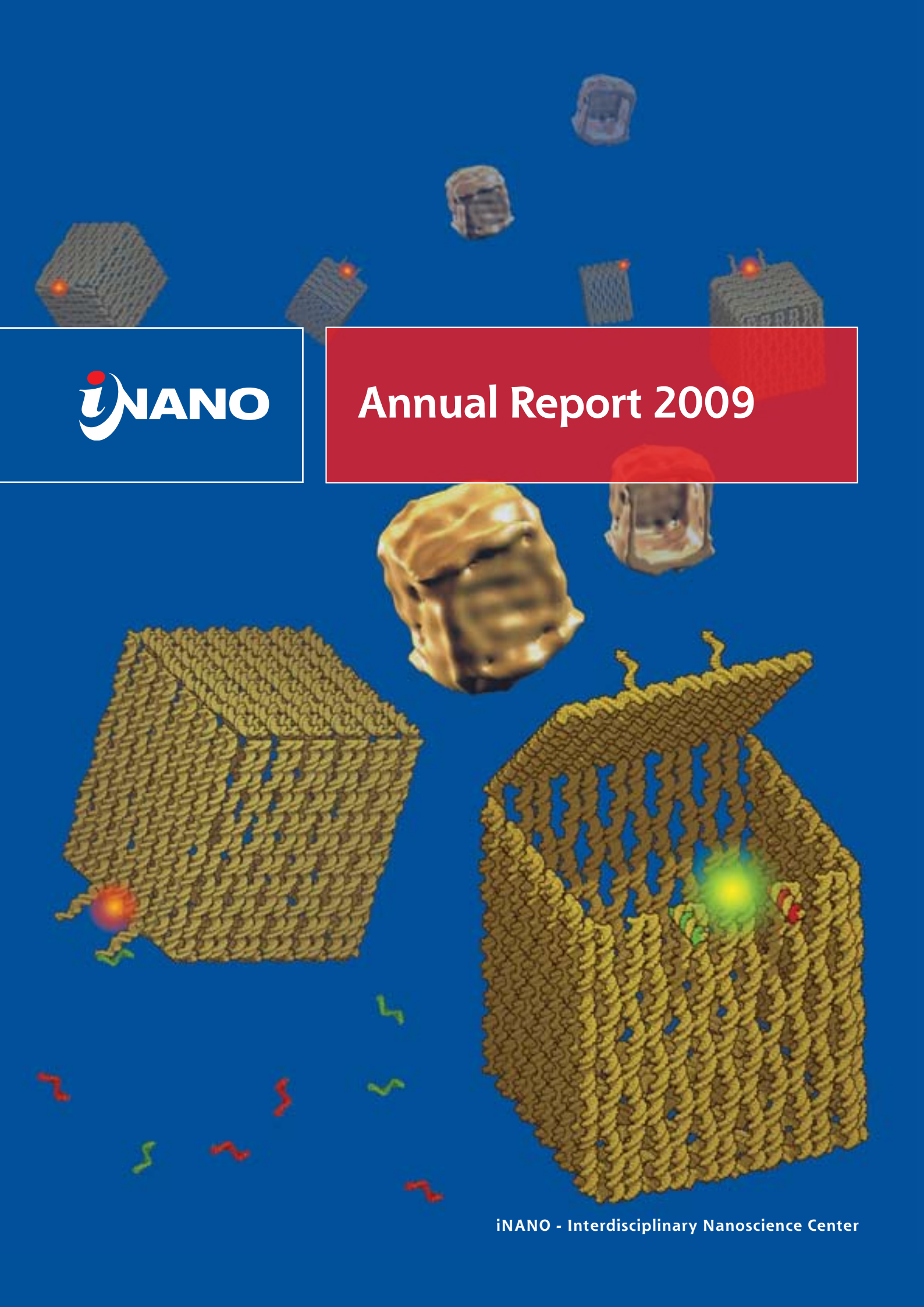
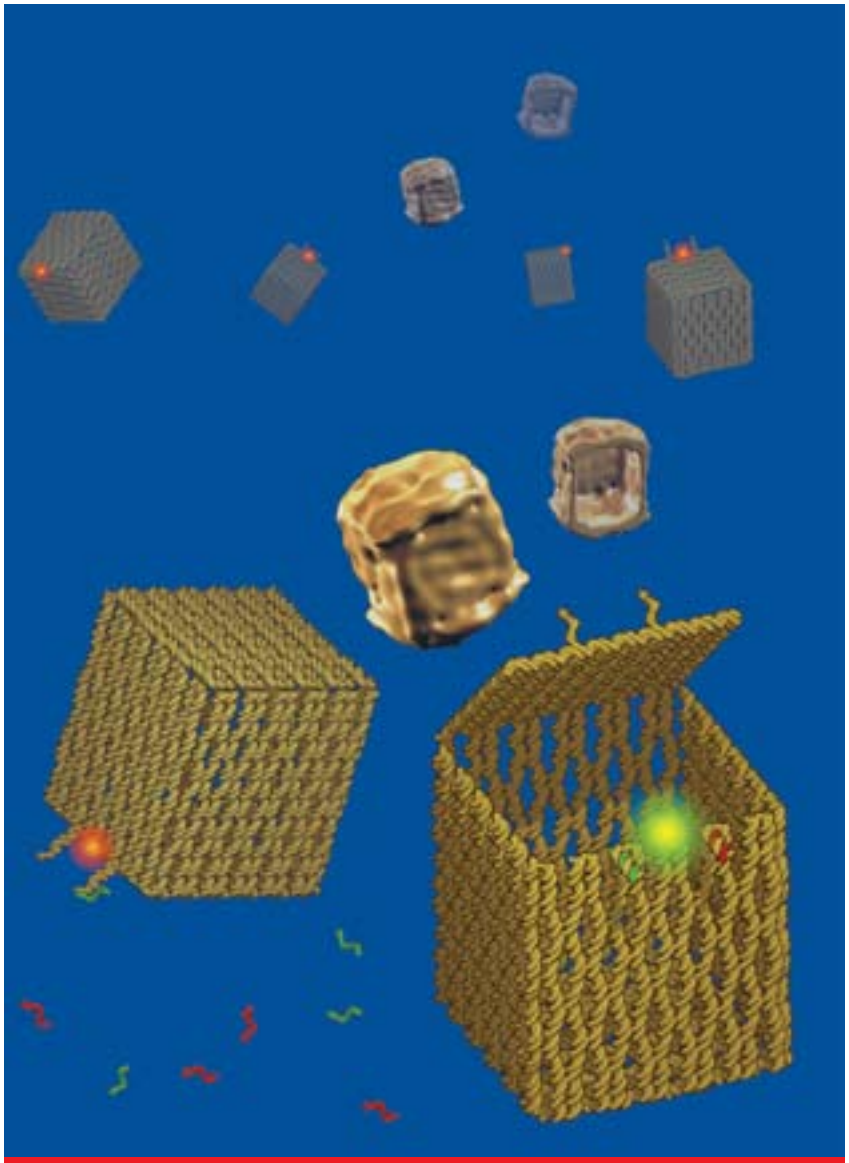


# Annual Report 2009

iNANO - Interdisciplinary Nanoscience Center



*The cover illustration shows the DNA box with dimensions of 42 x 36 x 36 nm³ that was designed and self-assembled by the DNA origami technique. Theoretical models of the DNA box is shown in the open and closed state. Models based on cryo electron microscopy data are shown in the full model and cut in half to reveal the inner cavity. The DNA box is designed with DNA helix "locks" that can be opened by externally added DNA "keys" (green and red strands). The resulting opening of the lid of the box is detected by a change in fluorescence of a donor/acceptor FRET pair (green and red light).*

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# Contents

# Message from the Director

*Jørgen Kjems, vice director,*
*and Flemming Besenbacher, director*

**It is a great pleasure for me to highlight some of the major advances and achievements by iNANO scientists during 2009. There are quite a number of highlights to choose from, which clearly demonstrates that the iNANO organization is thriving and ever-expanding into new, interesting interdisciplinary research areas.**

*By Flemming Besenbacher*

**Flemming Besenbacher**
director

## Research management and hierarchies

The ongoing mission of iNANO rests on three equally important pillars that go hand in hand: Education, Research, and Innovation. We put great emphasis on constantly strengthening all three pillars and simultaneously keeping all three pillars interdisciplinary (the small i in iNANO), as we find that many breakthrough discoveries in science today are made at the borders between the traditional scientific disciplines – and this will be even truer in the years to come. However, one should bear in mind that interdisciplinary collaboration has its own challenges on both the organizational and the scientific level, e.g. when scientists do not speak a common language. Nevertheless, I find that the iNANO organization and its research are blossoming.

