

Annual Report 2005

iNANO - Interdisciplinary Nanoscience Center



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Message from the Director

It is with pleasure that I present the second annual report for iNANO, the Interdisciplinary Nanoscience Center at the University of Aarhus and Aalborg University. In 2005, we have witnessed exciting developments and new important additions to iNANO's blooming activities, while our established research projects and extrovert initiatives progressed at a brisk pace.

By Flemming Besenhacher

The single most important development in 2005 was undoubtedly the decision of the Board of the University of Aarhus to fully approve iNANO's plans for a large laboratory/office building including clean-room facilities. The general ideas and arguments for building the iNANO House will follow at the end of this message.

Organisation

At the moment about 55 senior researchers, 35 postdocs, and 85 PhD students are associated with iNANO, and the activity level has been ever-rising since the center was inaugurated in 2002. This has necessitated a strengthening of the iNANO organisation. Besides the director, the daily management team now consists of Brian Bech Nielsen and Kjeld Pedersen, who hold the positions as Vice-directors of iNANO, supported by Signe Osbahr and Sanne Olofsson Dolmer, who have been promoted to scientific coordinator and head of the administrative staff, respectively. In order to ensure an efficient communication channel to all iNANO researchers, a new management committee headed by the director has been established with representatives from each of the involved departments at the University of Aarhus: Niels Christian Nielsen (Chemistry), Jørgen Kjems (Molecular Biology), Brian Bech Nielsen (Physics), Rikke Louise Meyer (Biology), Thomas Vorup Jensen (Medicine) and Kjeld Petersen from Aalborg University.

The iNANO mission

The mission of iNANO is based on three equally important pillars:

- 1. To play a key role in the education of the next generation of researchers in nanotechnology at the Bachelor, Master, PhD, and Postdoctoral levels.
- 2. To strengthen interdisciplinary research in the area of nanoscience and nanotechnology and to catalyze international collaborations within the field.
- 3. To promote innovation and thereby provide transfer and transformation of basic knowledge in nanoscience to nanotechnology in Danish industry. We wish to assist in the creation of spin-off companies and catalyze innovative projects in existing Danish companies.

The developments of the three pillars constituting iNANO's activities during 2005 are briefly described below:

New Education initiatives in 2005

Pioneering undergraduate education

The nanotechnology education at the University of Aarhus was initiated in September 2002 and has attracted an increasing number of new students each year up to 2004, when more than 60 new students were enrolled. In 2005, the Faculty of Science thus found it necessary to impose a quota of 60 students – an unusual, but correct decision by the Faculty.

In 2005, our first nanostudents became the first Danish Bachelors in nanotechnology and in their fourth year of study they will achieve a high degree of specialization in one of the branches; Nanophysics, Nanochemistry, or Nanobiology.

In addition to specialized courses in nanoscience, iNANO now offers a course on innovation and

entrepreneurship in collaboration with Aarhus School of Business. The objective is to provide the students with solid knowledge about researchbased innovation and entrepreneurship, and thereby strengthen their ability to create new companies or new business areas within existing companies.

iNANOschool - graduate education at iNANO

After their fourth year our brightest nanotechnology students will be ready to apply for admission to our graduate school, iNANOschool, in 2006. With their broad background in nanotechnology they will constitute an invaluable addition to graduate students, who have attended the more traditional undergraduate programmes.

In 2005, iNANOschool expanded its volume to reach a current peak of 85 graduate students. Many graduate projects are carried out and financed in collaboration with industrial partners according to the so-called 1/3-1/3-1/3 model, where the Faculty of Science, the Danish Research Training Committee (FUU), and an external company or a public institution each contribute one third of a PhD Scholarship. In 2005, FUU granted iNANO an additional 10 such co-financed projects, and the number is expected to increase in 2006. iNANO receives an increasing number of applications for grants from international students, and we hope to get additional funding to allow many more of these to join us.

New research activities in 2005

iNANO researchers received a very large number of grants in 2005, and I will restrict myself to emphasizing a few of the new and truly interdisciplinary projects:

Bioimaging using nanoparticles

Advanced biomedical imaging is becoming increasingly important in combating diseases. Nanoscience may provide efficient tools for targeting specific tissue markers, allowing new avenues in diagnostic imaging and individualized therapy. This project integrates cuttingedge nanotechnology and bioimaging (Magnetic Resonance Imaging) to create novel platforms for

Bernhache. Flemming Besenbache

director

diagnosing and treating common diseases, such as cancer and atherosclerosis. This project builds upon an established collaboration between the Center for Functionally Integrative Neuroscience, the Center of Insoluble Protein Structures (inSPIN), the Department of Oncology at Aarhus University Hospital, all associated with iNANO, and the Danish company H. Lundbeck A/S.

NanoNonwovens, a High-Technology Foundation project

At the end of 2005, iNANO and the Aalborgbased company Fibertex A/S were granted 20 million DKK for a highly innovative project, which combines nanotechnology and polymerbased fibres. Fibertex A/S is among the world's largest producers of nonwoven polymer-based textiles, which are used in hygienic and medical products as well as in a number of technical applications, such as in automobiles, filters, furniture, and construction materials.

Collaboration with industry

iNANO houses a regional office of NaNet, the Danish National Knowledge Network on Nanotechnology, which is a collaborative effort between the major Danish universities and national laboratories. NaNet offers assistance, in particular, to small and medium-size companies with an interest in nanotechnology.

Aalborg University has recently assisted in forming a new company, Nanolab (www.nanolab.dk), which specializes in consulting on products based on nanotechnology. One objective of Nanolab is to offer companies access to Aalborg University's clean-room facilities, which were put into operation in 2005.

The "Nanofood" consortium, established in 2005, focuses on improved food safety and healthy nutrition. The partners include strong industrial players, such as Arla Foods, Danisco, Aarhus Karlshamn, Danish Crown, and Systematic Software Engineering in collaboration with the University of Aarhus (iNANO), Danish Technological Institute and the Engineering College of Aarhus.



Invest in Denmark, Aarhus

Foreign direct investments in Denmark have been biased towards the capital region. As a consequence the West Danish counties have decided to expand their investment promotion activities. iNANO now hosts Invest in Denmark, Aarhus, which aims at attracting investments in life sciences and targets biotechnology and big pharma companies. The objective is to attract international companies to Denmark and facilitate access to international partnerships and thereby create new jobs and strengthen the region's overall competitiveness.

Collaboration between iNANO and a Danish company often begins as a co-financed PhD Scholarship for a project under the auspices of the iNANOschool. In a number of cases, such projects have enabled the identification of larger collaborative projects. The iNANO organisation currently prepares for an expansion of the portfolio of such projects, which will be housed in the upcoming iNANO House.

The iNANO House

Nanoscience and nanotechnology were announced as a focus area in the "Development Contract 2005" between the University of Aarhus and the Ministry of Science, Technology and Innovation. In 2005, the Board of Directors of the University showed their commitment and decided to establish a clean room research facility with an area of about 120 m² excluding service areas. Recently, the Board took the next major step and approved the building of an iNANO House with a total area of about 8000 m² including the clean room. The clean room research facility is expected to be operational in the autumn of 2007, while the rest of the building will be inaugurated in 2008 according to plans. This development represents a major breakthrough for nanoscience and nanotechnology research at the University of Aarhus. The iNA-NO House will give researchers from different departments excellent opportunities to collaborate closely in well-equipped competence laboratories, and consequently the interdisciplinary research will be strengthened significantly. Furthermore, the new building will bring together students in nanotechnology and PhD students in the iNANOschool and give them outstanding possibilities to conduct first-class research in nanoscience and nanotechnology.

Finally, the iNANO House will strengthen the interaction with Danish Industry and further promote innovation. The presence of key interdisciplinary scientists, central synthesis facilities, and a range of first-class analytical techniques, implies that companies will have easy access to state-of-the-art technology and knowledge. In the medium to long-term, we expect approximately 25% of the iNANO House area to be occupied by employees from private companies, who work on special projects and collaborate with key iNANO scientists. In parallel with the strengthening of the contact with industry and increasing the awareness about innovation among students, we expect new companies to be formed on basis of research activities in the iNANO House

Acknowledgement

Finally, I would like to express my deep appreciation for the excellent achievements, which are results of the hard and dedicated work carried out by the scientific, administrative and technical staff associated with iNANO in the past 12 month period. I am confident that we are well prepared to successfully meet the challenges in 2006.

Educational activities

Undergraduate studies

A new interdisciplinary study line was introduced in September 2002, where 37 new students commenced their nanotechnology studies at the University of Aarhus. In 2004 the experience gained from the education of these frontrunners and the feedback they gave us led us to redefine the 3rd and 4th year of the nanostudy programme curriculum and to introduce three specialisations: nano-physics, nano-chemistry, and nano-bio (www.inano.dk/studerende). The course programme for the 4th study year is planned individually in consultation with iNA-NO researchers who will act as future supervisors on Master or PhD projects. During the 4th year, four new courses were introduced: Nanocharacterisation, Current Nanoscience, Student's colloquium, and a Patent/Innovation course. The former two courses ran for the first

time in 2005, when the "oldest" students initiated their 4th study year. The two courses introduce a number of experimental characterisation techniques for nanoscience and important subject matters for nanoscience research. The later two courses will run for the first time during spring 2006. The colloquium will give the students experience in presenting a subject of their own choice in a coherent manner to a wider audience. Finally, the patent/innovation course introduces concepts of commercialisation, which are highly relevant to anyone who wishes to enter into a commercial exploitation of nanotechnology. The experience gained from the first four years of teaching nanotechnology lead us to further redefine the studies slightly for the students to be accepted in 2006. The new study programme can be seen in figure 1.



In September 2005, 66 students were enrolled in the nanotechnology study programme. This number is comparable to the number of students admitted to the traditional disciplines at the Faculty of Science: A number of new initiatives, such as individual counselling, "nano café", extra instructors, etc. have been successful in lowering the drop-out frequency among the nanostudents to a very low level. A quota of 60 nanotechnology students per year has now been implemented to ensure the continued high level of the education.

In 2005 iNANO arranged a very successful fourday study trip for a group of 24 third-year students to the nanoscience centres in Hamburg, Munster and Enschede, with which iNANO have established collaboration regarding the Bachelor and Master educations.

Master project in nanotechnology			Master project		
			Semester project	Nano specialization: Physics, Bio, Health care or Production	
Specialisation - 4	Innovation/patent	Specialisation - 10	Semester project	Nano specialization: Physics, Bio, Health care or Production	
Specialisation - 3	Specialisation - 6	Specialisation - 9	semester project		
Specialisation - 2	Specialisation - 5	Specialisation - 8	e	Nano specialization: Physics, Bio, Health care or Production	
Specialisation - 1	Student's colloquium	Specialisation - 7	Semester project		
Current nanoscience	Theory of Science	Bachelor project		Nanofabrication and characterisation; Quality control; Physical Chemistry; Nanostructures in biological organisms; Biochemical reactions in the body: Optical, electronic, magnetic properties of nanostructures	
Nanocharaterisation	Experimental mol.bio.	Bachelor project	Semester project		
Solid state physics	Bionanotechnology	Nano project		Organic and inorganic nanostructures; Statistical mechanics; Solid state physics and chemistry; Biosensors; Fluid dynamics in small structures	
Statistical mechanics	Elective-2	Fourier analysis	Semester project		
Introduction to quantum mechnics	Elective-1	Statistics and data processing	e	Quantum mechanics; Structure of solids and liquids; Molecular	
	Chemical binding	Linear algebra - 1	Semester project	biophysics; Computer modelling; Spectroscopy; Data processing; Differential equations	
Experimental exercises	Inorganic chemistry	Basic molecular biology		Quantum mechanics; Structure of solids and liquids; Molecular biophysics; Computer modelling; Spectroscopy; Data processing; Differential equations	
Introduction to programming	Thermodynamics/kinetics	Basic biochemistry	Semester project		
Waves and optics		Nano intro	C	The composition of matter; Chemical and biological molecular structures; Scientific communication and methods; Mathematics;	
Electromagnetism	Organic chemistry	Basic biology	Semester project	structures; Scientific communication and methods; Mathematics; Mechanics; Thermodynamics; Scientific models of the universe	
Mechanics/thermodynamics	Numerical physics	Calculus - 2	Semester project	Atoms and molecules; Basic chemistry; IT; Mathematics;	
Introductory mechanics	Introductory chemistry	Calculus - 1		Scientific models of the universe	

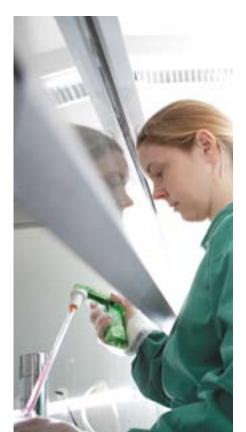
Course programme for new nanotechnology students.

