarily driven by immediate development applications. However, the funded projects address key challenges in nanoscience and as such, are likely to strengthen the scientific roots that the nanotechnology business sector needs for maturing. NANOSCI-E+ takes the view that only a decisive support for basic nanoscience can allow nanotechnologies to keep their promises. The project features twice as many projects compared to NanoSci-ERA, so it has a significantly bigger breadth.

SANDIE (Self-Assembled semiconductor Nanostructures for new Devices in photonics and Electronics, http://www.sandie.org/) is another NoE focusing its research on self-assembled semiconductor quantum dots. The self-assembly process allows fabrication of structures in the 10 nm size range, which can then be cemented in position by the deposition of further layers of the substrate material. By varying the semiconductor materials involved, the growth conditions, and by vertically stacking layers of nanostructures, a rich variety of novel materials has been produced for the study of the fundamental properties of strongly confined systems, and for the development of advanced electronic and photonic devices.

The project started and intensified many collaborations between the partners. These led to a high number of scientific results that were published in over 800 refereed papers and over 600 conference contributions. The developed methods for controlled fabrication of nanostructures and their characterisation and theoretical modeling are world-leading. Quantifiable goals with respect to the integration of people, facilities, research and training events were achieved. SANDIE has established itself as a stable structure with well-defined decision making processes and a lively and amicable working atmosphere. Several joint projects and investigations have been performed and progress in existing efforts has been made that would not have emerged without the network.

The project developed fundamental knowledge necessary for the evolution of advanced electronic and photonic devices for applications in telecom, quantum cryptography and secure communication among others, so its achievements have an impact on everyday life. The safety of embedded self-assembled nanostructures is high. Results of the scientific programme of SANDIE helped the five industrial partners to develop better and cheaper products.

NANO-STRAND (Standardization related to Research and Development for Nanotechnologies) was generated by the real need for management strategies of pre-normative research and standardisation of nanotechnology. One of these provided guidance to the European Commission to suggest where new calls and funding should be directed. The second was targeted to CEN (European Committee for Standardization) and covered standardisation in nanotechnology.

The project had the very important role of road-mapping standardisation, which is going to be fed into European policy, and was very well received. Its main topics address consumer health and safety, which are major issues for society.

NANO-STRAND also facilitated European industrial development, by enhancing integration between nanotechnology research and production, and provided several institutions and organisations with valuable information about the needs of the different nanotechnology stakeholders.

The theory and simulation of electronic spectroscopies in matter was addressed by **NANO-QUANTA (Nanoscale Quantum Simulations for Nanostructures and Advanced Materials, http://www.**

cmt.york.ac.uk/nanoquanta), a NoE gathering 10 groups across Europe, which was set up because expertise in this field was previously difficult to locate and access.

The project set up a European Theoretical Spectroscopy Facility (ETSF) that provided access to state-of-the-art expertise for researchers from industry and academia. It also trained scientists, particularly young, early-stage researchers, and encouraged multidisciplinary research. The results are long-lasting, as good communication continues among the research groups involved.

The project also created a number of permanent jobs for scientists. The network included academic and government researchers, but it actively encouraged proposals from the industry.

EURONANOBIO (European-scale infrastructure in nanobiotechnology, http://www.euronanobio.eu) provided definitions of nano-biotechnology and its main clusters and looked into standardisation regulation and ELSA issues in this field at European and local level. It also provided education and training. As a follow up to the Nano2Life project, it aimed at formulating practical solutions for the nano-biotech community. Its results are going to be fed into European policymaking.

REACHING OUT TO THE FUTURE

Communicating nanotechnology towards a broader dialogue within European society is essential for its responsible and integrated development

The EC singled out the real need for a fresh approach to communicating nanotechnology and building mechanisms allowing all stakeholders to get involved and give feedback. In order to increase confidence and trust in nanotechnology, the potential benefits and the potential risks or challenges need to be properly addressed.