Any minor or major roadblocks are in our experience best prevented by efficient research management, an almost heretical concept a few years back due to a strong mistrust in what was perceived as the manager meddling with the individual scientist's autonomy. But research management has come of age and in our interpretation it merely acts as a facilitator and catalyst for establishing interdisciplinary collaborations, and I think all but the sourpuss have come to realize that everyone stands to gain.

A second aspect of successful interdisciplinary collaboration is to avoid a too-rigid hierarchy. In the iNANO organization we go to great lengths to maintain a flat organizational structure where information and opinion flow unimpeded. I have learnt from several foreign colleagues that they face great difficulties when trying to promote interdisciplinary research and education within their own organizations, often owing to rigid hierarchies. The strategy at iNANO has been to build the organization via a bottom-up approach, where the strongest groups are handpicked to join a strong interdisciplinary research effort that eventually cannot be ignored.

## Education

Over the last few years, enrolment to our annual undergraduate programme has stabilized at around 35 new nanoscience bachelor students. The nanoscience curriculum serves an important role as a counterweight to the standard mono-disciplinary education offered at Aarhus University and the tendency for students to specialize in a very narrow topic quite early in their career. It is a great satisfaction to witness the students' skill and enthusiasm, which reaffirm my impression that our nanoscience curriculum attracts bright and dedicated young students.

Indeed, it has almost become a tradition that a group of handpicked iNANO students presents a very strong case at the annual "Grundfos Challenge" and also in 2009 our students brought home the top Engineering Prize. To underline my case, I need only mention that our first-year tutors won the Aarhus University-wide Tutor Prize 2009. Congratulations on jobs well done! In the graduate arena, iNANOschool now has an impressive total of 153 enrolled PhD students. Excitingly, our first batch of bone fide nano PhDs from the class of 2002 has started its last year of studies. We are doing our utmost to assist them in making appropriate career choices based on their interests and abilities.

## Research

Without doubt the most prominent publication from iNANO scientists in 2009 was on the "DNA box" (see article elsewhere in this Annual Report) published in Nature, which is probably the most complicated object yet constructed by means of DNA nanotechnology. In this context, I want to emphasize that this kind of work would simply not have been possible in a mono-disciplinary department, and I see the collaboration that led to this and other outstanding publications as a prime example of what we can hope to achieve by working together in interdisciplinary teams.

The year 2009 also saw the influx of a number of prominent grants to create centres managed under the iNANO umbrella. For example, professor Bo Brummerstedt Iversen was awarded the Danish National Research Foundation's Center for Materials Crystallography (CMC), which conducts research into advanced applications of synchrotron radiation. The tasks here tie in well with professor Iversen's work on energy materials and nanoparticle synthesis.

At the end of 2009, a strong group of medical doctors and iNANO nanoscientists was able to attract a large grant to establish the "Lundbeck Foundation Nanomedicine Centre for

Individualized Management of Tissue Damage and Regeneration" (LUNA, detailed elsewhere in this report). iNANO has long promoted large-scale cross-faculty collaboration and I am happy to see that our efforts to establish a visionary nanomedicine programme have borne fruit in this exciting way.

These and the many other grants awarded in 2009 fall to a large extent into one of the iNANO focus areas: Energy, Nanomedicine, Nanomaterials, Nanofoods, and Self-assembled nanostructures. These areas have been chosen because they represent strong basic research competences at iNANO and Aarhus University and at the same time have the interest of Danish industry.

Indeed, I see no contradiction or exclusion in conducting world-class fundamental and independent research in unison with more applied/strategic research. To be frank, to make a distinction between the two seems rather artificial because any research has both basic and applied aspects and pretending to do just one or the other is to exclude oneself from learning new things and creating fresh ideas.

To this end, I want to stress that scientists should bear in mind that they work not for themselves but together towards a common goal, which is why we should all ask ourselves what good our research can do for society; I refer to this as Scientific Social Responsibility.

## Innovation and collaboration with industry

Examples of such admirable behaviour can for example be found in a new Danish National Advanced Technology Foundation project awarded to iNANO scientists: "Strontium-functionalized titanium implants for accelerated bone ingrowth" with participation from Jørgen Bøttiger and Morten Foss.

On an even more advanced stage on the road to commercialization, iNANO research has in 2009 crystallized into two new start-up companies: i) CABRA (Computer Aided Biological Response Assessment), with participation from iNANO scientist Jens Vinge Nygaard, which constructs patient-specific computer models that can predict the risk of catastrophic plaque ruptures leading to strokes and heart attacks, and ii) Nanoference (Kenneth Alan Howard and Jørgen Kjems), which secured capital from the venture company Novo Seeds and works with nanoparticle-based delivery of small interfering RNA for the treatment of infectious pulmonary diseases such as influenza, and inflammatory disease such as rheumatoid arthritis.

## Infrastructure

2009 saw the completion of the clean room whose construction was initiated by iNANO but from 2010 is managed by the Department of Physics and Astronomy, where a fantastic technical infrastructure already exists. The first clean room activities started already in 2009 and, towards the end of the year, we were successful in securing funding for a number of expensive pieces of equipment by a generous grant from our Dean, Erik Meineche Schmidt. The clean room should become fully functional in the summer of 2010 with a suite of equipment, the choice of which clearly reflects our focus on enhancing our synthesis capabilities. iNANO is already strong in multiple characterization techniques, but the power to create real structures will strengthen our overall goal of conducting research for the benefit of society.

After long deliberations, the iNANO-house project, which is to be constructed in conjunction with the existing clean room, is finally back on track. Construction is scheduled to begin in August 2010 and should be finished in August 2012.

# An interdisciplinary curriculum for Nanoscience

*By Trolle Linderoth*

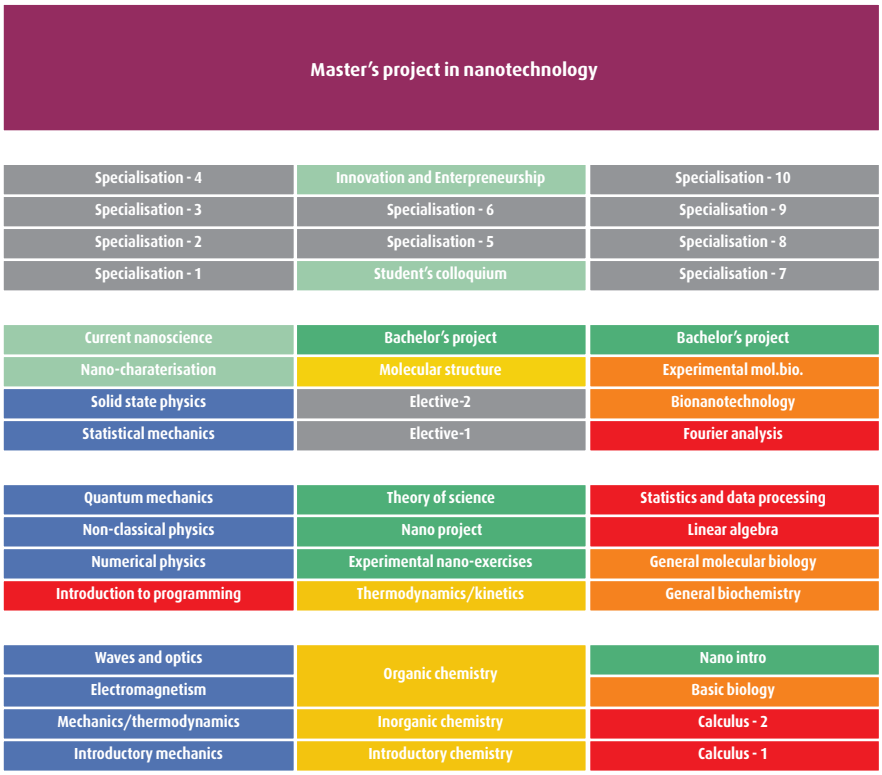
Interdisciplinarity lies at the core of nanoscience and nanotechnology. Many of the most groundbreaking, current developments take place at the boundaries between the traditional disciplines of physics, chemistry, molecular biology and biology. This observation, along with the fact that the years of undergraduate education to a large extent define our mental framework and approach to science, call for an early introduction to all the core disciplines of nanoscience. At iNANO we offer dedicated Bachelor's and Master's programmes in Nanoscience where the goal of disciplinary breadth has been realized without sacrificing scientific depth. This has been accomplished by developing a fixed course programme involving carefully selected elements from the core disciplines combined with dedicated nanoscience courses and elective specialisation modules during the last years of study. Since its introduction in 2002 the annual uptake on this new study programme has counted 40-60 highly motivated and dedicated young students.