Legend: blue: physics courses, yellow: chemistry courses, orange: molecular biology courses, red: mathematics/computer science courses, green: nanoscience courses, grey: specialisation modules.

Course programme for the Bachelor programme in nanotechnology at the Aalborg University.



At Aalborg University, a new engineering programme focused on nanotechnology started in 2003 (www.physics.aau.dk), and in 2005 70 students were enrolled. The programme consists of a combination of courses and projects with different themes for each semester (see Figure 2).



A Two-year Master programme with specialisations in physics, biotechnology, health care, and production techniques is currently being planned in detail.

Graduate studies - iNANOschool

A vocationally oriented graduate school, iNA-NOschool (www.inanoschool.dk), was started in 2002 shortly after the inauguration of iNANO. The activities in iNANOschool (mainly PhD projects and graduate courses) are based on a large grant of DKK 12 mill. from the Danish Research Training Council (FUR). This grant covers 1/3 of PhD scholarships in a so-called co-financing scheme, where the Faculty of Science and the Faculty of Health Sciences contribute another 1/3 and the remaining 1/3 coming from private companies or a public body, in our case the County of Aarhus.

Currently, 21 PhD projects are financed by the FUR funds. The total number of PhD students enrolled in iNANOschool is, however, as high as 80, the remainder being financed by e.g. faculty funds or funds obtained by individual research groups in iNANO from other sources. The original funded scholarships have all been allocated, and an application for new scholarships was recently submitted. During 2005 21PhD students completed their PhD studies, and 22 new PhD students were enrolled in the iNANOschool (a list of the PhD titles is listed under PhD Theses 2005)

In 2005, a number of graduate courses were held as part of the iNANOschool activities:

- N9: Bionanotools and protein structure
- N15: Biochemistry and molecular biology for nanoscientists
- N17: Formidlingskursus (in Danish)



Finally, iNANO organised a very successful autumn school with attendees from eight countries at Fuglsøcentret near Aarhus on October 7-11, 2005. The autumn school gives the students an opportunity to interact with each other and with the lecturers in an informal setting. This year we were able to present the following excellent lecturers:

- David Oupicky, Wayne State University, USA: "Nanomedicine and Drug Delivery: Gene nanothereapeutics with stimulus-controlled activity"
- Lisbeth Illum, IDentity Ltd, UK: "Novel Approaches for the Nasal Delivery of Vaccines – are nanoparticles the answer?"
- 3. Z. G. Tang, UKBioTEC, University of Liverpool, UK: "Nanoscience & Tissue Engineering"
- 4. Anders Bentien, Max Planck Ins. Dresden, Germany: "Thermoelectric Materials "
- Anders Palmqvist, Chalmers, Sweden: "Nanostructured Materials Prepared by Molecular Templating and Self-Assembly"
- 6. Jacob Fage-Pedersen, Technical University of Danmark: "Nanostructure in Photonics"
- Lyubov M. Belova, Royal Inst. of Technology, Sweden: "Nanostructured Carbon. Inorganicbio Interfaces for Biomedical applications"
- Horst Vogel, Ecole polytechnique fédérale de Lausanne: "Investigating cellular signalling by micro- and nanotechnology"
- 9. Jan O. Jeppesen, University of Southern Denmark: "Supramolecular Chemistry and Nanoscience" "
- 10. Thomas LaBean, Duke University, USA: "Self-Assembling DNA Nanostructures and DNA-Based Nanofabrication"
- Raz Jelinek, Ben-Gurion University, Israel: "ĐNano-patchĐ bio-mimetic sensors for studying biological membrane processes"
- Niels Bent Larsen, Risoe, Denmark:
 "Interfacing the Living and the Non-Living: Can We Trick Nature?"
- 13. Johannes Barth, UBC, Canada: "Controlling Matter at the Nanoscale through Supramolecular Engineering at Surfaces"
- 14. Fredrik Höök, Lund University, Sweden: "Towards Label-Free Single–Molecule Detection of Lipid-Membrane Mediated Biomolecular Reactions"

Nanorama

Description of the student

organization; Nanorama

By Celia Haldan Voetmann

Nanorama is a student organization run by undergraduate students at iNANO and was first started in the spring of 2005. Nanorama arranges a range of different social activities, such as "Friday NANOBar" once every quarter - sometimes in collaboration with other student organizations. Last year, we also arranged a Christmas lunch for nanostudents where about half of the undergraduate students at iNANO participated.

Besides these social activities, Nanorama also arranges visits to industrial companies, whose research and development activities are of great relevance to nanostudents. We have recently arranged two visits; one to Danisco and one to the Danish Technological Institute, both situated in Aarhus. These visits were a great success with more than 30 participants at Danisco and 60 at the Danish Technological Institute. About 20 of these 60 nanostudents were from other Danish Universities, and for them we arranged a tour at iNANO, where one of iNANO's researchers gave a talk about nano-biocompatibility.

So far the support for our activities has been overwhelming, and since the number of students increases every year, we expect to expand our activities in various ways. We have lots of ideas, and it seems as if time is our only limit.





4th annual iNANO meeting 2006: **A glimpse of the future**

Today it is still basic science. But in the years to come nanotechnology may change society and affect almost every aspect of life – industry, consumer goods, transport, information technology, health and medicine, and even the food we eat. The speakers at the 4th annual iNANO meeting 2006 described recent breakthroughs and gave clues to a tantalising future.

By Rolf Haugaard Nielsen, science journalist

Nanoscience has provided us with a wonderful toolbox of functional nanostructures that may serve as building blocks for electronic components, industrial and environmental sensors, superior materials, molecular motors, diagnostic kits, vehicles for drug delivery and even selforganised systems designed to improve the human uptake of neutraceuticals such as antioxidants from food. Still, it is a major challenge to integrate these nanostructures into functional devices. The traditional top-down approach used by, e.g. the semiconductor industry is too coarse to construct the minuscule nanoscale components, and building functional nanodevices bottom-up from atoms and molecules is difficult, time-consuming and too expensive for industrial applications.

A promising solution is clever combinations of the top-down and bottom-up approaches. David Reinhoudt from the University of Twente in The Netherlands reported recent success in doing just that - his research group has created nanoscale organic field-effect transistors (FETs). First nano imprint lithography is applied to make a molecular print board on a gold surface coated with a polymer. This is achieved by a stamping out a pattern of elevated polymer lines. Then layer-by-layer self-assembly is used to build up tiny organic semiconductor channels between the polymer stripes. After removing the polymer the semiconductor pattern of thin lines measuring only two nanometres across is transferred to a silicon wafer and tiny gold electrodes are added to construct functional nano FETs. "Our goal is to create FETs small and fast enough to build computers that work with the decimal number system rather than binary system used today", David Reinhoudt said.

The layer-by-layer method is based on supramolecular chemistry. The first monolayer consists of D-cyclodextrin molecules that are adsorbed onto the gold surface. On top these molecules display circular cavities ready to support the next monolayer made from dendrimers that bind to the cavities by multivalent - and reversible - hydrophobic interactions. The dendrimers are self-assembled molecular containers that can be filled with guest atoms giving them a variety of functionalities. The dendrimers also display cavities able to bind yet another layer, and this makes it is possible to build nanodevices consisting of alternating layers with different properties.

Nanotubes in quantity

Of all the nanostructures made so far, the stars are carbon nanotubes that can be electrically insulating, conducting or semiconducting making them ideal building blocks for nanoelectronics. Nanotubes are also incredibly strong and flexible and may pave the way for the development of ceramic or polymer composites with superior strength, and maybe even one day space elevators! Their cost, however, is a bit of a problem – high-quality single-walled carbon nanotubes are more than thirty times as expensive as gold. "We are struggling to produce large quantities, and we are still talking grams, not kilograms or tonnes", said Sumio lijima from the Meijo University in Japan.

lijima, who discovered carbon nanotubes back in 1991, described a new and highly efficient way to grow the tubes. The standard method is chemical vapour deposition, in which hydrocarbon gasses are fed into a superheated chamber containing nanoparticle catalysts. The heat breaks the hydrocarbons apart, creating a vapour of carbon atoms that link together to form nanotubes grown from the catalyst particles. Unfortunately, in most cases an amorphous carbon layer coats the cat-

A glimpse of the future



alysts preventing the growth of nanotubes, and the catalysts usually stop working after only one minute, which makes it difficult to grow long nanotubes.

Iijima's group has solved this problem by adding water to the process. Water is weakly oxidising and capable of removing amorphous carbon from catalyst particles without oxidising - that is burning - the nanotubes themselves. In this way it is has been possible to grow 3 mm long carbon nanotubes, and by starting with catalysts patterned in circles or lines, macroscale sheets or pillars of nanotubes can be made. Such pillars could be used as electron emitters for flat-panel displays. "The goal of a new research programme is to be able to grow 10 cm long single-walled carbon nanotubes on a 10 cm2 substrate by the end of 2008", Sumio Iijima said in an interview after his speech. Other programs aim at applications. "We are developing carbon nanotube supercapacitors able to deliver current for the start-up of fuel cells in hydrogen cars".

Learning from biology

Cees Dekker from the Delft University in The Netherlands stressed "that nanotechnology has a lot to learn from biology. Just look at a bacterium, it is a wonderful box of nanotech". An example of exploiting biological processes is hooking single-stranded DNA on carbon nanotubes. In this way the unique ability of DNA to recognize and combine with complementary DNA sequences may be used to assemble functional nanodevices. Biological research benefits equally from nanotechnology. Dekker's group has used nanoimaging techniques such as atomic force microscopy to study DNA repair proteins in action, and recently they have made silicon nanopores that resemble ion channels in cell membranes. When the nanopores are placed in solution they are able to suck in DNA strands when a voltage is applied and push out the strands when the voltage is reversed. These nanopores are currently used for studying DNA folding behaviour and protein binding to DNA. "Our dream is that nanopores can be developed into a tool for extremely fast DNA sequencing", Cees Dekker said.

Drug delivery and bone grafts

Nanotechnology has great potential for developing highly efficient vehicles for drug delivery. Jackie Ying from the Institute of Bioengineering and Nanotechnology in Singapore reported how tiny nanoscale capsules made of a biodegradable polymer may one day enable diabetes patients to take insulin by tablets or nasals spray instead of having to inject their medicine. The capsules release insulin only when the concentration of blood glucose is high, and as soon as the level is normalized, the capsules stop delivering the drug. In this way patients will have neither too much nor too little glucose in their blood, and frequent monitoring will no longer be necessary. "The polymer chains surrounding the insulin depots are linked together with glucosyl groups, which are removed by glucose, when the blood sugar is high. This dissolves the capsules, but as soon as

the blood sugar is lowered, the process stops". The system has performed well in diabetic rats. "Next step is to test it on larger animals before moving to clinical trials", Ying said.

Progress has also been achieved in developing new treatments for bone defects. Recently, natural growth factors called bone morphogenetic proteins have been hailed as an alternative to bone grafts due to their ability to elicit new bone formation. Today, clinical use involves loading the protein solution onto collagen sponges, which are subsequently implanted. Unfortunately, the sponges release the growth factors within two weeks, and this limits the effect of the treatment because healing of large fractures in humans takes approximately six months. To slow down the drug release, Ying's group uses apatite particles - apatite is the main bone mineral - onto which the proteins have been preadsorbed. The particles are coated with a biodegradable polymer, and as the polymer slowly degrades, it releases acids that dissolve the apatite particles setting the drug free at a controlled rate. "So far we have demonstrated perfect healing of bone fractures in rats, and the newly formed bone is comparable to natural bone", Jackie Ying told the audience.

Towards personalized medicine

Today, most of our drugs typically work well on 80 percent of the patients, but for the remaining 20 per cent the treatment is inefficient or leads to adverse effects. This is the reason for the on-



going effort to develop personalised medicine, where the drug formulation or the dosage is tailored to match the individual's genomic make-up. "To maximise the therapeutic effect and minimize adverse effects, treatments should be targeted to modulate specific molecular pathways in specific tissues. During the treatment selective biomarkers are needed to monitor the response non-invasively, so that the treatment can be modified on a rational and on-going basis. Combined targeted imaging and therapy may prove very useful for achieving personalized medicine" said King Li from the National Institutes of Health Clinical Center in Washington, USA.

Li gave a fascinating example. A promising strategy in cancer therapy is to kill the growing blood vessels that support hungry tumours, and in 2002 the American group applied lipid based nanoparticles to deliver the drug right at the target. The nanoparticles are coated with small organic molecules that bind to specific membrane receptors, which are abundant on the growing blood vessels that nourish cancer cells, but rare on already established ones. The receptors propel the nanoparticles into the blood vessel cells, where the cytotoxic drug is released. Each blood vessel supports 50-100 cancer cells, which die in the aftermath. The researchers were able to follow the effect of the treatment non-invasively by monitoring the very radionuclide that also kills the cells. The strategy was tested with success in mice, and delivering toxic genes to the cells of blood vessels also worked well.