Responding to the EC's requirement to develop a safe, integrated and responsible nanotechnology, a whole range of specific communication projects focused on the involvement of young people, a balanced information of public opinion, with the ultimate aim to set up a solid dialogue mechanism about nanotechnology within the whole of Europe's society.

SPOTLIGHT ON...

NANOYOU

The first, creatively extensive and comprehensive educational programme in nanotechnology to reach tens of thousands of young people is being spearheaded by **NANOYOU (Communicating Nanotechnology to European Youth, http://www.nanoyou.eu)**, which is systematically designing and undertaking a broad communication and outreach programme in nanotechnology aimed at European youth, targeting students between 11 and 18 years old through school programmes and the upper age bracket between 19 and 25 through science centres.

Ten EC languages are being spoken within NANOYOU, whose effective outreach is very big as the project's school programmes involve at least 400 schools on a regular basis, which means more than 25 000 students altogether throughout the project's lifespan. Having devised and distributed a very creative panoply of materials and activities, NANOYOU is informing young people in most EU Member States and Associated States about R&D nanotechnology concepts and their applications in medicine, ICT and energy.

All the project's materials have been carefully targeted to different age groups, specifically gathering 11-13, 14-18, 19-25 year-old participants. The teacher trainings, survey and evaluation, online materials, portal and ongoing dissemination efforts pinpoint the originality of the project.

NANOYOU also encourages the participation of young people in dialogue about the ELSA of nanotechnology through a specific communication and outreach programme. Among the project's other main instruments to reach its target groups there is also a highly organised online project portal. The communication and outreach activities in schools are taking place in two stages, with feedback from the first stage being used to improve the programmes in the second stage.

During this first phase, NANOYOU completed the work on the survey and requirements analysis and it successfully finalised the development of tools and activities related to nanotechnology dialogue and the development of teacher training materials. For instance, teachers noticed that this way of dealing with the technology and its related ELSA aspects sharpened the way students used this information to improve their higher-order and critical thinking skills in the course of further discussions and games. For instance, results of the online questionnaire highlighted the concerns by half of the students that the benefits of the technology may only be felt by wealthy countries or individuals.

The seminal development of teacher training materials has so far enabled science teachers in schools to educate, motivate and inspire young people about nanotechnology and its applications. The highly innovative NANOYOU pilot teacher training involving 50 representatives of pilot schools from different European countries was a great success and the materials provided positively stimulated the interest of the other teachers involved in the project, who responded with some very good feedback. This initiative was a success, as all the teachers implemented the programme materials in their schools and a sample of 500 students participated in the first phase of the evaluation procedure.

All the tools, materials and activities developed during the first year of the project are available on the NANOYOU web portal. For instance, the virtual dialogue comprises six animated stories presenting a problem, a nanotechnology solution and its possible effects. For each story a 'dilemma' is presented and students are asked to justify their opinion. Card and memory game workshops involve groups of students experiencing and studying three nanotechnology clusters, namely medicine, energy/environment and ICT.

Because of its inclusive approach to outreach, the project's dissemination programme is an integral part of the project. It is aiming to spread awareness and promote a much wider adoption of the programmes by reaching out to young people way beyond the project itself, by involving them in a debate on the ethical, legal and social aspects of nanotechnology, together with scientific and technical background and current research.

On a broader scale, NANOYOU's dissemination activities, which include a nanotech digital travelling exhibition, are also aimed at university students, science museums and science centres, the relevant government authorities in education, science and technology and the general public. The project's activities and results have been featured in magazine articles, conferences and exhibitions, the YouTube channel and some educational networks such as e-Twinning and e-Skils.

All of NANOYOU materials are creative and can be shared. They are free for use on a non-commercial base for educational purposes.

NANODIALOGUE (Enhancing dialogue on nanotechnologies and nanosciences in society at the European level) involved citizens from eight European countries in the debate around the ELSA of nanotechnologies through activities and debates. All this, together with the public's feedback assessment, was centred around an interactive exhibition module. The interdisciplinary characterisation of the project, involving experts from different backgrounds, was also reflected at the final conference at the European Parliament in Brussels, which encouraged the debate on cutting-edge science.