## Bachelor's programme

During the first three years the students receive basic, interdisciplinary training in physics, chemistry, biology, molecular biology, mathematics and computer science. Many of the courses are followed along with students from these core disciplines. In addition, a number of courses address issues specific to the nano-area. In the course "Introduction to Nanotechnology" the first year students are introduced to key nano-concepts such as scanning probe techniques and bottom-up/top-down synthesis of nanostructures. The course ends with a two-week project which enables students to make close contacts with research groups at iNANO already at their first year. In the subsequent courses more advanced, experimental exercises and a bigger project, currently involving fabrication and characterisation of a dye-functionalised solar cell, are carried out. In the final year of the Bachelor's degree programme students can follow the courses "Nano-characterisation" and "Current Nanoscience" which introduce a number of experimental nanoscience characterisation techniques as well as important subject areas for current nanoscience research. A course on the theory of science dedicated to the nano-area places the subject in a societal context and emphasises ethical aspects. Elective course modules at the third year of study allow fine-tuning of the course programme to the particular interest of individual students. The Bachelor's degree programme is terminated by an individual Bachelor's project typically carried out in a research laboratory and supervised by iNANO researchers.

## Master's programme

During their Master's study students are required to specialize in either of three different fields: nano-physics, nano-chemistry or nano-molecular biology. In doing so they choose from the extensive course catalogue at the Faculty of Science and follow course programmes developed through individual counselling. In the compulsory 'Student's Colloquium' the students gain experience in presenting a subject of their own choice to fellow students, and in the 'Enterpreneurship and Innovation' course they are introduced to concepts of commercialisation. The specialisation courses followed on the fourth year of study enable the students to commence their one-year master's project or alternatively to seek admittance to the iNANOschool PhD programme.




*Course programme for the interdisciplinary Bachelor's and Master's degree in nanoscience offered at iNANO. Each academic year (starting from the bottom) is divided into four 7-week quarters and typically three courses are followed in each quarter. Legend: Blue: Physics courses, yellow: Chemistry courses, orange: Molecular biology courses, red: Mathematics/computer science courses, green: Nanoscience courses, grey: Specialisation modules.*

# Giving new nanoscience students a good start

*Kristian Sneskov, Jonas Lerche Hansen, Martin V. Kristensen, Thomas Tørring, Karin Doolewerdt, Thomas Kollin Nielsen, Anders B. Olesen, Rasmus Havelund, Maj Frederiksen (Morten Karstoft Rasmussen absent)*

*The team of instructors offering class-based teaching in the first year of the bachelor's degree programme in nanoscience during the academic year 2009/2010. Nearly all have followed the programme themselves and are now graduate students at iNANOschool. Kristian Sneskov (at extreme left) comments: "A major motivational factor for me as instructor is when I succeed in putting the various exercises into a broader scientific context so that a math problem goes beyond "crunching numbers" and the students realize how it is relevant for my own research in computational nanochemistry."*

*By Morten Karstoft Rasmussen and Trolle Linderoth*

Every year in September, a new group of students commences the bachelor's degree programme in nanoscience offered at iNANO. During their first year of study they encounter a highly qualified team of teaching assistants, or instructors, most of whom are PhD students with a master's degree in nanoscience. Providing such a team is a major benefit of an established education institute and ensures that the instructors can act as inspirational role models who know how the course they teach fits into the curriculum of the nanoscience programme and are also able to place relevant aspects of the elementary teaching into a nanoscience context.

Most courses followed during the first year of study are offered as a combination of lectures, given by senior academic staff, and problem-solving classes and laboratory exercises, which are undertaken by the instructors. In addition to 10 weekly hours of lectures, this facilitates approximately 15 hours of class-based, direct student-instructor interaction with dialogue, help and feedback, ensuring a high academic gain. The nanoscience students are divided into fixed classes of 20-25 persons who follow all their class-based activities together. This ensures cohesion and a sense of belonging, and numerous activities, academic as well as social, take place within these groups. Each class is assigned its own classroom, which also functions as a home base for individual study and group work between lectures or after hours.

A very important focus of the instructors' work is to help the new students get off to a good start at the university. This includes keeping an eye on the students so a friendly SMS can be sent to those who need encouragement. After the first two months of studies the instructors consult each other on the performance of the students and offer brief one-on-one conversations where the students also have the opportunity to raise their possible concerns. At the Friday afternoon café, held in the classrooms, the students have an opportunity to discuss the past week's lectures or the coming week's problems informally with their instructors. As a new initiative, the instructors this year took turns to present and discuss core subjects selected in dialogue with the students. Additionally, former iNANO students now employed in private companies have given inspirational talks on the opportunities offered by an interdisciplinary nanoscience education.

*The five award-winning tutors: Signe Grønborg, Niels Bøje, Mie Birkbak, Rudi Stallbohm, Christina Krogsgård Nielsen*

*When new students arrive, they are greeted by a team of tutors who introduce them to university life during a freshman week. In 2009, four nanoscience tutors received a prize from the Danish Association of Masters and PhDs. In their motivation for the award, the nanoscience students wrote: "Owing to the tutors, our class quickly became a cohesive group. The tutors made it possible for us to create networks across both the different classes and the year groups... They also did a great job teaching us about daily life at the university, informing us about study techniques and otherwise simply passing on their personal experiences."*

# International-level graduate studies at iNANOschool

**Since it was set up in 2002, iNANOschool has developed into a nanoscience graduate school of international stature. There are currently 153 PhD students. A broad range of specialized graduate courses has been established, and iNANOschool students have access to highly advanced research facilities. iNANOschool provides interdisciplinary competences in nanoscience and nanotechnology at the highest international level.**

*By Tina Fredsted*

iNANOschool (www.iNANOschool.dk) was established in 2002 with the objective of giving highly qualified, internationally competitive PhDs training in interdisciplinary competences in nanoscience and nanotechnology. iNANOschool offers a broad range of PhD courses in nanoscience and nanotechnology and provides facilities for and supervision of an increasing number of PhD students. Besides the focused PhD courses, activities include a major annual meeting, an autumn school, student networks, and initiatives to promote exchanges with other international institutions. The research areas at iNANO and iNANOschool are highly integrated as well as truly interdisciplinary and at present cover such diverse research fields as functional nanomaterials, nanoscale energy materials, nanomedicine, self-assembled molecular nanostructures, nanofood,

nanophotonics and nanoelectronics, and nanotoxicology. Overall, the research activities are at the international forefront of science and serve as an ideal framework for education and industrial collaboration. During 2009, 38 new PhD students were enrolled in iNANOschool and 17 PhD students completed their studies.

## Courses at iNANOschool

An important task for iNANOschool has been to establish a fairly large number of new PhD courses in nanoscience and nanotechnology. These courses serve to educate the students in high-priority research fields together with innovation, commercialisation and ethical aspects of nanotechnology. Most courses are offered on an annual or biannual basis and are primarily structured as intense one- or two-week courses. In this way, the interference between courses and research projects or stays abroad is kept to a minimum. It is worth noting that other national and international institutions also benefit from the iNANOschool courses by sending their students to iNANO for short visits. In return, iNANOschool's PhD students get excellent networking opportunities with students from other institutions.