A problem still remained, however. Some tumours defend themselves by drawing in a lot of water. This builds up the pressure in the tumour, and the pores between the cells are closed tightly, preventing the entry of nanoparticles into the blood vessels. "Fortunately physics comes to the rescue. By applying ultrasound pulses, we can shake the cancerous tissue. The repeated movements open the pores of the tumour, and water leaks out while the nanoparticles rush in. The ultrasound is also used to monitor the tumour during the treatment", King Li said. The first clinical trials of the combined imaging and therapy approach will be carried out on cancer patients in 2007.

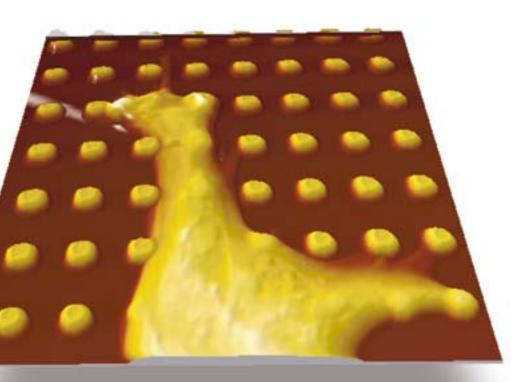
Food goes nano

Nanotechnology has a great promise for creating advanced foods, and Nasim Garti from The Hebrew University in Israel described how selforganised nanodroplets may improve the human uptake of neutraceuticals – these are food supplements mostly derived from plants and able to provide health benefits, including prevention and treatment of diseases.

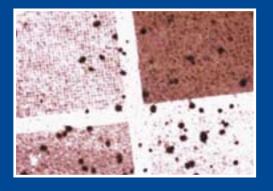
One example is lycopene, the colouring agent that makes tomatoes red. Lycopene is an antioxidant and anticarcinogenic as well, but unfortunately it has a very low solubility in water and is not absorbed into the blood stream. "It is not possible to benefit from the health effect of lycopene simply by eating a lot of tomatoes. But the bioavailability can be improved by loading lycopene into nanodroplets", Garti said. These nanodroplets are self-assembled micellar structures, which are soluble in water as well as in oil. The droplets are made from amphiphilic molecules. In oil they turn out their lipophillic side, and in water the hydrophilic parts of the molecules are displayed on the outside of the droplet. By loading lycopene into such nanodroplets it becomes soluble in blood and available to the human body.

Another neutraceutical that may be of great interest to a lot of people is phytosterols from soybean oil that reduce the concentration of cholesterol in the bloodstream. The human uptake of phytosterols is also improved significantly by loading these neutraceuticals into bicontinuous nanodroplets that emulsify in water just as well as in oil. "One could envisage water-based drinks containing bioavailable phytosterols packed in nanodroplets. When you have enjoyed a large steak for dinner, you wouldn't need to worry about your cholesterol level if you swallowed such a drink afterwards", Nasim Garti pointed out.

The art of growing homogeneous cell populations



Micron sized pillars guide a primary human bone forming cell, an osteoblast.



Murine bone forming cells grown on 4 different topographic microstructures for 3½ weeks. The wafer was stained for calcium deposition (red). The structure top-right shows enhanced mineralization as compared to the others. The cross separating the squares is not structured and serves as control surface. Each square is approximately 4'4mm². A major challenge today is to form homogeneous cell populations for cell replacement therapeutics and industrial drug validation. Array technology provides important information on how cells are guided by topographic micro- and nanoscale features. Large-scale screening is a promising tool to identify just the right topography for the desired cell type.

By Morten Foss and Mogens Duch

For any type of cell replacement therapy a homogeneous cell population is a prerequisite for success – no one would want, e.g. bone to develop inside cartilage. Homogeneous cell populations are equally important in industrial drug testing, where uniform cell cultures would be beneficial in large scale testing. However, it is a challenging task to produce homogeneous populations of specific cell types such as neurons, bone forming cells, insulin producing cells and stem cells.

Interactions between cells and artificial surfaces are influenced by a variety of factors including surface topography and chemistry. Since the size of a typical cell is in the micron range, this is the relevant length scale for the creation of features that influence cells. Unfortunately, we do not possess a detailed and thorough understanding of the cellular behaviour in relation to variation of parameters such as repeat-distance, height or feature shape.

To interact with their surroundings cells use proteins with sizes in the nanometer range, and very little is known about how nanoscale surface topography influences their interaction with cells. It has been demonstrated, though, that cells do



react to topographical cues from substrates with features in the nanometer range. This indicates that the use of surface topographies in both the micron and nanometer ranges can be utilized to guide cells in a certain direction during expansion and differentiation. This may open novel possibilities of tailoring new generations of surfaces with specific cell-guiding properties.

The BioSurface Structure Array

At iNANO, we are developing a method for largescale screening of topographic micro- and nanostructures by exploiting a new technology called BioSurface Structure Arrays (BSSA) for identification of structures facilitating expansion and differentiation of cultured cells.

The concept is to create a large number of different topographic structures on individual test squares on a single wafer coated with biocompatible tantalum. The cell population is plated on the wafer, and the cells are screened for relevant attachment and differentiation parameters. At present the BSSA wafers consist of 169 different structures, but we expect to increase the amount of structures to more than 1500 on a 6-inch wafer within the next year. So far the BSSA wafers have been generated using standard photolithographic techniques to create microstructures on the surface. However, cheaper BSSAs may be produced in a variety of polymer materials using hot embossing or injection moulding. When promising structures are identified by the array screening technique, they are produced individually and used for a variety of experiments utilising, e.g. Atomic Force Microscopy (AFM) and fluorescence microscopy. These techniques enable investigation of cellular interactions with structured artificial biointerfaces. By combining fluorescence microscopy with cells expressing stably transduced fluorescent fusion proteins we are able to visualise changes in the cytoskeleton in real time and correlate them with surface nano- and microstructures.

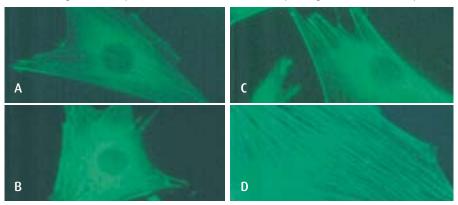
For bone formation purposes we have already identified one microstructure with a specific size

and pitch that strongly enhances mineralization as compared to other structures using a murine osteoblastic cell line. This structure was further defined according to height where only structures above a certain threshold height induce mineralization.

A new start-up company

The research at iNANO has resulted in a patent application on the BSSA technology, and a start-up company, InVitroQ ApS, has been established by the four inventors Morten Foss, Mogens Duch, Finn Skou Pedersen and Flemming Besenbacher.

Reporter cells are important tools for monitoring subcellular responses to topographical patterns in real time. The cytoskeletons of the cells are visualized by yellow fluorescence protein (EYFP) fusion proteins. The images show the preosteoblastic cell line MC3T3-E1 expressing an actin-EYFP fusion protein.



Making implants last a lifetime

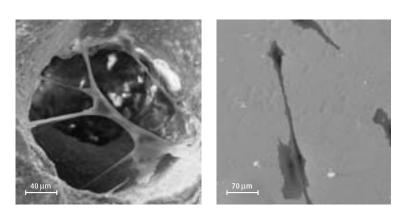
The demand for bone and joint implants is increasing among old as well as young patients. A vision at iNANO is to create nano-functionalized 3D scaffolds for bone reconstruction. These new scaffolds may radically improve clinical therapies and prolong the lifetime of implants.

By Jørgen Kjems, Cody Bünger, Jens Vinge Nygaard and Tina Mygind

The population is aging all over the industrial world, and degenerative disorders of the musculoskeletal apparatus such, as rheumatism, arthritis, osteoporosis and bone cancer, are a dramatically increasing problem. Additionally, more young patients need bone and joint implants due to road accidents or sport accidents, and this creates a demand for implants with a longer lifetime. Despite progress in implant technology, improving bone ingrowth and implant fixation are still important challenges with potential to improve the patients' quality of life.

Our vision is to create nano-functionalized 3D scaffolds as advanced bioactive materials for bone reconstruction. A scaffold material is a microstructure tailored to act as a medium for the transfer of drugs and cells to the body. These new multifunctional scaffolds may even be tailored to individual patients for a specific application and may radically improve clinical therapies, including enhancement of spinal fusion, reconstruction of traumatic bone lesions, fixation of revision implants, and treatment of bone cancer.

For a number of orthopedic surgical procedures the use of autologous bone graft is the standard method to stimulate bone ingrowth and implant



Scanning electron microscopy pictures of bone forming human mesenchymal stem cells (hMSC) cultivated on a 3D substrate (left) and a 2D substrate (right). Cultivation of cells in 3D is closer to real life as cells in tissue will practically always exist in a three-dimensional environment.

fixation. These grafts are usually taken from the hip bone, but limited amounts of bone are available, and the harvest procedure may damage the donor site and cause the patient pain. Allografts from bone banks are readily available, but the complication rate is even higher with the risk of immunological rejection or transmission of infectious diseases. Therefore, alternative methods are currently being investigated within the scientific fields of tissue engineering and regenerative medicine.

Nano-functionalized 3D scaffolds

One strategy is to develop synthetic bone graft substitutes as a replacement for allografts and autografts. These substitutes could be bioactive coatings on implants, or they could be bone void fillers. Ideally, bone graft substitutes should be porous scaffolds with a micro- and nanoscale architecture similar to the central part of natural bone.

At the microscale the porosity enables cultivation of bone cells in the internal 3D structure or recruitment of cells upon implantation into the patient. The layout of the microstructure controls the local environment to each cell growing in the scaffold, and the design of this structure is crucial. At the nanoscale the scaffolds can be functionalized to promote the attachment, proliferation and differentiation of bone forming stem cells by incorporation of bioactive nanoparticles into the scaffold. These nanoparticles act either as sustained release drug delivery centres or attachment foci for cell specific signalling peptides, thereby promoting cellular recruitment and differentiation.

New bone from stem cells

A promising strategy applied at the iNANO center combines preculture of osteogenic stem cells and a porous nano-functionalized scaffold. Using this approach, we will be able to produce viable semi-mature bone in the laboratory for regenerative and fixative purposes, and this approach may be a good solution in cases where synthetic bone grafts are not sufficient or perhaps unable to recruit enough cells for bone generation.

Autologous bone forming stem cells are used to improve the fixation of the implant to the bone. These stem cells are isolated from bone marrow of the patient, and they can be multiplied and differentiated into osteoblasts either in culture or upon implantation. When the cells are grown in culture prior to implantation, a good distribution of cells,



oxygen, and nutrients throughout the scaffold is achieved with dynamic cultivation systems able to vary the amount of fluid flowing through the scaffold. The intention is that after implantation the scaffold degrades as cells, and the bone matrix they produce slowly incorporates into the patient tissue.

The scaffold is functionalized with nanoparticles that actively promote this process. To enhance the active ingredient of the nanoparticles, we have at iNANO screened and identified a number of cellular constituents that appears to be actively involved in controlling the differentiation of human bone forming stem cells into boneproducing osteoblasts. Jens Vinge Nygaard Tina Mygind





Fluorescence microscopy on sections of scaffolds cultivated with hMSC. Cell nuclei were stained with a DNA binding dye. On top: Human bone forming stem cells cultivated on a 3D scaffold in a normal cell culture tray for 21 days.

Below: Bone forming stem cells cultivated with dynamic fluid flow conditions for the same period. The number of cells (small blue dots) increased significantly compared to the normal cell culture.

Nanocomposite coatings for extremely hard and tough industrial tools



Industrial tools for cutting and moulding of plastics and deep drawing of steel sheets are subjected to rough conditions and often fail prematurely. Nanocomposite coatings can improve their performance, prolong the lifetime of the tools and enable considerable cost savings.

By Jørgen Bøttiger and Klaus Pagh Almtoft

Many industrial tools need to be extremely hard to perform their job, but hardness comes at a price. The harder the tool, the more brittle it will usually be, and the greater the risks that it cracks like glass. New nanocrystalline composite coatings developed at the iNANO Center have the potential to solve the problem. These coatings consist of very small grains, and the propagation of cracks is halted at the grain boundaries. Furthermore, the nanocomposites can be synthesized from two materials, one that provides hardness and another that provides toughness. Such coatings can be applied to produce extremely robust and durable industrial tools for cutting and moulding of plastics and deep drawing of steel sheets.

Left: Electron microscopy image of nanocrystalline silver with argon bubbles in the grain boundaries.

Right: Schematic of a nanocrystalline material.