The exhibition was seen by more than one million visitors in the countries in which it was displayed. This audience took part in events, demonstrations, science theatres and lectures. Over 700 visitors completed a socio-demographic questionnaire to determine their perceptions and expectations about nanotechnology and their assessment of its potential benefits and risks. Some of the respondents were also involved in a series of 16 focus groups across Europe.

Prior to visiting NANODIALOGUE's exhibition, the majority of respondents rated their level of understanding of nanotechnology as low (55%). A significant proportion (20%) stated that they had no understanding about it at all. When asked what effect they think nanotechnology will have on their way of life in the next 20 years, 60% said it would be positive, while only 3% envisaged negative effects.

Benefits to human health and environment were the most keenly anticipated while risks to national security and the economy posed the most concerns. Of the respondents, 88% agreed that the Nano-Dialogue exhibition had increased their understanding of nanotechnology. Significantly, 62% of respondents believed the public should be involved in decisions about the research and development of nanotechnology. The project established solid relationships with companies and industries, which provided samples of nanomaterials and used the exhibition as a place to meet the visitors.

NANODIALOGUE was the first project at European level focused on an intense dialogue with citizens and stakeholders on the ethical, legal and social aspects of nanotechnologies. The novelty was also related to the important role of science centres to communicate and to collect visitors' perspectives. From this project on, several other projects involved science centres in communication campaigns over nanotechnology science and society topics.

NANOTOTOUCH (Nanosciences Live in Science Centres and Museums, http://www.nanototouch.eu/) is creating innovative environments for the public to learn about nanotechnology by putting visitors directly in contact with scientists for further learning and debate. The project has achieved this by recreating some laboratory environment and research conditions in the middle of museums and science centres.

Here the public can access a range of very successful 'open nano labs' and 'nano researcher live' areas, where people can have a personal, close-up look at practices and processes of nanotechnology. By engaging visitors on an equal footing with researchers, especially young scientists, the project aims to answer individual questions and tackle wider issues relating to nanotechnology in a hands-on manner. This includes discussions about ethical issues and wider implications for society (ELSA).

The project aims to make full use of the strengths of science centres and museums, so it is establishing new role models for those students intending to undertake a career in science, while young researchers will learn first hand that communication of their research is part and parcel of their professional identity. NANOTOTOUCH is very keen on this exchange, which will benefit the scientific community by allowing it to pay more consistent attention to the ideas and needs of the public. The relationship between education and science will as a consequence be strengthened, too. These experiences will be recorded in the project's 'cookbooks'.

The open labs are permanently staffed by PhD students throughout the project and are trained in science communication. The flagship 'open nano lab' is at the recently opened centre of new technologies at the Deutsches Museum in Munich, the other two are in Milan and Gothenburg.

On top of this, a series of dedicated events called 'Open campus days' completes the experience of bringing the public into direct contact with the scientists.

'Understanding by doing' in science centres and museums, with a special attention to young people, is at the core of **TIME4NANO (http://www.timefornano.eu)**, which has devised a range of informal education products on the benefits and risks related to nanoscale research, engineering and technology. The highlights include a nano-kit and the organisation of a 'Nanolympics' web contest to coincide with each school year throughout the project, which will be the basis for the realisation of 'nano days' events and debates aimed at the public to collect opinions and feedback.

The nano-kit, translated into the EU languages of the participant countries, contains activities related to nanosciences, objects containing nanotechnologies and materials, and a Decide game that aims to challenge students to debate nanotechnologies. It can be used in the web contest, science museums and in classrooms by teachers. Also, 1 000 copies of the prototype were produced and distributed across the 10 science centres of the consortium. Each science centre organised at least five nano days, which were an overall success.