During 2009 iNANOschool offered the following courses: Bionanotools and Protein Structure, Drug Delivery, Innovation and Entrepreneurship, Reactivity of Nanoparticles, and Toxicology, as well as the annual Autumn School.

Two of the courses were held at Aarhus University: Bionanotools and Protein Structure and Drug Delivery. Bionanotools and Protein Structure was held 10-14 August; the aim was to introduce the students to a number of analytical measurements and analytical tools used for structure-function analysis of biological macromolecules or biological nanomachines such as functional proteins, membrane pumps and channels. The aim of the Drug Delivery course was to provide insight into the theory and technical requirements for delivery of nucleic acid-based gene-silencing therapeutics in established cell lines, primary cells and animals. Innovation and Entrepreneurship was held on eight days in April and May and the purpose of the course was to impart a broad knowledge of the basic concepts of innovation and entrepreneurship. The Toxicology course was held at the Fuglsoecentret on 22-24 June with contributions from experts with high recognition internationally and covering a broad range of sub-disciplines within the field of toxicology. The last course, Reactivity of Nanoparticles, was held at Sandbjerg Estate on 22-27 August. The focus was on more efficient and sustainable energy production and covered a long list of topics dealing with nanoparticles and catalysis. The program consisted of tutorial lectures delivered by specially invited leading international experts, student exercises and poster presentations by the attending students.

## iNANO Autumn School 2009

A very important event at iNANOschool is the annual Autumn School, where all PhD students enrolled at iNANOschool are brought to a conference centre, Freshwater Centre, close to Silkeborg, from Friday morning to Monday afternoon. Every year a given topic or focus area is chosen for the Autumn School and this year the focus was on areas like networking, project handling, stress handling, coaching, innovation, management, presentation techniques/communication - topics that are considered to be highly relevant for PhD students, both in their research studies and in their later careers. Ten excellent speakers were invited from different areas of our society to present these topics, and from the feedback from the participating PhD students it appears that this year's topics were well chosen and highly useful for the PhD students. In addition to their work with the overall topic, the students presented their research projects either orally or in a poster session. The intention is to catalyze discussions and stimulate collaboration among the students on research activities. The PhD students receive feedback on their oral presentations and there is a competition for both best oral presentation and best poster.

## Workshops/seminars

In order to stimulate interdisciplinary research activities and give all students direct access to the most recent international nanoscience research, a series of weekly Friday iNANO lectures has been held with remarkable success. At these lectures, highly esteemed international scientists give tutorials on different aspects of nanoscience, and scientists associated with iNANO present their most recent results. The lectures are very popular, and typically about 80-100 graduate students and researchers broaden their horizons on current issues in nanoscience through these iNANO lectures. In addition, there is a series of iNANO specialized lectures, where more specialized topics are presented. Finally, all PhD students at iNANOschool also participate actively in the iNANO Annual Meeting, where outstanding, international scientists present talks on hot topics in nanoscience and nanotechnology. A poster session for PhD students and postdocs allows them to present and discuss their own projects and to gain knowledge about other current projects at iNANO.

# Industrial PhDs – two case studies

**An industrial PhD project is a special, company focused PhD project. The project is conducted in cooperation between a private company, an industrial PhD student and a university.**

*Karina Matthiesen*

*By Christina Trojel-Hansen and Karina Matthiesen, MSc in nanoscience*

An industrial PhD project is a three-year research project and research training programme with an industrial focus conducted jointly by a private company, an industrial PhD student and a university. The student is employed by the company and enrolled at the university.
The industrial PhD programme as such strengthens research and development in Danish business communities by providing scientists with an insight into the commercial aspects of research and development and by developing personal networks in which knowledge can be disseminated between companies and universities.

As a starting point, the student must divide his or her time equally between the company and the university. Hence, the student is supervised by at least two supervisors: a main supervisor from the university and a second supervisor from the company. In addition, one or more third-party supervisors may also be attached to the project. Hence, the industrial PhD differs from the ordinary PhD as follows:

- The industrial PhD is employed by the company.
- The industrial PhD training is a full-time education, where the PhD candidate shares his or her time between the university and the company.
- Industrial projects have a commercial perspective. However, the company must be aware that the industrial PhD programme is a research-training programme, and the candidate must carry out research. The university ensures that the research level is acceptable.
- The Danish Agency for Science, Technology and Innovation provides a wage subsidy to the company to hire the candidate and also pays the university to act as a mentor for the industrial PhD student.

More information can be found on the website www.industrialphd.dk

At iNANO we have a number of industrial PhD students and here we present two case studies of research projects carried out in cooperation between iNANO and TopoTarget A/S and H. Lundbeck A/S, respectively.

My name is Christina Trojel-Hansen and I am MSc in nanoscience from Aarhus University. I began my studies in 2003 and I am now an industrial PhD student working at the cancer-focused biotech company TopoTarget A/S, where I have been employed for two years.

My PhD project at TopoTarget A/S aims at determining the molecular mechanism of action of a new promising class of anti-cancer drugs, which means identifying a molecular target for the drugs, and describing the way they mediate cancer cell death. As such, this project allows me to try and use many different approaches and methods that give me a broad experience of and great insight into drug discovery and drug development. With knowledge about the mechanism of action, the process from pre-clinical/experimental in vitro and in vivo studies to clinical trials is simplified and shortened, as this knowledge enables us to predict potential adverse effects as well as identify patient groups who will effec-

*Christina Trojel-Hansen*

tively respond to and benefit from treatment with the anti-cancer drugs.

On a more scientific level, a description of a mechanism of action of potent anti-cancer drugs could help the author identify novel targets and provide new approaches to treat cancers. I chose to go in the industrial PhD direction since this would give an ideal opportunity to move to the borderline between business and research, to have the opportunity to contribute to the development of commercial products and to gain insight into the factors that are important for a research-based company. Therefore I also chose to do my PhD in a smaller company since the distance from the PhD students to the management is significantly smaller than in a large company. This smaller distance between the different layers in the company has certainly given me great insight into how to operate a research-based company, also in periods of financial crisis.

With an industrial PhD you feel well equipped to take the next career step – both into industry and university. There are plenty of job possibilities – it is just a matter of figuring out what your vocation is!

My name is Karina Matthiessen and I have chosen to carry out an industrial PhD at H. Lundbeck A/S, a Danish pharmaceutical company. Lundbeck specializes in the treatment of psychiatric and neurological disorders, and my project is aimed at understanding some of the processes associated with schizophrenia and Parkinson's Disease. In both these diseases, signalling cascades involving the intracellular messenger cyclic adenosine monophosphate (cAMP) are impaired. cAMP is involved in the regulation of many processes in the cell, eventually determining the mode of communication between nerve cells in the brain. However, the way cAMP is regulated is not yet fully understood.

To measure cAMP in nerve cells I use two related bio-nanotechnological tools called FRET (Förster resonance energy transfer) and BRET (bioluminescence resonance energy transfer). Lundbeck has a well-established research division in biology and molecular biology, but nanotechnology based methods such as FRET and BRET have not previously been a part of the experimental portfolio.

In connection with this industrial PhD project, Lundbeck has used resources on setting up a number of new methods. In addition, through me the company can draw on the knowledge that my university supervisor brings into the subject. Besides any new information on the mechanisms of cAMP regulation that my PhD project may result in, Lundbeck can therefore also obtain know-how on new techniques for use in the future.

In addition to the laboratory and general skills that a PhD study gives me, an industrial PhD project provides inside knowledge about how the research process is coupled to other aspects of the company. This awareness can be valuable both for a future position as a researcher in the industry as well as at a university. But it also opens up for several alternative job possibilities, linked to other aspects of a research-based company. With a year left of my PhD studies, I still do not know what future career path I will choose, but I know for certain that I will make good use of the alternative perspective I have obtained on research in my industrial PhD project.