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Nanocrystalline coatings are grown by magnetron sputtering. A negative cathode, denoted the target, is biased with -500 V and placed in a growth chamber with an argon gas at a pressure of 0.005 mbar, whereby a plasma is formed. Positive argon ions are accelerated towards the cathode by the voltage drop, and when hitting the target the energetic ions sputter off atoms of the material, which are subsequently deposited onto the substrate creating the nanocrystalline coating. To increase the plasma intensity, magnetic field lines are placed parallel to the cathode for electrons to spiral around. By applying a negative voltage on the growing coating, argon ions from the plasma are accelerated towards the coating and deliver energy that plays an important part for the nanostructure of the film. Another parameter that strongly influences the nanostructure is the substrate temperature.

rystalline materials grain growth takes place even at room temperature. To avoid this problem nanocomposites containing two different crystalline phases, e.g. silver and copper, have been introduced. In these nanocomposites, a typical onset temperature for grain growth is about 600 oC.

It is possible to further improve the mechanical properties of nanocomposites by using a hard phase such as titanium nitride and a tough phase such as copper - in this way the coating becomes not only extremely hard, but also very ductile. Nanocomposites have been synthesised with a hardness value equal to that of diamond.

Multilayer coatings

Nanocomposites can also be produced as multilayer coatings with a layer thickness of 3-10 nanometres. In a multilayer coating consisting of alternating layers of a metal and a ceramic, hardness increases with decreasing layer thickness. Such multilayer coatings synthesized at the iNA-NO Center will be commercialised and brought to market by CemeCon Scandinavia A/S.

deposition in real time For a specific coating it is immensely important to be able to tailor the nanostructure for optimum properties. This requires knowledge of the mechanisms of growth during deposition as well as the relationship between the deposition parameters and the nanostructure. In order to obtain this knowledge, realtime growth studies of nanocrystalline coatings have been carried out by X-ray diffraction and reflectivity at the European Synchrotron Radiation Facility in Grenoble.

X-ray studies show

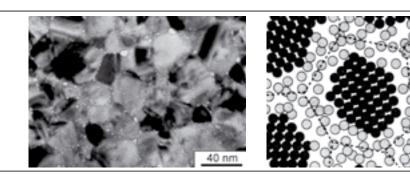
Nanocrystalline materials are a new class of materials. They are characterized by grain sizes between a few nanometres and 100 nanometres, resulting in extremely large grain-boundary areas. This gives the nanocrystalline materials a variety of improved properties compared to the conventional polycrystalline counterparts with grain sizes in the micron range. Nanocrystalline materials may, for example, exhibit unique mechanical, magnetic, and catalytic properties.

Stopping the cracks

The mechanical properties are of paramount importance to the successful performance of nanocrystalline hard coatings. Hardness and plastic deformations are controlled by the movement of line defects in the crystalline lattice called dislocations. Grain boundaries restrict the dislocation movement, and therefore smaller grain sizes lead to increased hardness. When going from a polycrystalline material to the nanocrystalline counterpart, hardness typically increases by nearly an order of magnitude. In conventional polycrystalline materials the capability to resist cracks is reduced with increasing hardness. However, as the grain boundaries are effective barriers to crack propagation, the smaller grain size of nanocrystalline materials and the enlarged grain-boundary area improve both hardness and toughness.

Thermally stable nanocomposites

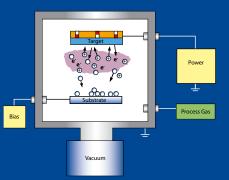
Grain growth can deteriorate the unique properties of nanocrystalline coatings, and hence thermal stability is a key issue. The large, stored grainboundary energies result in significant driving forces for grain growth, and thus in some nanoc-











Exploring the biological nanomachinery of insoluble proteins

More than half of all human proteins are insoluble in water. In cell membranes they act as switch-boards and serve as drug targets. Insoluble proteins also form the fibrils that are the hall-marks of deadly neurodegenerative diseases. Now their atomic structures are finally within reach, opening a bounty of nanotechnological applications.

By Niels Chr. Nielsen and Thomas Vosegaard

One of the biggest challenges in molecular biology is to obtain detailed insight into the structure, dynamics, and functional properties of proteins located in cell membranes and other insoluble biological structures. The current lack of knowledge is due to technical difficulties in using traditional high-resolution techniques. It is often impossible to obtain crystals for X-ray diffraction, and liquid-state NMR cannot be applied to insoluble proteins.

Less than one per cent of the 32,000 protein structures determined so far belong to the class of insoluble proteins. This is in striking contrast to their importance in biology and medicine. About half the human proteome consists of insoluble proteins, including the important cell membrane proteins that most biological processes rely upon, and which are the targets for the majority of all current drugs. Many deadly neurodegenerative diseases such as Alzheimer's and prion diseases involve the formation or degradation of insoluble protein aggregates and fibril structures, and solving these structures may lead to long-sought treatments. Other types of insoluble proteins form the framework around the cells - the extracellular matrix - and may be involved in aging, bone remodeling, and distribution of cancer metastases. Furthermore, the fascinating new field of bionanotechnology, aiming to create artificial biological devices, can harvest enormous inspiration from nature. Some examples are signaling over membranes and materials inspired by fibrillating structures.

All membrane proteins may be within reach

We have applied solid-state NMR structural analysis to bacteriorhodopsin, the protein that absorbs sunlight in photosynthetic bacteria and converts it into energy. Bacteriorhodopsin is of nanotechnological interest because it may be used in holographic devices for optical data storage or may act as a light sensitive power plant in nanodevices in combination with the enzyme ATPase. Niels Chr. Nielsen and Thomas Vosegaard

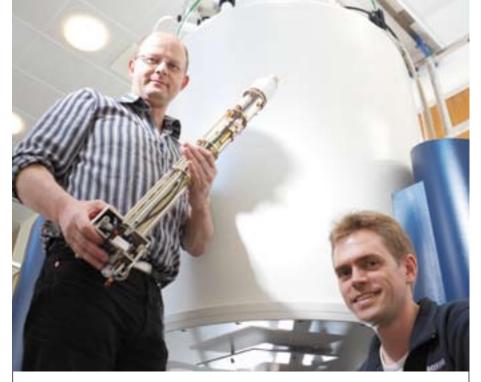
From our point of view bacteriorhodopsin was a major challenge, since it required us to take a giant leap forward towards structure determination of large membrane proteins, with bacteriorhodopsin being nearly five times larger than other membrane proteins whose structures have been determined by solid-state NMR.

Bacteriorhodopsin is one of the few membrane proteins, whose structure is known from X-ray crystallography, and this made it possible to validate our method, which hopefully will be applicable to most membrane proteins. Therefore, it is now possible to get detailed insight into conformational changes of these molecules as they carry out their nanoscale operations.

Nanotech with antimicrobial peptides

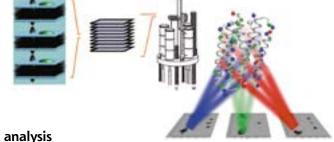
Antimicrobial peptides kill bacteria by puncturing their cell membrane. These peptides may be exploited as a new class of powerful antibiotics, and they have interesting nanotechnological applications as well.

One such peptide is alamethicin that forms a channel in the membrane through which ions may be transported in a voltage-gated manner. These self-assembled channels illustrate how peptides may be used to establish artificial channels in biological or synthetic membranes in order to create externally regulated and controllable transport systems. Our interest in alamethicin is many-fold and truly interdisciplinary. Exploiting the synthetic organic chemistry group's expertise in synthesis of modified peptides, we will synthesize various modified alamethicin oligomers to achieve better control of the channel properties and eventually equip these molecules with programmable activators, e.g. light-driven gates. We anticipate that our structural and dynamic NMR analyses of these artificial channels will enable nanotechnological applications such as ion channels or transporters in sensors.



The world's first shielded 700 MHz widebore NMR spectrometer at the University of Aarhus.

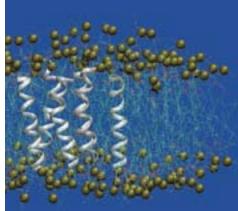
The structure and dynamics of the transmembrane helices of membrane proteins can be determined from uniaxially aligned samples.



Solid-state NMR analysis

In NMR analysis a strong magnetic field is applied to the sample aligning the magnetic dipole moment of atomic nuclei with a nuclear "spin". A radio frequency pulse of a specific frequency can disturb the alignment of the spins for a chosen isotope, and as the pulse stops, the spins precess around the magnetic field and return back into the alignment. The precessing spins induce a radio frequency signal resulting in an NMR spectrum. Such spectra yield information on the structures that the isotope is imbedded in.

One of our approaches relies on residue-specific 15^N labeling and uniaxially aligned membrane samples. By simultaneous analysis of the characteristic line shapes of the resonances in these spectra, we have established procedures for determining the scaffold structure of the transmembrane helices of large membrane proteins.

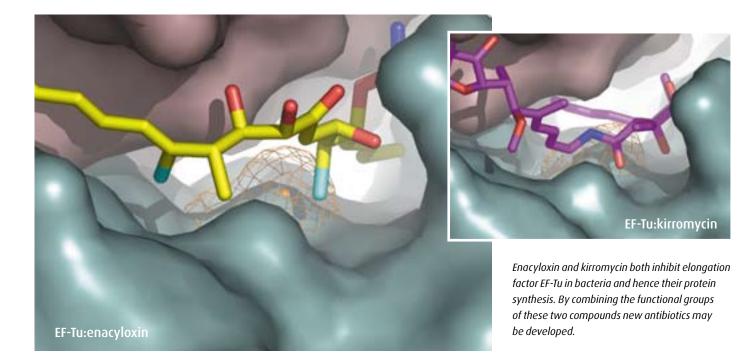


The alamethicin ion channel.

The inSPIN interdisciplinary research center

Four iNANO groups have merged their research activities into the "Center for insoluble protein structures" (inSPIN) founded by the Danish National Research Foundation. The combined effort takes the analysis all the way from identifying relevant proteins by proteome analysis, large scale expression and purification, organic synthesis of peptides, ligands and inhibitors, functional characterization by biophysical methods to highresolution determination of structures and dynamics using NMR spectroscopy and molecular dynamics calculations.

Drug design at the atomic level



The atomic structures of promising drug targets complexed with experimental medicines can be revealed by X-ray crystallography. At iNANO such crystal structures are exploited in the development of new antibiotics and a promising prodrug strategy to treat hormone-insensitive prostate cancer.

By Anne-Marie Lund Jensen, Morten Grøftehauge and Poul Nissen In biology and medicine structure at the atomic level equals function. Drug molecules must fit into their receptors as a hand in a glove to exercise their therapeutic effect, and medicines should only interact with specific targets to avoid undesired side effects. One way to achieve these goals is to determine the three-dimensional atomic structures of drug receptors and analyse their interaction with a drug.

Most drug targets in the human body are proteins, and the Protein Data Bank currently holds about 32.000 atomic structures. They have mainly been determined by X-ray crystallography, which provides a direct three-dimensional image of the molecular structure. X-ray crystallography has become an integrated tool of molecular biology, and new frontiers such as membrane proteins and multicomponent complexes are now being challenged. These are the most common drug targets, and solving their structures may open a bountyland of opportunities to go from basic research to nanotechnological application, such as rational drug design at the atomic level.

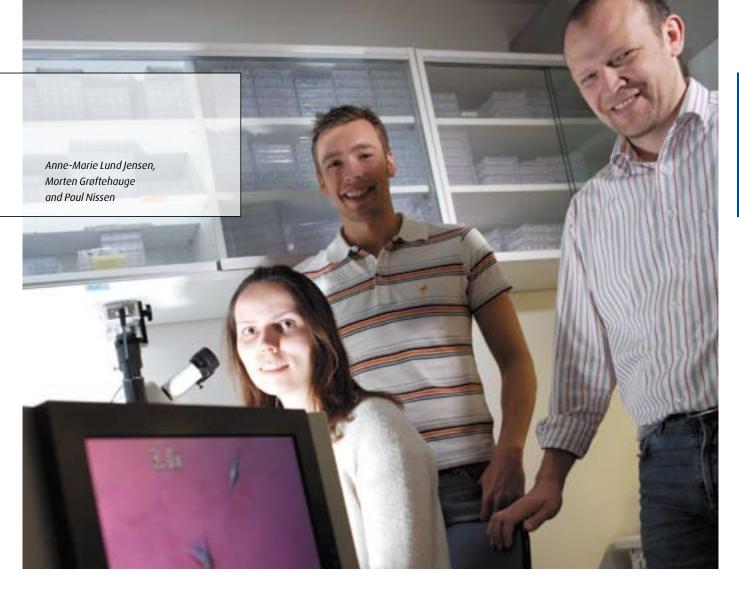
An important question is, however, whether a given protein is at all a useful target for medical drugs? Nature often gives a good indication. An example is the bacterial translation elongation

factor EF-Tu, which is indispensable for protein synthesis. Some bacteria such as Streptomyces and Frauteria gain an edge in their environment by releasing EF-Tu inhibitors to fight other bacteria. The interesting point is the attacked bacteria develop resistance only with difficulty because the price of introducing changes in EF-Tu is high, generally making the mutants unfit compared to the wild type bacteria. Thus, EF-Tu is a "proven target" for antibiotics tested in the powerful selection of nature. Drugs that inactivate EF-Tu may therefore circumvent a major health problem of increasing importance - the limited number of available antibiotics to fight infectious multiresistant bacteria.