The 'Nanolympics' video web contest, which is open to young people aged between 14 and 20, was organised on a national level in 9 countries (Belgium, Finland, France, Germany, Italy, Poland, Portugal, Turkey and the UK). The European winner of the first edition was chosen on the basis of the best and most original way five nano-dilemmas were addressed, each one of which carried a 'killer question' about healthcare, privacy, the environment, the socioeconomic divide and about ethics and a potential human enhancement scenario.

In order to encourage young people's creativity, the artistic partner of the project's consortium made stop motion videos that are posted on the TIME4NANO website and on the YouTube channel. Tutorials posted on the YouTube channel as well as video workshops organised during the nano days had helped to increase the involvement and the participation in the contest. Eventually, 87 self-made videos were posted for the first edition on the project's website.

Specific training courses in each of the participating science centres (at national level) and by Ecsite (at European level) also reached a large number of knowledge multipliers. Dissemination takes place through each partner's national and regional relationships with science centres, science festivals and schools, and particularly through Ecsite and its large community of science centres and science museums all over Europe.

NANOLOGUE (Facilitating the dialogue between research, business and the civil society to improve the quality of life, create wealth and reduce impacts to society, http://nanometer.nanologue.net) addressed the keen question of a dialogue about nanotechnology in three main steps. First came a mapping study on the ELSA of nanotechnologies and a background paper on the application areas of energy conversion and storage, food packaging and medical diagnosis.

Then the project carried out a consultation on the ELSA of nanotechnologies with representatives from research, business and civil society, and finally the partners developed three scenarios on the future of nanoscience published in the study 'We need to talk: the future of nanotechnology', which included three possible scenarios about how nanotechnology will have developed by 2015. Insights gained throughout the project have also been used for the design of the NanoMeter – an Internet-based tool, the first of its kind, assessing societal implications of nanotechnology-based applications in the R&D phase.

The results helped to lay the ground for a structured public debate on the impacts and implications of nanotechnologies. While NANOLOGUE by design could not reach a significant number of European citizens, content and recommendations were regularly taken up by subsequent projects aiming at widespread impact and public information.

The NanoMeter self-assessment tool introduces companies to relevant social, ethical and legal concerns. Guiding questions link these aspects to actual nano-enabled applications under development, aiming to prevent a loss of R&D investments due to a lack of customer acceptance. In the meantime, this well-working tool is still being used. In fact, it has been taken up and further developed by the ObservatoryNano project, tailoring it towards different technology sectors in the diverse nano industry. The social, ethical and legal impacts of nanotechnologies defined from our literature studies were among the first of its kind and are still used and referred to for structuring current debates.

The project was among the first providing clear (and still updated) recommendations on how public dialogue on nanotechnologies should be organised and carried out, and the accompanying brochure is regularly quoted as helpful guidance to introduce the public to the issue and challenges of nanotechnology.

ICPC NANONET (http://www.icpc-nanonet.org, http://www.nanoarchive.org) aims to foster collaborations between Europe and International Cooperation Partnership Countries (ICPC), thereby assisting in the transformation of nanotechnology from a resource-intensive to a knowledge-intensive industry across the globe. The project aims to bridge the technology gap between developed and developing countries, and ensure that developing countries have the opportunity to exploit nanotechnologies for their own benefit.

The four-year project is providing an updated electronic archive of nanoscience publications that is freely accessible to researchers around the globe. Such an archive currently hosts over 7 000 items and all researchers are encouraged to file their papers. ICPC NANONET also makes publicly available an electronic database of nanoscience organisations and networks in ICPC, with the corresponding links to nanoscience researchers and stakeholders worldwide, allowing for the identification of research expertise and capacities in ICPC regions. The organisation database can be searched by name, type, country and region, discipline, application area and keywords; to date it features 1 015 organisations from 72 countries and 5 world regions.