# Nanovidensbank

## – a popular web portal for nanoscience and nanotechnology

*All the writers on Nanovidensbank since it started: Jeppe Lyngsø, Kristian Kollind, Esben Kjær Unmack Larsen, Jonas Ørbæk, Anders Bodholt (Dorthe Ravnsbæk absent)*

*By Esben Kjær Unmack Larsen, Tina Fredsted and Trolle Linderoth*

Where do you turn to if you are a high-school student who has been asked to write an essay on nanotechnology? Or a concerned consumer who would like to distinguish fact from fiction when it comes to the many fancy "nanoproducts" now on the market? The Internet abounds with information, but far from all is trustworthy. And most of it is written in English or using much technical lingo, which can be a barrier for some.

To meet this demand, iNANO hosts Nanovidensbank (nano knowledge bank), which is a Danish web portal about nanoscience and nanotechnology. Since its creation in 2005 more than 65 articles and 300 blogs have been added, and with more than 7,500 page views per month Nanovidensbank is among the most popular nanotechnology portals in Denmark.

The goal for Nanovidensbank is to communicate interesting and important stories about nanoscience and nanotechnology to an audience of non-experts who are curious and interested. The website features topical overviews as well as "hot stories", often illustrated with examples from research carried out at iNANO. Essentially, every important aspect of nanoscience and nanotechnology is covered, ranging from nanomaterials for cleaner energy conversion to nanoparticles that can revolutionize cancer treatment. About half the stories on Nanovidensbank are about research themes, but there is also a long list of articles about nano-products already on the market or ethical issues arising from the new opportunities offered by nanotechnology.

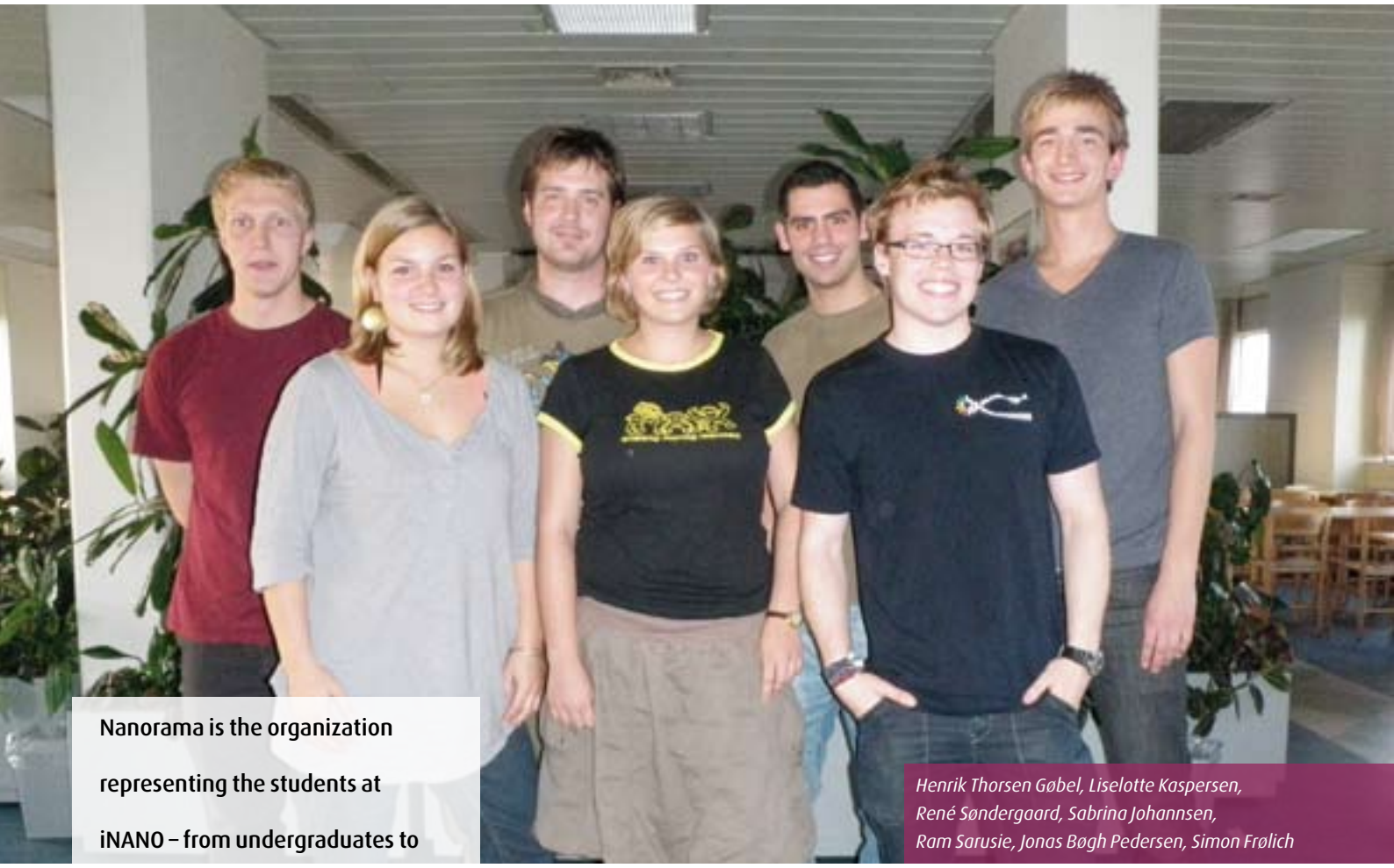
All the Nanovidensbank writers since 2005 are graduate students at iNANOschool and are selected for their interdisciplinary competences and commitment to communication and outreach. Esben Kjær Unmack Larsen says: "We try to write the articles in a language that is easy to understand, and our focus is to explain the often complicated science using common non-scientific words as much as possible. This can be tricky when dealing with concepts such as polymers, probe microscopy or even nanoparticles, but as writers of Nanovidensbank articles we always remember to explain such terms and use many illustrations and fact boxes to make the information easily accessible. The fun part of being a Nanovidensbank writer is that you learn so much yourself!"


Nanovidensbank is steadily growing; there is at least one new article and several new blogs on the web site each month. Active work with search engine optimization ensures that the portal has a high score in e.g. Google.

Monthly visitors to the blog part of Nanovidensbank:
2007: 530
2008: 1242
2009: 2056

Top stories on Nanovidensbank in 2009 (in Danish):
1: What is nanotechnology?
2: Nanotechnology applications in real life
3: Nanoshow
4: Nano this and nano that
5: Harness the power of the sun with nanotechnology

# Nanorama
– an iNANO-student organization



*Henrik Thorsen Gøbel, Liselotte Kaspersen, René Søndergaard, Sabrina Johannsen, Ram Sarusie, Jonas Bøgh Pedersen, Simon Frølich*

**Nanorama is the organization representing the students at iNANO – from undergraduates to PhD students. The organization is run by students and was established in the spring of 2005. By arranging various nano-related scientific arrangements and different social activities, such as the "iNANO Friday bar", the goal is to make the everyday life for each student at iNANO a great experience.**

*By the Board of Nanorama*

The aim of Nanorama is to strengthen the contacts between nanoscience students from different year groups and give the students a broader perspective with respect to their possibilities after their education in nanoscience at iNANO. We make an effort to achieve this by arranging numerous social as well as educational activities each year.

Nanorama's board consists of seven students representing different year groups. To attain efficient schooling of new members, the board is elected by other students twice a year, thereby allowing a time overlap between new and more experienced board members.

In 2009, Nanorama arranged a wide spectrum of activities, such as iNANO student teams joining the annual Aarhus 1900 relay race, Friday bars, and the traditional birthday party. Furthermore, we have promoted industry contact by company visits; in the autumn we visited Lundbeck and Haldor Topsøe on a trip to Copenhagen. We believe that students are encouraged in their studies if they know about possibilities for their future careers. Furthermore, we arranged an end-of-year dinner, where students could meet each other in a relaxed atmosphere before leaving for the summer break.