Another "proven target" is the mammalian calcium pump, which is the subject of our attempts to devise a prodrug strategy against prostate cancer. When the calcium pump does not work properly, the affected cell commits suicide by apoptosis.

EF-Tu as target for new antibiotics

EF-Tu is a universally conserved protein and a critical component of the protein synthesis machinery. It brings tRNA with amino acids, the building blocks of proteins, to the protein factory of the cell, the ribosome. The natural bacterial inhibitors, kirromycin and enacyloxin, impose a specif-



ic conformation of the EF-Tu protein, which then becomes trapped on the ribosome and blocks protein synthesis, killing the bacteria. However, these and all other known EF-Tu-targeting antibiotics are very difficult to synthesise and not attractive as clinical drugs.

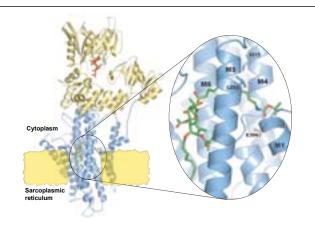
We have been able to determine crystal structures of EF-Tu in complex with kirromycin and enacyloxin, and we observe that kirromycin and enacyloxin bind at overlapping binding sites. In collaboration with the chemists of iNANO we now exploit the design and synthesis of new compounds, combining the functional groups of kirromycin and enacyloxin. In this way we seek to identify a lead compound for the development of new antibiotics.

A prodrug strategy for treating prostrate cancer

The compound thapsigargin is produced by the plant Thapsia garganica, and it is a potent inhibitor of the calcium pump inducing apoptosis in any affected cell due to loss of control of Ca2+-mediated signalling. The plant is therefore toxic and avoided by grassing animals.

Together with local collaborator Jesper Vuust Møller as well as Søren Brøgger Christensen at the Pharmaceutical University of Denmark and international collaborators, we now investigate the prospects of using thapsigargin in a prodrug strategy against prostate cancer. The hormone-insensitive forms of prostate cancer are slowly proliferating and resistant to traditional chemotherapeutics that generally target fastdividing cells. A new cure is therefore needed. The prodrug strategy is based on the fusion of a thapsigargin derivative with a peptide extension. The peptide makes the compound inactive in the body, but when the peptide is cut off, the drug becomes cytotoxic. Here is the trick: Only an enzyme specific to prostate cells is able to make the cut, and the thapsigargin derivative is therefore only released to kill prostate cells - in the prostate gland or in prostate cancer tissue anywhere in the body.

We have determined structures of the calcium pump complexed with thapsigargin derivatives with the aim of improving drug properties of the active component of the prodrug. The structures identify hotspots that can be further exploited by modification, and we aim at developing new cancer drugs in the future.



The calcium pump, Ca2+-ATPase, is a transmembrane protein. When the pump is inactivated by derivatives of thapsigargin, the cell commits suicide. The binding site of the drug is shown to the right.

The proteome of the human cornea may shed light on vision disorders

The Nano HPLC and Q -Tof tandem ESI-MS/MS mass spectrometer used in the cornea proteome study.

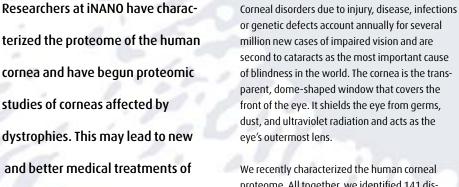
studies of corneas affected by

corneal disorders and maybe even

to development of artificial corneas

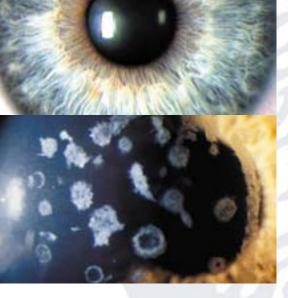
By Henrik Karring and Jan Johannes Enghild

for transplantation.



proteome. All together, we identified 141 distinct proteins from the normal human cornea of which 99 had not previously been identified in any mammalian cornea, and 118 proteins were identified from wound healing corneal fibroblasts. Furthermore, by comparing the proteome analysis with gene expression data using bioinformatics we showed that many of the proteins in the normal cornea are not synthesised in the cornea, but are imported from surrounding tissues. These results now provide the basis for detailed studies of diseased corneas, and the functions of the identified proteins.

Better vision with nanomedicine Identification of the differences in the protein expression profiles between normal and diseased



Top: A healthy human eye. Bottom: A human eye affected by the inherited disorder granular corneal dystrophy in which a specific protein forms opaque aggregates that impair vision.

Henrik Karring and Jan Johannes Enghild

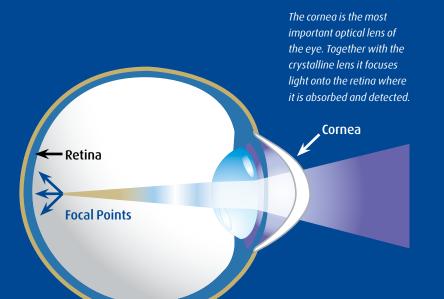


Fast liquid chromatography systems for protein purification.

corneas may lead to new avenues for therapeutic interventions. Because the cornea is so accessible, the potential for developing effective drugs and nanodevices for the treatment of corneal diseases is good. In addition, specific knowledge of the corneal proteome during normal and pathological conditions may lead to improved molecular classifications of corneal diseases, which will facilitate the development of new treatments, including gene therapy.

Nano-engineering of artificial cornea

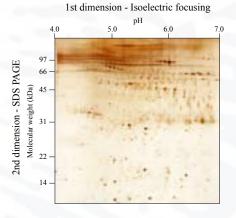
Due to the lack of donor tissue, there is a demand for efficient and safe artificial corneas for transplantation. By studying the cells and proteins of the cornea, we hope to identify the mechanisms that control the assembly of collagen fibrils into ordered nano-networks. Construction of nanoscaffolds resembling those found in the cornea may be an important step towards the design of artificial corneas. At iNANO we are trying to reach this goal by manipulating corneal cells to produce highly ordered nanostructures in culture.



The transparent cornea

The cornea is the only transparent connective tissue of the body, and it is responsible for approximately 70 per cent of the refractive power of visible light in the eye. The cornea is a highly ordered tissue mainly consisting of lamellae formed by collagen fibrils. The transparency is thought to arise from the uniform diameter and regular spacing of the collagen fibrils allowing visible light to be transmitted.

The proteins in the human cornea are separated by 2D gel electrophoresis. Each dot contains a distinct protein. Afterwards each protein is identified by mass spectrometry



Analyzing the corneal proteome

In the experiments we use human donor corneas that are no longer fit for transplantation. For the proteomic analyses the soluble proteins from the cornea are extracted and analysed by 2D polyacrylamide gel electrophoresis, in which proteins are separated according to charge in the first dimension and according to size in the second dimension. The method permits simultaneous analysis of hundreds or even thousands of proteins. On the 2D gel each spot contains a distinct protein.

Each protein is identified by mass spectrometry. The protein is digested with a protease, and the accurate masses of the resulting peptides are determined. These masses are compared to the theoretical peptide masses generated from all genes in the human genome. If a significant match is found, the protein has been identified.

Insoluble proteins such as those associated with the nano-network of collagen fibrils in the cornea are converted into soluble peptides by chemical digestion and also identified by mass spectrometry.

Learning from Mother Nature: **Designing nanocatalysts** with enzyme-like activity

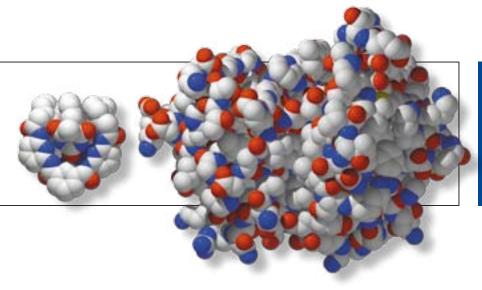


Today synthesis of chemicals typically requires organic solvents, heavy metals and high reaction temperatures and pressure, and it often leads to formation of undesired by-products. A novel class of green catalysts with enzyme-like activity may promote chemical reactions under mild and environmentally friendly conditions.

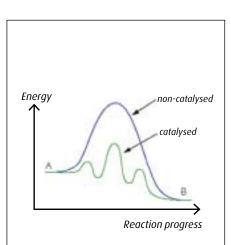
By Brian Schou Rasmussen and Troels Skrydstrup

Technological and pharmaceutical advancements constantly require access to new molecules with specific structures and functions. Polymers, drugs, petroleum products and fine chemicals represent some of the many classes of chemical compounds continuously being developed to meet these needs. However, synthesising new molecules with existing technology can lead to additional waste products, which can burden our already over-strained environment. At iNANO we are striving to meet this challenge by preparing a novel class of green catalysts which can promote chemical reactions under mild and environmentally friendly conditions.

The synthesis of chemicals is not always an easy task. It requires identification of just the correct conditions to prepare a specified compound with a precise function. Failing to do so often leads to the formation of unwanted by-products, where separation procedures can be a timely and costly affair. Sometimes such problems can be prevented by adding a catalyst which accelerates a given reaction and thus avoids undesired side reactions. Catalysts are constantly being developed The natural enzyme to the right is a big and complex molecule. The artificial enzyme to the left is much smaller and simpler, but still capable of recognizing and binding a specific compound and catalysing a specific reaction.



or improved to promote many new reactions, for example in the synthesis of new pharmaceutical products.



Over the activation barrier

Every chemical reaction has to overcome an activation barrier to convert the starting material into the product. The larger the activation barrier, the slower the reaction will proceed. A catalyst is a chemical substance that provides an alternative pathway which lowers the activation energy and thus makes the reaction proceed faster. The catalyst is not modified or consumed in the process, so it continues to promote the same reaction over and over again. An example is the exhaust catalysts in cars that accelerate the conversion of toxic combustion products into non-toxic compounds.

Pros and cons of enzymes

Nature has its own catalysts, a class of proteins known as enzymes, which are in many respects superior to man-made catalysts. Whereas enzymes catalyse reactions at moderate temperatures and in an aqueous environment, transformations promoted by synthetic catalysts typically require organic solvents, heavy metals and high reaction temperatures and pressure, and therefore enzymes play a significant role in industry.

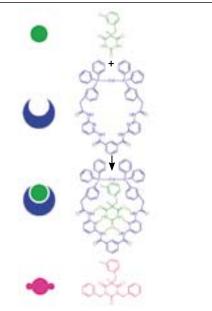
However, enzymes have disadvantages as well. Enzymes have evolved over billions of years to catalyse a specific reaction for a particular compound, and hence there are numerous industrial processes which enzymes simply cannot catalyse. Furthermore, enzymes can be expensive, and in many cases they display limited stability, restricting their application over longer periods.

Introducing molecular recognition

In Aarhus, we are attempting to combine the positive properties of man-made catalysts and enzymes by introducing a molecular recognition domain – present in all natural enzymes into known industrial catalysts. By synthesising nano-sized molecules with both a catalytic site and a recognition site, we can in many regards prepare catalyst systems which resemble natural enzymes.

Our design criteria is centred on the hypothesis that introduction of a recognition site on the catalyst will allow the substrate to be oriented in close proximity to the catalytic site, resulting in increased reaction rates. Only substrates able to fit into the recognition site will experience substantial rate accelerations, and hence the catalyst will be able to distinguish between different reactants. Molecular recognition also has the advantage that reactions can be directed to take place at a certain part of the substrate and in this way the large artificial enzyme will protect the molecule from unwanted side reactions.

A long-term goal is to exploit molecular recognition to permit reactions that are impossible with traditional catalysts. The effect of placing two reactants in close proximity by recognition can be sufficiently large to promote the unthinkable reaction!