On its website, the project publishes annual reports on nanoscience developments in Africa, Asia, the Caribbean, Central Asia, Eastern Europe, Latin America, Mediterranean Partner Countries, Pacific and Western Balkan Countries. These focus on areas for collaboration, funding, national, regional and inter-regional initiatives and networks and are peer reviewed by partners and the ICPC Nanonet steering committee. Furthermore, ICPC NANONET actively provides online networking tools, such as forums and workshops for scientists and researchers. Any scientist or researcher can host a workshop, and one annual workshop is respectively held in China, the EU, India and Russia, which are webcast live to facilitate access. So, two annual region reports have been published.

ICPC NANONET also hosts many live 'webinars'. This year, these events addressed nanotechnology for water purification, renewable energy, nano-biosensors and biomedical applications. The latest sessions on nanotechnology for a knowledge-based society in collaboration with Nano Rights and Peace attracted participants from Argentina, Brazil, Egypt, India, Ivory Coast, Morocco and Uruguay among others.

The project is implementing the guidelines set up by the EC's Action Plan for Nanotechnologies, stating that the EC places great emphasis on global collaboration, which needs to bring together economically and industrially advanced countries and the countries that are less advanced, in order to secure their access to knowledge and avoid any 'nano divide' or 'knowledge apartheid'. It is unique in that it supports international research cooperation in nanotechnology between the EU and ICPC among the emerging economies and developing countries, thereby transcending geographic, economic and political boundaries.

NANOFORUMEULA (Nanoforum EU Latin America) aimed to foster lasting research relations and stimulate communication between European and Latin American nanotechnology research organisations. Brazil and Mexico were chosen as they are the most active countries in nanotechnology R&D in Latin America and working relationships were established to enable the industry in these countries to set up a working relationship with European research.

NANO TV (Enhancing public awareness on the results of European research actions on_nanosciences and nanotechnologies through the professional use of television media) is due to produce 14 free-of-rights video news releases about key results of European research and the key issues related to it. The target is the distribution of these videos to mainstream TV news programmes across all EU Member States and beyond.

NANOFUTURES: The European Initiative on Nanotechnology (http://www.nanofutures.eu)
NANOfutures is a European Technology Integration and Innovation Platform (ETIP) created in a joint initiative of the European Commission together with industry, SMEs, NGOs, financial institutions, research institutions, universities and civil society, and with contacts to Member States at national and regional level.

NANOfutures aims to be a nano-hub, linking together European Technology Pplatforms and other nano related initiatives. NANOfutures will create synergies among European Technology Platforms and other initiatives on nanotechnology; identify key strategic nanotechnology nodes addressing issues of cross-sectorial and nano-specific relevance and develop and disseminate a 10-year Roadmap for European Nanotechnology with a detailed medium term implantation plan.

NANOfutures conducts its activities within Horizontal Working Groups addressing issues like regulation, research & technology, regional/national networking, standardisation, skills and education, industrial safety strategy, industralisation & nano-manufacturing, communication, technology transfer and innovation financing and nanosafety research.

Participation is invited from all parties having an interest in promoting the use of nanotechnology.

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In order to think ever bigger, you have to go ever smaller. Science today is looking for the key to greater achievements by turning its full attention to the manipulation of structures in the order of a few millionths of a millimetre, the nano domain. However, this new industrial revolution implies the mastery of an intricate web of interdisciplinary connections, as demonstrated throughout the research projects of the different clusters described in this publication. Nanomedicine is represented by its three main branches: Diagnostics, Drug Delivery and Regenerative Medicine; Energy and Environment reveal the potential to give the world cheap access to clean water and energy; Electronics/ICT and Nanomaterials cross over into virtually all nano-territories, including Industrial Applications, Security, Textiles and Agrifood. The safety of nanomaterials and processes is being very actively researched as shown by the large portfolio of projects under the cluster Environmental and Human Safety, while societal issues of nanotechnology are addressed under the cluster Ethical, Legal and Social Aspects. Finally, the clusters on Outreach and policy Coordination and Support are closing the loop building nano-networks within the scientific world, structuring nano-educational platforms and communicating nanotechnology research to the whole society.

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