The current board members will carry on the work of Nanorama until the beginning of 2010, and several events are already on the drawing board. With the first nanoscience candidates finishing, it is now possible and very relevant to hear their stories and draw on their experiences. In the years to come, more PhD students will finish, and we are convinced that an alumni network will prove very valuable.

iNANO students awarded the

# Grundfos Challenge Prize 2009


*Carsten Bjerg, Rasmus Schøler Sørensen, Louis Nilsson, Marie Østergaard Pedersen, Niels Due Jensen*

**A rising demand to develop energy efficient housing led three iNANO students to come up with an innovative concept for collecting solar energy and reducing air-conditioning costs by circulating water in windows.**

*By Marie Østergaard Pedersen, Rasmus Schøler og Louis Nilsson*

There is some concern that the climate is changing due to our extensive combustion of fossil fuels. To meet the future challenges brought about by these changes, there is a political and commercial push towards the development of buildings with a low $CO_2$ impact. As the world's largest sustainable energy source is radiation from the Sun, it is a dilemma that buildings in areas with a lot of sunlight, such as the southern parts of USA or China, do not exploit this resource. On the contrary, the buildings consume large amounts of energy to sustain a cool indoor climate by air conditioning.

Against this background, a team of three iNANO students, Rasmus Schøler Sørensen, Louis Nilsson and Marie Østergaard Pedersen, set out to solve the assignment presented in the Grundfos Challenge 2009 on how Grundfos can reach the goal of having one-third of the company's turnover in 2025 come from products other than or more than pumps, with sustainability being a main priority. The solution from the iNANO team was a very innovative concept in which circulating water in windows can be applied to serve dual goals: collect solar energy and reduce the costs of air-conditioning. Specifically, this design presents a new type of functional window, which has a thin laminar flow of water between two panes of double glazing. When water flows down through these windows, it can effectively absorb infrared radiation from the Sun. Hence, the construction limits the amount of heat entering the building, which thereby reduces the need for air-conditioning. Using a heat conversion system, the captured thermal energy is used for heating water, for the air-conditioning system or as electrical energy. Applying a new concept like this may lead to a situation where smarter houses can help the environment in a more intelligent manner than is the case today.

The Grundfos Challenge is a unique competition sponsored by Grundfos between students from top Danish institutions offering education in engineering, natural sciences and economics. The Grundfos Challenge takes place at the Poul Due Jensen Academy, and during an intense week all participants are given a thorough introduction to a set of innovation tools, which they can use to create the most innovative solutions to real-life problems. In the process of finding the winners, it is not solely the most innovative ideas themselves that are evaluated, but also the innovation process, scientific development and the ability to interact as a team. The committee of judges, which was made up of a number of highly respected directors and research directors from Danish industry, was impressed with the very ambitious and innovative project the iNANO team came up with and awarded the team the prestigious Grundfos Challenge Prize.

# iNANO study tour 2009

**In 2009, as in previous years, iNANO students who had just finished their second-year nanoscience studies also went on a week-long international study tour, seeking inspiration for their continued nanoscience studies, but also to gain insight into the scientific environment at some of iNANO's international scientific partners.**

*By Liselotte Kaspersen and Maria Kragelund*

When we first heard about the opportunity to go on a study trip we did not hesitate to volunteer as organizers. Funds had to be applied for, travel arrangements had to be made, and hostels had to be booked for the group of fellow students and for Leif Schauser, senior scientific coordinator at iNANO, the organizer of the scientific programme.

Based on last years' experience, a study tour to Switzerland, Leif had decided to avoid tedious, excessively long bus transportation and make use of Ryanairs' affordable route Aarhus-Barcelona instead. Hence, we were filled with anticipation when we went to Aarhus Airport Tirstrup in the early hours of 21 June.

Upon arrival at Girona airport in Spain, our hired VIP bus brought us to Toulouse in France where we on the following day visited professor Christian Joachim, head of the nanoscience group at the Center for Material Elaboration & Structural Studies under the French National Center for Scientific Research (CEMES-CNRS). The day was an interesting mixture of lectures in chemistry, surface physics and theoretical physics, and we gained insight into their outstanding research on surface-rotating nanomachines. After a great French-style lunch there was a very exciting tour through the laboratories, where enthusiastic researchers introduced the experimental set-ups and hardware. After an inspiring day in Toulouse we continued in a bus to our next destination: San Sebastian.

On our first day in San Sebastian we walked 5 km along the sunny beach to the cooperative research centre CIC nanoGUNE. After an introductory lecture on nanoGUNE's organizational model and mission, as well as on selected scientific highlights, we were guided through the laboratories in the basement, where PhD students and postdocs explained experimental approaches, with concise introductions to the theory behind the experiments. We also went on a guided tour through the clean room, which was highly relevant to us now that iNANO has acquired its own clean room. We were informed about the possibilities of carrying out a PhD project at nanoGUNE, although we were warned that the fantastic sunshine of the day was a rare exception in the normally misty and cloudy Atlantic climate of Biscay.

The following day we took the day off, enjoying the wonderful beach and city, before heading to Barcelona in the late afternoon. When we arrived in Barcelona we went for a little sightseeing before retreating to the hostel. The next day we took the metro and train to Barcelona University campus, where we visited professor Arben Meroci, who heads the Catalan Institute of Nanotechnology. He had arranged a great breakfast snack table for us, and we heard about exciting results in the areas of electrochemistry, biosensors and improvement of nanomaterials. Again, enthusiastic PhD students presented the theory behind their projects in their laboratory settings, a very inspiring approach. We moved back to downtown Barcelona in the late afternoon and had dinner in a cosy restaurant, and, to memorize the end of the trip, several entertaining speeches were held.

A few early-leavers took the plane to Copenhagen on the following day, whereas most of us stayed on in Barcelona for a couple of additional days, enjoying the nice weather and the beautiful city. All the participating iNANO students realized that studying abroad as an undergraduate or a PhD student would be a great experience and a career as a researcher in nanoscience could indeed be very attractive.

TUBORGFONDET
We acknowledge the kind support from TUBORGFONDET and HEDE NIELSEN FONDEN which made this tour possible.

# 8th iNANO annual meeting 2010

**The 8th iNANO annual meeting took place on 20 January 2010 as a whole-day event with six invited lectures, a poster session with an impressive 95 poster contributions, and an evening dinner, which included a glorious Haydn trumpet concerto recital by iNANO professors Kurt Vestager Gothelf and Daniel Otzen. As always, iNANO managed to attract high-profile speakers from three continents who delivered inspiring nanoscience-related talks.**

*By Liselotte Kaspersen and Maria Kragelund*

## Graphene: A cornucopia of new nanoscience

The first speaker of the day was Russian-born University of Manchester professor Andre Geim. Among other important scientific contributions, such as the development of gecko tape and demonstrations of diamagnetic levitation, Geim famously invented a practical method for producing single-layer graphite sheets, graphene. In 2004, Geim and his team published a very simple mechanical way to produce manageable sheets of graphene, which can subsequently be characterized mechanically, electronically, magnetically, etc. Geim also proposed an alternative route to graphene, which involves epitaxial growth on a planar crystal and subsequent chemical removal of the backing substrate. This method is now also in practical use with up to 30-inch, perfect graphene layers now being produced.

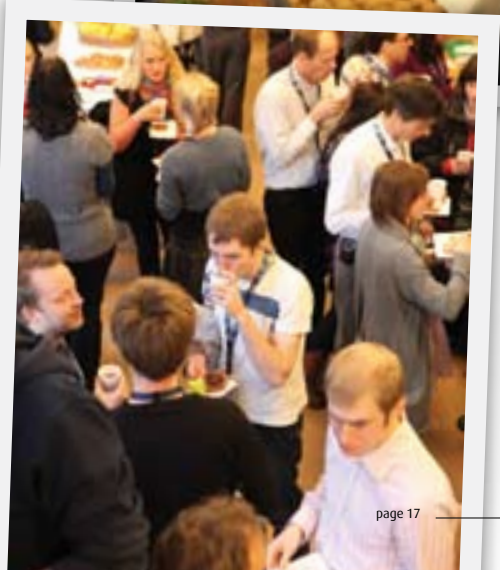
Other than being the thinnest material imaginable, graphene has a number of record-breaking properties: it is the strongest, stiffest, and most stretchable (up to 20% elastic deformation) material ever found; it can support the highest current density (one million times that of copper); it has a record thermal conductivity; it has the highest-known intrinsic carrier mobility (100 times that of silicon); it is the lightest charge carrier (in fact it has zero mass); it has the longest electron mean free path. Indeed, the list goes on.