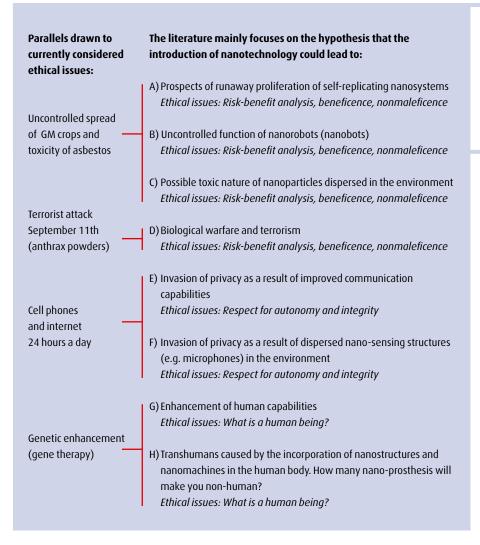


How an artificial enzyme makes the distinction

In our work we have been exploiting hydrogen bonds to join two molecules together in a selective reaction. A class of compounds known as barbiturates, which were once used as sedatives, are exploited because of their potential to generate six hydrogen bonds. The artificial enzyme in blue recognises and binds the little barbiturate in green via a hydrogen bonding network indicated with red dashed lines. No binding can take place with the other barbiturate in purple as it cannot bind with enough hydrogen bonds. In this way the artificial enzyme distinguishes between the two types of barbiturates. When the correct barbiturate binds to the recognition site, it is placed in close proximity to the active catalytic site, in this case the palladium atom (Pd). This molecular recognition allows the catalyst to react with the green barbiturate several times faster than the red barbiturate.

Nanoethics – Not from Scratch

Nanotechnology has been proclaimed the source of a revolution comparable to the emergence of the steam engine, electrification or computer technology. However, nanotechnology also raises concerns. We should address any negative impacts on humanity, public health, safety and environment as an integral part of nanoscience and the technological development process.



By Mette Ebbesen

Does research into nanotechnology make headway, while ethics lag behind? Canadian researchers at the University of Toronto Joint Centre for Bioethics recently concluded that there is a paucity of thoroughly published research into the ethical, legal and social implications of nanotechnology. They believe there is a danger of derailing nanotechnology if serious studies of nanotechnology's ethical, environmental, economic, legal and social implications do not reach the speed of progress of science. This essay challenges the worry that ethics lag behind science by raising the question whether one can infer that too little reflection on ethical issues of nanotechnology has taken place simply because only a few articles have been published so far.

The ethical issues of nanotechnology fall into three groups: Risk problems, privacy problems and problems of transhumanism. None of these can be regarded as unknown hitherto.

Risk problems

As to risk problems one can draw parallels between the fear of the uncontrolled spread of genetically modified crops and the prospects of runaway proliferation of self-replicating nanosystems. In a similar way the discussion of the possible toxic nature of nanoparticles can be compared with the debate on the toxicity of asbestos, which has been ongoing for years. Such issues can be dealt with by risk-benefit analysis, where risk is defined as possible future harm, and benefit refers to things of positive value, such as life or health. Risk-benefit relations may be conceived in terms of a ratio between the probability and magnitude of an anticipated benefit and the probability and magnitude of an anticipated harm.

The privacy issue

It is a general acknowledged ethical principle that the autonomy and integrity of humans ought to be respected. The fact that nanotechnology could lead to an invasion of privacy as a result of improved communication capabilities is a currently debated issue, and the ethical problem could grow in the future if spying nanomicrophones can be released in the environment. The principle of respect for integrity means, then as now, that

Mette Ebbesen

Parallels can be drawn between ethical issues of nanotechnology and currently analysed ethical issues. Especially, bioethics provides a useful knowledge base for the ethical discussion of nanotechnology.

nobody has the right to access information that is intimately linked to the life and identity of another human being.

Transhumanism

In the future nanodevices and nanomachines may be incorporated into the human body, raising the question of whether such nanoprostheses will make you non-human? As to problems of transhumanism, one can draw a parallel to the issue of genetic enhancement. Since the first experiments of gene therapy, ethicists have warned that gene therapy may lead to the enhancement of normal characteristics in contrast to treatment of disease.

A knowledge base from bioethics

In light of the parallels drawn between ethical issues of nanotechnology and ethical issues of biotechnology and biology, a reasonably sound knowledge base has already been acquired in the field of bioethics that can be extended to nanotechnology. There is no reason the ethical discussion of nanotechnology should not gain from this knowledge base. The fact that only a few articles dealing specifically with ethical reflections of nanotechnology have been published so far does not imply that the ethical discussion of nanotechnology needs to start from scratch.

The existing knowledge base from bioethics is currently being put to use at the iNANO Center where the author of this essay has received a two-year research grant dedicated to studies of the challenging field of nanoethics.



Does small mean risky?

Herman Autrup

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Humans may be exposed to nanoparticles by cosmetics, medicine, food additives and contaminants. The standard methods for determining toxicity of products may not be sufficient to detect all possible adverse effects of nanoparticles.

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By Herman Autrup

The paradigm in toxicology is that health effects are correlated to the mass of the agents to which the individual is exposed. For nanoparticles the concentration number and the resulting total surface area determine the interaction with biological system and may thus be of great importance. In addition to the surface area, the chemical composition and physical properties of the nanotechnology products may also influence their toxic properties.

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In view of the specific characteristics of nanoparticles and nanoparticle formulations, the assays usually performed for determining toxicity of products may not be sufficient to detect all possible adverse effects of minuscule particles. Human could be exposed to nanoparticles either by inhalation, by intake of food additives and contaminants, by topical contacts with cosmetics and by injection and implantation for some medical products.

Risk assessment of nanoparticles

Risk assessment consists of four elements: Hazard identification, dose response, exposure assess-

Cell cultures are used to determine the toxicity of a range of nanoparticles.

ment and risk characterisation. The dose-response curve is a major focus area in the toxicological evaluation of nanotechnology products. A complication in establishing this relationship is that smaller particles appear to clear less efficiently from the human body, and thus have potential for bioaccumulation in humans.

The toxicological mechanism of nanoparticles is presently unknown, but one mechanism of toxicity is likely to be induction of reactive oxygen species and the consequential oxidative stress in cells and organs.

Investigations of the toxicological effect of nanoparticles as a function of dose and chemical composition have been initiated at the Department of Occupational and Environmental Medicine, Institute of Public Health. Studies will be conducted in cultured human cell lines and in human blood cells.

Assays with human cells

The studies in cell lines will focus on cytotoxicity, membrane damage and induction of stress genes that may make cells commit suicide by apoptose, and the formation of products that is a consequence of damage induced by reactive oxygen species. Cell lines representing relevant organs for toxicity will be explored. The response of individual cells to nanoparticles will be studied in human blood cells using inflammatory markers, e.g., induction of cytokines and other mediators, as indicators of effects. The effect of particle size, surface area and chemical composition will be investigated in these preliminary studies, and will form the baseline for future studies of the mechanism of the toxicity of nanotechnology products and individual susceptibility.

Furthermore, the studies in cell cultures should be complemented with established animal models using relevant routes of potential exposure to study systemic effects.

Nanononwovens

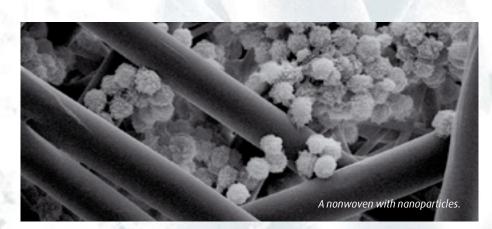
- Intelligent textiles of the future

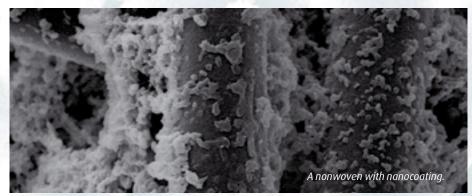
Nanostructured nonwovens are about to introduce intelligence into textile products: Carpets that clean themselves like the leaves of a Lotus plant in the rain, medical textiles that eliminate pathogenic bacteria, and new environmentally friendly and fire-retardant nonwovens. The Nanononwovens will be developed jointly by Fibertex A/S and the iNANO Center.

By Thomas Broch-Nielsen, Jens Bøndergaard and Flemming Besenbacher

The Danish High-Technology Foundation has donated 20 million DKK in support of the four-year project called 'Nanononwovens' to be carried out in joint collaboration between the only Danish nonwovens manufacturer, Fibertex A/S, and the iNANO Center. Fibertex A/S and iNANO also contribute with 20 million DKK to the project.

Fibertex A/S produces nonwovens, which are used for applications such as raw materials for diapers, furniture and bedding, car parts, and geotextiles for use in road and harbour construction. Through this innovative high-technology project the partners plan to utilise nanotechnology to give nonwovens unique properties that open entirely new avenues of application. An example is the use of nanoparticles to improve the mechanical and functional properties of fibres to produce environmentally friendly and fireretardant nonwovens. Other high-priority applications are antibacterial nonwovens for medical textiles and water repellent nonwovens for selfcleaning textiles.





Antibacterial nonwovens could be based on recent nanotechnological discoveries of the antibacterial properties of nanoscale particles, such as copper or silver. Ions released by these particles are toxic to certain microbes and non-toxic to humans. Increased hydrophobicity can be achieved by placing certain well-defined topographic features on the surface of nonwovens. This phenomenon of water repellence is inspired by surfaces of certain plants in nature. The effect is best illustrated by watching water rolling off the leaf surfaces of the Lotus plant: a phenomenon frequently referred to as the Lotus effect.

During the past year, Fibertex and iNANO have jointly examined the possibilities of employing nanotechnology in Fibertex's manufacturing processes. The efforts will now be intensified with the expected results contributing to entirely new development trends in the nonwovens technology. The project will strengthen Fibertex's global position in the nonwoven business, while the universities will benefit from the general know-how obtained from the project. A drop of water on a superhydrophobic non<u>woven.</u>

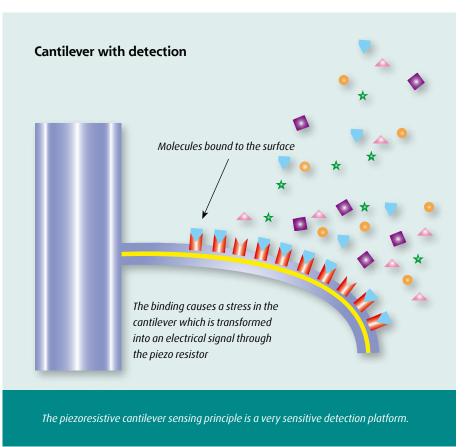


NanoNord: Cantilever sensors spot the offender

Minuscule cantilevers that bend when specific molecules bind to their nanoscale receptors are the "electronic noses" of the future. Such cantilevers are able to detect bacteria, viruses, chemical weapons, explosives, smells, and impurities in water.

By Dorthe Mindorf, Ole Jensen, Erik Lægsgaard, Flemming Besenbacher og Jørgen Kjems

The cantilever technology is extraordinarily simple and based on the principle that molecules capable of recognizing and binding to a target are chemically attached to the surface of a tiny flexible rod called a cantilever. The binding of these molecules induces surface stress that causes the cantilever to bend, which in turn changes the resistance of an in-built piezoresistor in the cantilever. In this way, the binding is quantitatively transduced into a measurable electrical signal. The unique readout system will enable miniaturization of the instrument and a high degree of parallelization. The technology is a multifunctional, highly sensitive, real-time method for a variety of sensor applications, including gas sensors, sensors for detecting entire microorganisms and viruses, sensors for protein studies in liquid environments, and olfactory sensors; hence these cantilevers can detect salmonella, bird flu, chemical weapons and plastic explosives, as well as aromatic substances in the air or impurities in water.



Because of its many applications, the cantilever technology is of great interest as a label-free biosensor system, a very efficient industrial tool, but also very useful for education purposes.

A new generation of cantilevers

Nanonord had recently taken over the CANTION cantilever technology, and in collaboration with iNANO the biosensor system is being upgraded, and a new generation of cantilever sensors is being developed. To put these sensors to work it is important to rely on robust recognition between the biomolecules and the analyte. To accomplish this strong emphasis is put on further development of surface chemistry and biomolecule design.

Another important focus is the development of a digitally based signal processing system that will enable internet access to the sensors from all over the globe.

The following improvements and new applications are currently being developed:

- New advanced analog/digital front end for optimum signal-to-noise measurements with separation of system stray capacitance from the cantilever.
- Implementation of dynamic measurement mode to measure real-time mass adhesion to the cantilever in addition to the surface stress measurements.
- The use of biomolecular interactions to detect contaminants in food and drinking water.
- Genotyping of human pathogenic viruses including HIV-1.
- High throughput screening of drugs that interferee with oncogenic products in cancer cells.
- Development of a specialised fuel detection sensor.

iNANO and industry

As Chairman of the Board of iNANO, I would like to express my satisfaction with the steps taken by the University of Aarhus and the iNANO staff during the last year to facilitate closer interaction between nanoscience research and its application in industry. In particular, the decision to build an iNANO house including a clean room in 2007-2008 will promote collaboration with industrial partners in the future.

The vision remains to demonstrate proof-of-concept of a given product or process, which subsequently may be transferred from the iNANO environment to an existing company or to a start-up company. The fulfilment of this vision will require hard and dedicated work by the iNANO staff in the time ahead. However, industry must also be prepared to play its constructive role, and the flow of information must be reciprocal to ensure that collaborative projects are based on a mutual agenda setting. Finally, but not least important, the funding bodies such as the High-Technology Foundation and the Danish Strategic Research Council must show willingness to more massive and longer-term commitments. Too much valuable research time is spent on writing numer-



ous applications for small programmes, which offer insufficient funding. The political goodwill to strengthen research within nanotechnology has been announced, and we look forward with high expectations.

Hans Jørgen Pedersen, Danfoss A/S, Chairman of the Board



Industrial Partners

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Boldt, Henning B., Characterization of individual domains in PAPP-A

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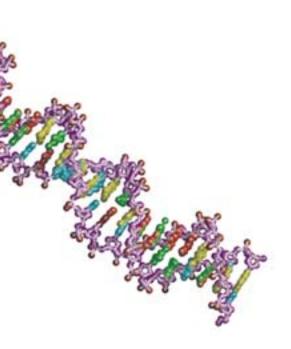
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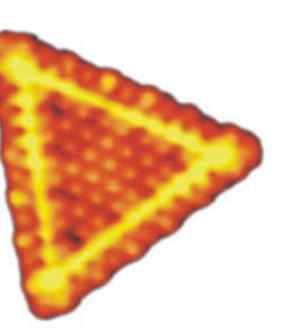
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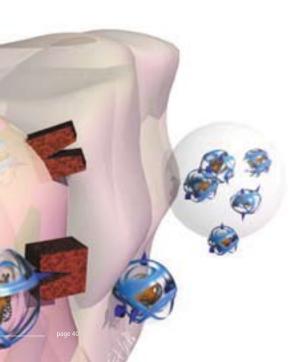
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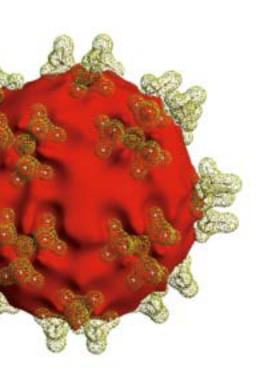
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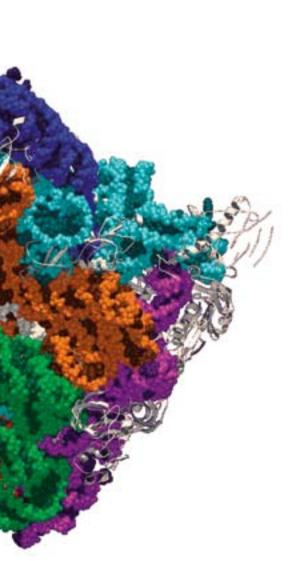
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Lars Diekhöner, Magnetic nanostructures and single atoms: What a couple!, Seminar, Max-Planck-Institut für Mikrostrukturphysik, Halle, Germany

Lars Diekhöner, Nanovidenskab og -teknologi, Foredrag for Rotary-klubben, Nørresundby, Denmark

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Jan Johannes Enghild, Thrombin activatable fibrinolysis inhibitor (TAFI), Sanofi-Aventis, Frankfurt, Germany Angela Fago, Hemoglobin as a (glutathionedependent?) nitrite reductase: a vasodilation study, International Minisymposium What's New in Oxygen Binding Heme Proteins and Red Blood Cell Physiology, Aarhus, Denmark

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Torben R. Jensen, renewable energy and hydrogen society, Dept. of chemistry, AU, Aarhus, Denmark

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Torben R. Jensen, renewable energy and hydrogen society, Denmark

Torben R. Jensen, Nano er vejen til hydrogen samfundet, forskningens døgn, AU, iNANO, Aarhus, Denmark

Torben R. Jensen, Hydrogen samfundet, Kystcentret Thyborøn, Denmark

Torben R. Jensen, renewable energy and hydrogen society, Dept. of chemistry, AU, Aarhus, Denmark

Torben R. Jensen, Hydrogen-samfundet - et nyt energisystem, Jydsk Selskab for Fysik og Kemi, Kemisk Institut, Aarhus Universitet, Aarhus, Denmark Torben R. Jensen, Hydrogen-samfundet, Dept. of Chemistry, University of Aarhus, Aarhus, Denmark

Jørgen Kjems, Bionanotechnology at iNANO, 15.03.2005, Odense, Denmark

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Jørgen Kjems, HIV, Ungdommens Naturvidenskabelige Forening (UNF), Århus, Denmark

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Jørgen Kjems, Identification of targets in viral treatment, IGMM-CNRS, Montpellier, France

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Jørgen Kjems, RNAi, ECB 12 on Biotechnology, DTU, Copenhagen, Denmark

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Martin Kristensen, Achievements of the GLAMOROUS project on poling, BGPP, Sydney, Australia

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Arne Nylandsted Larsen, Capacitance-transient spectroscopy on irradiation-induced defects in germanium, The 2nd ASPECT Workshop, Warsaw, Poland.

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Niels Chr. Nielsen, Solid-State NMR and Functional Characterization of Proteins in 'Insoluble'Biological Structures, Inauguration of the inSPIN research Centre, University of Aarhus, Aarhus, Denmark

Poul Nissen, A modulatory ATP binding site of SERCA1a, Seminar, CEA Saclay

Poul Nissen, Pumping calcium ions across the membrane: structure and function of the Ca2+-ATPase" Danish Chemical Society, general meeting 2005, Denmark

Poul Nissen, Strukturel biologi og molekylær medicin" Annual meeting for high-school teachers in biology (gymnasielærerdag), University of Aarhus, Aarhus, Denmark

Poul Nissen, Large complexes and membrane proteins, International Workshop in recent advanc-

es in phasing methods for high-throughput protein structure determination, Peking, China

Poul Nissen, Pump Fiction – transporting calcium ions across the membrane, Seminar, Yale University, USA

Poul Nissen, Understanding the Structure and Function of the Calcium Pump, European Congress on Biotechnology, Copenhagen, Denmark

Poul Nissen, Calcium transport and proton counter-transport by the Ca2+-ATPase, Workshop on transmembrane transport, Sigtuna, Sweden

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Poul Nissen, Structure and function of the yeast ribosome and elongation factors, Annual meeting of the Human Frontier Science Program Organization, Bethesda, Maryland, USA

Poul Nissen, Structure and Function of Biological Macromolecules, Symposium for Research Centers of the Danish Natural Science Research Council (FNU), Denmark

Poul Nissen, Combining structural and functional data of the Ca2+-ATPase into a model, Transmembrane proteins, fourth meeting (TRAMP IV), Gothenburg, Sweden

Finn Skou Pedersen, The role of Septin 9 as an oncogene/tumor-suppressor gene in lymphomagenesis by murine leukemia virus, International Septin Workshop. Fuglsøcentret, Knebel, Denmark

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Kjeld Pedersen, Quantum well states in thin metal films, photoemission and optical second harmonic generation, Ankara University, Turkey

Jan Skov Pedersen, Low-resolution structure determination of proteins in solution by smallangle x-ray scattering (SAXS), Technical University of Denmark, 2nd Scandinavian, Workshop on Scattering from Soft Matter, Lyngby, Denmark Jan Skov Pedersen, Low-resolution structure determination of proteins in solution by smallangle x-ray scattering (SAXS), Centre for Structural Biology, University of Aarhus, Aarhus, Denmark

Jan Skov Pedersen, First Annual Meeting of Marie-Curie Training of Research network 'Selforganization in Confined Geometries, Aarhus, Denmark

Jan Skov Pedersen, Introduction to Small-Angle Scattering, Firenze, XX Congress of the International Union of Crystallography, Firenze, Italy

Jan Skov Pedersen, Studying bio-macromolecules in solution with Small-Angle Scattering, Bente Vestergaard og Lise Arleth, Danmarks Farmaceutiske Universitet, BIOSAS Conference, Copenhagen workshop on BIO-macromolecules in solution studied with Small-Angle Scattering, Copenhagen, Denmark

Peter R. Ogilby, The Singlet Oxygen Microscope: From Phase-Separated Polymers to a Single Biological Cell, Gordon Research Conference on Photochemistry, Smithfield, Rhode Island, USA

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Peter R. Ogilby, The Creation and Detection of Reactive Oxygen Species in Microheterogeneous Environments, International Symposium on Redoxactive Metal Complexes, Erlangen, Germany

Peter R. Ogilby, Creating and Detecting Reactive Oxygen Species, Particularly Singlet Oxygen, at the Sub-Cellular Level, Plant Stress Network, International Workshop, Odense, Denmark Jeppe Olsen, Properties of Quantum Dots Studied by Quantum Mechanical Methods, International Karlsruhe Nanoscience Workshop, Computational Tools for Molecules, Clusters and Nanostructures, Karlsruhe, Germany

Jeppe Olsen, Higher Excitations using Firstorder Interaction Subspaces, The 2005 Sanibel Symposium, St. Thomas Island Georgia, USA

Jeppe Olsen, Internal Contraction for Triple and Higher Excitations, Quantum Chemistry Applied : From H3 to Biocatalysis, An International Conference to Celebrate the 60 th Birthday of P.E.M. Siegbahn, Stockholm, Sweden

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Daniel E. Otzen, Mechanisms of membrane protein folding in lipids and detergent. Institute of Microbial Technology, Chandigarh, India

Daniel E. Otzen, Thermodynamics of membrane protein folding, Institute Tecnico Superior, Lisbon, Portugal

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Daniel E. Otzen, Folding and unfolding of membrane proteins in mixed micelles, ECB12 Conference, Copenhagen, Denmark

Daniel E. Otzen, Physics meets biology: Protein aggregation and deposition diseases, EMBL, Heidelberg, Germany

Rui Pereira, Local modes of hydrogen defects in Si:Ge and Ge:Si, 23rd International Conference on Defects in Semiconductors (ICDS-23), Awajii Island, Japan

Niels Peter Revsbech, Marine biotechnology and biofilm research at University of Aarhus,

Nato symposium on environmental challenges in marine biotechnology, Ålesund, Norway

Niels Peter Revsbech, Measurement of microbial activity at a microscale, SAME9, Symposium on Aquatic Microbial Ecology, Helsinki, Finland

Niels Peter Revsbech, Nitrogen cycling in Stratified Microbial Communities, Full Cycle: Microbial cycling of elements, Delft, the Netherlands

Niels Peter Revsbech, Det store I det små, "Husdyrgødning – guldgrube eller gravsten". Symposium arranged by SDU and DJF, University of Southern Denmark, Odense, Denmark

Birgit Schiøtt, Why drug discovery in academia?, Workshop on IT solutions for integrated drug discovery, Aarhus, Denmark

Jørgen Skibsted, Characterization of the Nanostructure of the C-S-H Phase by Solid-State 27Al and 29Si MAS NMR Spectroscopy, 107th Annual Meeting of the American Ceramic Society, Baltimore, USA

Troels Skrydstrup, Recent Applications of Samarium Diiodide for C-C Bond Formation via Radical Intermediates, Xth ICSN Symposium, Gifsur-Yvette, France

Troels Skrydstrup, Recent Applications of Samarium Diiodide in Organic Synthesis, 14th European Symposium on Organic Chemistry, Helsinki, Finland

Troels Skrydstrup, Recent Applications of Sm and Pd for Carbon-Carbon Bond Formation, En-dags symposium i anledning af Prof. David Tanners 50 års fødselsdag, Danmarks Tekniske Universitet, Denmark

Troels Skrydstrup, Recent Applications of Samarium Diiodide for C-C Bond Formation via Radical Intermediates, Pacifichem, Honolulu, Hawaii, USA

Troels Skrydstrup, Recent Applications of Sm

and Pd for Carbon-Carbon Bond Formation, Ecole Polytechnique, Palaiseau, France

Kjeld Søballe, Fælles årsmøde DSMM, DFFMT og Danske Fysioterapeuter, "Nye kirurgiske principper", Århus, Denmark

Kjeld Søballe, Ganz periacetabular osteotomy in acetabular dysplasia, EHS Meeting, 7th EFORT Congress, Lisbon, Portugal

Kjeld Søballe, Perioperative measures for pain relief and early rehabilitation, 7th EFFORT Congress, Lisbon, Portugal

Kjeld Søballe, Classification of Femoral Defects and Revision with Structural Allograft, Advances in Total Hip Arthroplasty, Rigshospitalet, Denmark

Kjeld Søballe, Minimally Invasive Total Hip Two Incission Approach, Advances in Total Hip Arthroplasty, Rigshospitalet, Denmark

Kjeld Søballe, Vorteile der HA-Beschichtung bei der unzementierten Knieenderprothetik, 54th Annual Congress NOV 2005, Hamburg, Germany

Kjeld Søballe, Ganz periacetabular osteotomy in acetabular dysplasi, International Hip Society, Closed Meeting, Vienna, Austria

Kjeld Søballe, Hvad kan man gøre, når man har fået slidgigt, kirurgi, Gigtforeningen, Frederiksberg Rådhus, Denmark