The discovery of graphene has also introduced a new kind of quasiparticle, whose behaviour must be modelled not by the conventional Schrödinger or Dirac equations but rather by a Hamiltonian equation describing massless Dirac fermions. These massless quasiparticles give rise to new physical phenomena, such as the two new kinds of quantum Hall effect (half-integer and "anomalous") first described by Geim's group.

These unique physical properties and their manifestation in new physical phenomena are expected to pave the way for graphene to become the electronic material of the future.

## A world of DNA assemblies

Professor William Shih from Harvard University then took the audience on a tour of the world of nanofabrication with three-dimensional DNA origami, in which long single strands of DNA are folded into a plethora of nanoscale structures. Folding happens through a self-assembly process aided by the addition of multiple shorter 'staple' strands designed to hybridize to specific positions in the longer DNA strand. The resulting two- or three-dimensional structure is a mirror of any arbitrary figure loaded into specially designed software.



Using this technology, William Shih and his colleagues have been able to construct a number of DNA objects, including a genie bottle, two kinds of crosses, a square nut and a railed bridge.

The aim of Shih's research is to explore design principles for self-assembling molecular machines, primarily using structural DNA nanotechnology to constantly push forward the complexity of programmable self-assembled systems. "A pivotal challenge for nanotechnology in the next half-century is to achieve precise positional control of material on the 1–100 nanometer scale. In the light of this challenge, our laboratory explores rational design and directed evolution approaches to developing self-assembling DNA structures and devices with application to problems of biomedical interest," says Shih. An outstanding problem in biology is the efficient structure determination of transmembrane proteins. The Shih laboratory is exploring the use of DNA nanotubes as an alignment medium for structure solution of lipid-bilayer-embedded transmembrane proteins. Also, Shih is investigating the utility of DNA nanotubes in the creation of artificial extracellular cell matrixes.

## In vivo bioreactor for tissue engineering

As a true nanotechnological field, tissue engineering is an interdisciplinary research field that applies the principles of engineering and the life sciences to the development of biological substitutes (which can restore, maintain or improve tissue function) in regenerative medicine. While natural scaffolds are seeded with cells and matured ex vivo in traditional tissue engineering, nanoscientists today are producing biomimetic synthetic scaffolds that are inserted acellularly or with cells seeded just prior to implantation.

In her talk, professor Molly Stevens from Imperial College London described the development of inorganic/organic hybrid nanocomposite porous scaffolds composed of a bioactive inorganic sol-gel and resorbable polymers built together by a foaming process, with covalent cross-linkers to provide physiological stability. The scaffolds can be tailored with mechanistic properties and Stevens showed how they had achieved a fully interconnected vasculature throughout these types of porous scaffolds. One of the current gold-standard treatments of large bone defects requires fresh autologous bone to be harvested and transplanted from the iliac crest. This procedure, though, is accompanied by extreme pain and morbidity. Thus, nanoscientists are exploring other alternatives in which harvested cells are combined with advanced nanotailored scaffolds and stimulated with exogenous molecules. Stevens and her colleagues extended the con-

# 8th iNANO annual meeting 2010

*Jørgen Kjems, Masaki Takata, Flemming Besenbacher, Molly Stevens, William Shih, Andre Geim, Geoffery A. Ozin, Kam Leong*

cept of in vivo tissue engineering by showing that large volumes of bone can be engineered in a 'bioreactor' and, importantly, without needing cell transplantation and growth factor administration. The 'bioreactor' space is created at the interface between the bone and the periosteum, a mensenchymal layer rich in pluripotent cells, by injection of a biodegradable calcium-alginate gel. The 'bioreactor' space is gradually infiltrated by periosteal cells and capillaries, resulting in the formation of compact bone within 12 weeks.

More fundamental research on how cells respond to different materials is needed to facilitate an increase in the level of biofunctional specificity of implantable scaffolds. Striving towards a deeper understanding of cell-material interaction, Stevens and her co-workers are exploring the chemical interactions between cells and proteins at the sub-nanoscale. "Cell adhesion strength is altered by sub-nanoscale patterns of chemistry," explains Molly Stevens.

## Nanomaterials research at SPring-8

Masaki Takata is a professor at the University of Tokyo and the research director of the "Super Photon ring-8 GeV" (SPring-8) facility in Hyogo Prefecture, Japan, which is the world's largest and most powerful third-generation synchrotron radiation facility. Scientists from around the world travel to SPring-8 to use one of the 60 beam lines, which can deliver ultrashort and nanosized X-ray pulses down to 40 ps in duration and 10 nm in diameter. These intense beams open the door to higher-precision structure determination in both nonbiological and biological materials and to investigations of fast physical phenomena with nanosecond resolution.

In his talk, Takata concentrated on a recent success story where SPring-8, Sony and Panasonic scientists together answered a longstanding question in materials science, which concerns the exact mechanism underlying the fast phase-change dynamics in the gallium/antimony/tellurium (GST) alloys used in today's digital versatile discs (DVDs). As is well known, DVDs are produced on a massive scale but surprisingly the structural changes occurring in write/erase cycles on DVDs are not well understood. A better understanding of the phase-change dynamics is a prerequisite for a rational design of faster next-generation data discs.

A DVD data track consists of alternating regions of amorphous and crystalline GST, which represent the binary data (zeros and ones). The readout mechanism is sensitive to the widely different optical properties of the amorphous and crystalline phases. A "write" laser pulse changes the affected GST region from the crystalline phase over the liquid state to the amorphous phase. Conversely, an "erase" laser pulse changes the material from amorphous to crystalline. These phase changes can be repeated over and over and occur on a 20-100 ns timescale.

Professor Takata's team was able to show that the surprisingly fast change from the amorphous to the crystalline phase is made possible by a loosely preserved sodium chloride (NaCl) crystalline imprint in the GST amorphous phase. In particular, adding antimony to a gallium/tellurium (GT) alloy restricts the composition of the amorphous phase to even-numbered member rings only, as opposed to both even- and odd-numbered rings in the GT alloy.

The team also investigated a new candidate material consisting of silver, indium, antimony and tellurium (AgInSbTe). This alloy can undergo phase changes even faster than the now-commercialized GST alloy, and Takata was able to show that these superior properties are due to an advantageous nucleation mechanism (edge growth), through which smaller, faster-growing crystallites form than is the case with GST. This kind of basic understanding of the factors underlying fast phase-change dynamics should pave the way for a rational design of the materials used in next-generation optical storage systems.

## Photonic bandgap structures: stacking the deck

Professor Geoffrey A. Ozin from the University of Toronto is a prominent figure in the field of nanochemistry and has written several textbooks on the subject. His research revolves around photonic bandgap (PBG) materials, a new class of dielectrics, which are the photonic analogues of semiconductors. The photonic band gap is a frequency interval where the linear electromagnetic propagation effects are turned off.

In 2000, Ozin invented a method for large-scale production of PBG structures based on an ordered 3D array of silica nano- or microbeads that serve as a template for infiltration with silicon depos-

ited via chemical vapour deposition. In his talk, professor Ozin presented an impressive number of applications of these PBG structures. Some are at the proof-of-concept stage but many are currently being commercialized by Opalux Inc., a company that he helped form.

For instance, Ozin showed examples of Bragg mirror stacks formed by nanoparticle infiltration into the PBG structure. With the right choice of material, the Bragg mirrors can be made highly flexible, and infiltration with differently sized nanoparticles imparts tuneability over a wide wavelength range. This kind of PBG structure has been commercialized in polymer-based electrically tuneable nanoparticle Bragg mirrors for display applications.

As a second, potentially revolutionary, example, professor Ozin presented as-yet unpublished results of his group's successful bottom-up synthesis of a nanoparticle silicon laser. Such lasers are key components in silicon-based optoelectronic applications as they allow for inexpensive integration of both optical and electronic components on the same wafer. The challenge has been silicon's bandgap, which is indirect, but Ozin's stable decyl-capped nanocrystals, which effectively have a direct bandgap due to their size, can be infiltrated into a PBG structure and coaxed to lase.