Kjeld Søballe, HA Coating – useful or not, Hydroxy-Apatite Ceramic 20, London, England

Kjeld Søballe, Nye aspekter inden for hoftekirurgi (ledbevarende kirurgi samt minimal invasive teknik, Staff meeting, Århus Sygehus, Nørrebrogade, Denmark

Kjeld Søballe, Minimal invasiv hoftekirurgi, Lægedag Århus, Scandinavian Congress Center, DK

Kjeld Søballe, Ortopædien i fremtiden – tværfaglig forskning inden for ortopædkirurgi, Afd. E's Temadag, Skejby Sygehus, Denmark **Kjeld Søballe**, Accelreret patientforløb i hofteog knæsektoren – ny postoperativ smertebehandling, Afd. E's Temadag, Skejby Sygehus, Denmark

Thomas Vorup-Jensen, New ligands for aXb2 integrin, MRC Immunochemistry Unit, University of Oxford, England

Thomas Vorup-Jensen, The innate immune system, polymer surfaces, and cell adhesion, Bioneer A/S, Hørsholm, Denmark

Thomas Vorup-Jensen, Creative destruction (of protein structure): new ligands for the leukocyte cell surface receptor aXb2 (CD11c/CD18) integrin, LEO Pharma A/S, Ballerup, Denmark

Thomas Vorup-Jensen, MBL structure and function, NatImmune A/S, Copenhagen, Denmark

Thomas Vorup-Jensen, Creative destruction (of protein structure): new ligands for the leukocyte cell surface receptor aXb2 (CD11c/CD18) integrin, iNano Seminar series, University of Aarhus, Denmark

Thomas Vosegaard, Towards the study of large membrane proteins using oriented-sample solidstate NMR" and "Numerical calculations and tools for biological solid-state NMR, Recent trends in solid-state NMR in biological systems, Bangalore, India

Thomas Vosegaard, Average Hamiltonian Theory, Euromar / EENC, Veldhoven, The Netherlands

Thomas Vosegaard, One week course of solid-state NMR, 15th Jyväskylä Summerschool, Jyväskylä, Finland



Colloquia

iNANO Annual Meeting

January 19, Ulrich Gösele, Max-Planck-Institut of Microstructured Physics, Halle, Germany, "Nanosilicon á la carte"

January 19, Carsten Werner, Dept. of Biocompatible Materials, Leibniz Institute of Polymer Research, Dresden, Germany, "Self assembly for the design of biomimetic materials"

January 19, Allan S. Hoffman, Department of Bioengineering, University of Washington, USA, "Smart polymer switches in separations, diagnostics and drug delivery"

January 19, Omar M. Yaghi, Department of Chemistry, University of Michigan, USA, "Nanoporous metal-organic frameworks designed for hydrogen storage"

January 19, Christoph Gerber, National Center of competence in Research, University of Basel, Switzerland, "Nanomechanics as a toolbox for the small"

January 19, Mauro Ferrari, Department of Biomedical Engineering, The Ohio State University, USA, "Nanomedicine"

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January 14, Arto Urtti, Dept. of Pharmaceutics, University of Kuopio, Finland, "Glycosaminoglycans inhibit cellular gene delivery with liposomal and polymeric nanosized carriers: physico-chemical and biological aspects"

January 14, Birger Lindberg Møller, The royal veterinary and agricultural University, Denmark, "Metabolic engineering of cyanogenic glucoside synthesis and plant-insect interactions"

January 21, Modern Trends in Chemistry Aarhus Winter Meeting. Organized by the Danish Chemical Society.

January 28, Jørgen Skibsted, University of Aarhus, Denmark, "Solid-State NMR studies of nanostructures in cement-based materials"

February 2, Henrik Birkedal, Dept. of Chemistry & iNANO, University of Aarhus, Denmark, "On Bites and Bones: Examples of Natures Materials"

February 18, Andrew J. Turberfield, University of Oxford, UK, "DNA Self-Assembly and Molecular Machinery"

February 25, Mischa Bonn, Leiden University, Germany, "Biosurface Spectroscopy"

April 1, Daniel Otzen, University of Aalborg, Denmark, "The changing faces of glucagon fibrillation: structural and energetic polymorphism"

April 15, Peter Hinterdorfer, Johannes Kepler University of Linz, Austria, "Sensing single molecule recognition with the atomic force microscope"

April 19, Joel S. Miller, Department of Chemsitry, University of Utah, USA, "New Chemistry and New Materials for this Millennium: Molecule-based Magnets and Molecule-based Electronics"

April 29, Jan J. Enghild, University of Aarhus, Denmark, "Proteome analysis of the human cornea"

May 13, Xiao-Dong Su, Life Science College, Peking University, China, "A high-throughput, cost-effective structural genomics platform"

May 20, Mette Ebbesen, University of Aarhus, Denmark, "Ethics in Nanotechnology – starting form scratch?"

May 27, Wolfgang Pompe, Technische Universitaet, Dresden, Germany, "Molecular bioengineering of metallic nanostructures"

September 9, Michael Lisby, University of Copenhagen, Denmark, "Nanobiotechnologies for studying DNA damage response in live cells"

September 16, Teresa Neves-Pedersen, Aalborg University, Denmark, "Photonic Biosensors: using light to create oriented as well as spatially defined multi-protein/DNA sensor arrays"

September 23, Peter R. Ogilby, University of

Aarhus , Denmark, "Creation and Detection of Singlet Oxygen with Sub-Cellular Resolution"

September 30, Bruce Milthorpe, USNW, Australia

October 14, Kurt Gothelf, University of Aarhus, Denmark, "Molecular self-assembly"

October 21, Fraser Stoddart, University of California Los Angeles, USA, "An Integrated Systems-Oriented Approach to Molecular Electronics"

October 28, Yves Dufrenes, Université catholique de Louvain, Belgium, "AFM force spectroscopy of biosurfaces: from single molecules to living cells"

November 4, David Phillips, Hofmann Professor of Chemistry, Senior Dean, Imperial College of London, UK, "Time-resolved fluorescence imaging studies in biological systems"

November 11, Miquel Salmeron, Berkley, USA, "Nanoscience and technology: Building new materials atom by atom"

November 18, Thomas Vorup-Jensen, Department of Medical Microbiology, AU

November 25, Jens Nørskov, DTU, "The Hydrogen Society"

December 2, Ole Hindsgaul, Carlsberg Laboratory, Denmark, "Introduction of labels into biomolecules using solid-phase reagents"

December 9, Leonid Gurevich, Section for Biotechnology, AAU, Denmark

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January 12, Thomas Schmidt, Physics Department, Leiden University, Germany, "Single-molecule microscopy for cell biology"

January 19, Omar M. Yaghi, University of Michigan, USA, "Nanoporous metal-organic frameworks designed for hydrogen storage"

January 26, Dr. Dylan Jaytilaka, Department of Chemistry, University of Western Australia,

Colloquia



Australia, "Wavefunctions derived from X-ray experiment: General philosophy, and review ofpast work, and future directions"

February 3, Poul Nissen, Dept. of Molecular Biology, University of Aarhus, Denmark, "The functional cycle of a cation pump"

February 7, Dr. Pawel Sikorski, Physics Department, Norwegian University of Science and Technology, Trondheim, Norway, "Amyloids and biopolymers. Solving crystal structures of semicrystalline polymersby use of fibre X-ray diffraction"

February 17, Kiyoshi Asakawa, University of Tsukuba and the Femtosecond Technology Research Association, Japan, "Fusion of quantum dots and photonic crystals – the application to ultra-fast alloptical switch"

March 1, Christian Bombis, Institut für Schichten und Grenzflächen ISG 3 Forschungszentrum Jülich GmbH, Germany, "STM studies of 2D-nanostructures: Monoatomic, high Au islands on Au(100) and the self-assembling system oxygen on Cu(110)"

March 2, Arnd Baurichter, Physics Dept. SDU, Odense, Denmark, "From dust grain catalyst for hydrogen and organic molecule formation in the interstellar space to hydrogen storage material: The system hydrogen on graphite"

March 9, Kiril Tsemekhman, Dept. of Chemistry, University of Washington, USA, "Self-consistent implementation of self-interaction corrected DFT and of the exact exchange functionals in the planewave DFT"

March 11, Kell Mortensen, Danish Polymer Centre, Risø, Denmark, "Block Copolymer Melts and Networks, Shear-Induced Texture and Shear-Induced Phase Transitions"

March 18, Nikolay Buzhynskyy,Lab. of Molecular Imaging and Nano-Bio-Technology University of Bordeaux, France, "Formation of supported proteolipidic layers, studied by QCM-D and AFM"

March 30, Roland Krämer, Universität Heidelberg, Germany, "Oligonucleotide - Metal Complex

Conjugates: Synthesis and Applications"

April 5, Alexander Shluger, University College London, UK, "When solids approach the defect size: modelling at the edges"

April 11, Kristian Thygesen, Dept. of Physics, Technical University of Denmark Wannier Functions

April 12, Heiz Ulrich, Technische Universität München, Germany, "Clusters on surfaces: Matter in the non-scalable size-regime"

April 21, Jean Pinson, Alcminer, France, "Electrografting of conductive and semiconductive surfaces by reduction of diazonium salts"

May 2, Alan C. Luntz, University of Southern Denmark, Denmark, "How adiabatic is activated adsorption?"

May 4, Wael Mandouh, Dept. of Chemistry, Lab. Photochemistry and Spectroscopy, Katholieke Universiteit Leuven, Belgium, "Two-dimensional Cyclic Structures As Templates At The Nanoscale"

August 24, Toyyaki Eguchi and Toshu Ann, The University of Tokyo, Japan, "High resolution Imaging of Surface Structure and Potential Profile by Atomic Force Microscopy"

September 20, Paul Ellis, Pacific Northwest National Laboratory, "67Zn and 25Mg Solid-State NMR Spectroscopy of Systems of Biological Interest. A Low Temperature Solid State NMR Experiment"

September 22, Jean-Paul Booth, Nicolas Bulcourt, Garrett Curley, Ecole Polytechnique, Palaiseau, France, "Production and destruction of reactive species in a dual frequency capacitive plasma in Ar/ C4F8 /02"

September 26, Markus Niederberger, Max Planck Institute, Germany, "Nonaqueous Routes to Crystalline Metal Oxide Nanoparticles: Formation Mechanisms, Assembly and Application in Gas Sensing"

October 17, Dietmar Stalke, Institut für Anorganische Chemie, Universität Göttingen, Germany, "Hypervalency - Experimental Charge Density Uncovers a False Concept"

October 18, Professor Alan Pinkerton, University of Toledo, USA, "X-ray crystallography - from structure to thermodynamics"

October 13, Professor Bonnie A. Wallace, Department of Crystallography, Birkbeck College, University of London, UK, "Synchrotron radiation circular dischroism spectroscopy: a new tool for structural and functional genomics"

November 3, Professor Thomas H. Foster, University of Rochester, USA, "Physical Determinants and Optical Signatures of Photodynamic Therapy"

November 15, Peter Kingshott, Senior Scientist, Danish Polymer Centre, Risø National Laboratory, "Playing with Surface Chemistry to Try and Stop Proteins, Cells and Bacteria from sticking"

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September 9, V. Renugopalakrishnan, Harvard, USA, "Protein-based memory: Next wave in information storage"

September 28, Sergey Bozhevolnyi, Harvard, USA, "Nano-plasmonics"

October 12, Ib Chorkendorff, DTU, Denmark, "Production and conversion of hydrogen on alloys and inorganic compounds"

October 26, Thomas Garm Pedersen, Aalborg University, Denmark, "Optical properties of carbon nanotubes"

November 11, Peter Wahl, MPI-Stuttgart, Germany, "Electronic correlation effects at metal surfaces"

November 23, Anja Boisen, DTU, Denmark, "Micro and nanomechanical systems for labelfree detection"

December 7, Thomas Tauris, Herlufsholm, Denmark, "Physics of radio pulsars"

Staff

Senior staff

d'Amore, Francesco, AU Andreasen, Peter, AU Balling, Peter, AU Besenbacher, Flemming, AU Birkedal, Henrik, AU Bozhevolnyi, Sergey, AAU Bünger, Cody E., AU Bøttiger, Jørgen, AU Christensen, Niels Egede, AU Daasbjerg, Kim, AU Duch, Mogens, AU Enghild, Jan Johannes, AU Fago, Angela Foss, Morten, AU Gothelf, Kurt Vesterager, AU Hammer, Bjørk, AU Hofmann, Philip, AU Iversen, Bo Brummerstedt, AU Jakobsen, Hans Jørgen, AU Jensen, Jan Egebjerg, AU Jensen, Torben Heick, AU Jensen, Torben René, AU Keiding, Søren, AU Kjems, Jørgen, AU Kristensen, Martin, AU Larsen, Arne Nylandsted, AU Lauritsen, Jeppe Vang

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