## Microfluidics platform related to nanomedicine

Finally, Kam Leong, professor in Biomedical Engineering at Duke University, introduced the audience to the latest advances in genomic therapeutics aimed at solving the inherent problem of premature dissociation or overly stable binding of self-assembled nanocomplexes carrying nucleic acid-based therapeutics. The heterogeneity of polyplexes resulting from bulk synthesis hinders the accurate assessment of the self-assembly kinetics and adds to the difficulty in correlating the polyplexes' physical properties to transfection efficiencies or bioactivities. To facilitate better understanding and control of the synthesis process of polyplexes, Leong and his colleagues have developed a new technology platform that combines nanophotonics (i.e. QD-FRET) and microfluidics to characterize the real-time kinetics of the nanocomplex self-assembly under laminar flow. QD-FRET provides a highly sensitive indication of the onset of molecular interactions and a quantitative measure throughout the synthesis process, whereas microfluidics offers a well-controlled microenvironment to spatially analyze the process with high temporal resolution (~milliseconds). For the model system of polymeric nanocomplexes, two distinct stages in the self-assembly process were captured by this analytic platform. The kinetic aspect of the self-assembly process obtained at the microscale would be particularly valuable for microreactor-based reactions which are relevant to many micro- and nano-scale applications. Further, nanocomplexes may be customized through proper design of microfluidic devices, and the resulting QD-FRET polymeric DNA nanocomplexes could be readily applied for establishing structure-function relationships. In their studies, Leong and his group have extended the QD-FRET nanosensor to follow nanoparticles in cells in time, including the study of nanoparticle unpacking and DNA degradation.

Getting a handle on protein aggregation:

# From insight to inhibition?

**Unwanted protein aggregation leads to devastating neurodegenerative diseases such as Alzheimer's and Parkinson's Diseases. Intensive efforts are underway worldwide to develop ways of inhibiting this process and thus prevent disease development. In collaboration with Wyeth Research Ltd, we have developed a high-throughput assay to screen upwards of a million compounds for aggregation inhibition. Small-angle X-ray scattering provides a rationale for the success of this assay: the formation of nanoscale beads on a string.**

*By Daniel Otzen, Lise Giehm, Cristiano Oliveira and Jan Skov Pedersen*

Neurodegenerative diseases (NDs) are very unpleasant afflictions. The gradual loss of cognitive abilities in a close relative suffering from Alzheimer's Disease (AD) can be a heart-wrenching process to watch, all the more so because nothing can be done to stop the inexorable decay, though there are ways to temporarily alleviate the symptoms. Parkinson's Disease (PD) is less harsh on the mental faculties and usually does not progress as rapidly as AD, but the decline in the patient's control over bodily movements remains distressing. The disease is caused by the loss of dopaminergic (dopamine-producing) neurons in the brain, which control the finer details of our movements (Fig. 1). Like other NDs, the molecular basis for PD is complex, involving many different factors, including the loss of mitochondria (the cell's energy generators), accumulation of reactive oxygen species and decline in the neurons' protein-recycling machinery. A central player is the small protein α-synuclein (αSN). Its normal physiological role is unclear, although it is likely to involve protein transport through the cellular membrane system and possibly fusion of membranes at the nerve synapses. Nevertheless, PD patients seem to have a problem with αSN lumps or aggregates. αSN is a natively disordered protein that does not have any persistent structure as a free monomeric protein. However, left to its own devices it slowly aggregates to bigger and bigger structures, which organize themselves as amyloid fibrils, where the proteins stack on top of each other by forming α-sheet structures (Fig. 2). In the cell, such aggregates eventually form so-called inclusions or precipitates named Lewy Bodies. This is not a problem per se, as these bodies are also found in the brains of many healthy elderly people. The problem arises at an earlier stage in the aggregation process, where αSN forms small soluble oligomers a few nanometers in diameter. These oligomers have a nasty habit of attaching themselves to the cell surface and rendering it leaky. It is thought that this allows precious calcium ions to leak out and upset the natural ion balance, leading to cell death. Thus interfering in the formation of these oligomers – rather than the fibrils themselves – is an obvious strategy to stop the development of PD.

## Finding a few needles in a million-straw haystack

To stop this oligomer formation, we have teamed up with the American pharmaceutical company Wyeth (recently merged with Pfizer) to develop a high-throughput screening assay, which, based on a library of close to a million compounds, will identify small molecules able to prevent or reduce oligomer formation from monomeric αSN. The big challenge has been to develop reproducible conditions for aggregation since αSN is notoriously unpredictable when it comes to aggregation. Otherwise identical samples can show markedly different aggregation behaviour both in terms of the start of aggregation formation (the lag time), the speed of growth (the elongation phase) and the extent to which fibrils form. Obviously, variations in these parameters impede the screening of an enormous HTS library. This library consists of almost a million different compounds which have been collected from various sources and represent a large collection of "chemical diversity", making the library an excellent place to start looking for compounds with interesting properties. While relentless shaking of the αSN solution in the presence of glass beads

*Jan Skov Pedersen, Daniel Otzen*

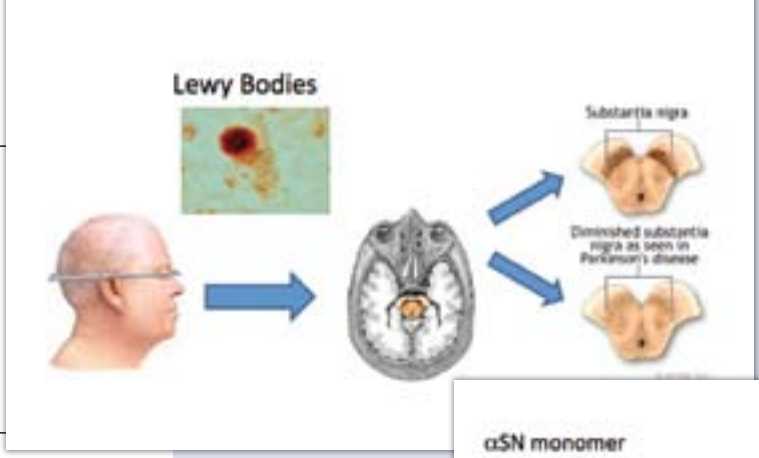



*Fig. 1. Cross-section of a brain showing the loss of dopaminergic neurons (localized in the substantia nigra) in Parkinson's Disease.*

can help the process along, this is just not compatible with HTS conditions, where the aggregation has to occur simply, rapidly and very reproducibly.

## Soap is the solution: sharing bubbles with your friends

This is where soap comes into the picture. Like other soaps, the well-known surface active agent sodium dodecyl sulphate (SDS) is generally used to prevent aggregation and solubilize or disperse greasy materials. SDS can do this because it forms roughly spherical self-assembled structures known as micelles above the so-called critical micelle concentration (cmc). However, below the cmc, SDS actually promotes protein aggregation. For αSN, it works like a charm. Add a little dollop of SDS and the aggregation starts after a very short lag time (less than an hour) (Fig.3). Using this approach to obtain reproducible aggregation conditions, we have, together with our colleagues at Wyeth, developed a simple fluorescence-based assay that allows us to follow either the loss of monomeric αSN or the formation of higher-order αSN aggregates (from dimers and up) (Fig. 3). Wyeth has screened 746,000 compounds and, of these, more than a hundred show significant aggregation inhibition. We are currently ranking them as starting points for a future drug development programme.

What is the basis for this amazing effect of SDS? It appears to be very simple: at low SDS concentrations, SDS is desperate to form micelles and enlists the help of αSN. It forms nano-scale clusters on the protein surface and by combining several (up to four) different proteins, enough SDS can coalesce to form a single micelle shared by several proteins. Individual clusters link up, presumably via intermolecular α-sheets, to form bead-on-a-string structures with an average distance of 8-9 nm between each bead. We were able to construct this model based on detailed small-angle X-ray scattering data, which can provide a remarkable level of structural detail on these slippery structures (Fig. 4).

So next time you wash your hands with soap, remember that the same type of material may ultimately help to keep the brain clear too...

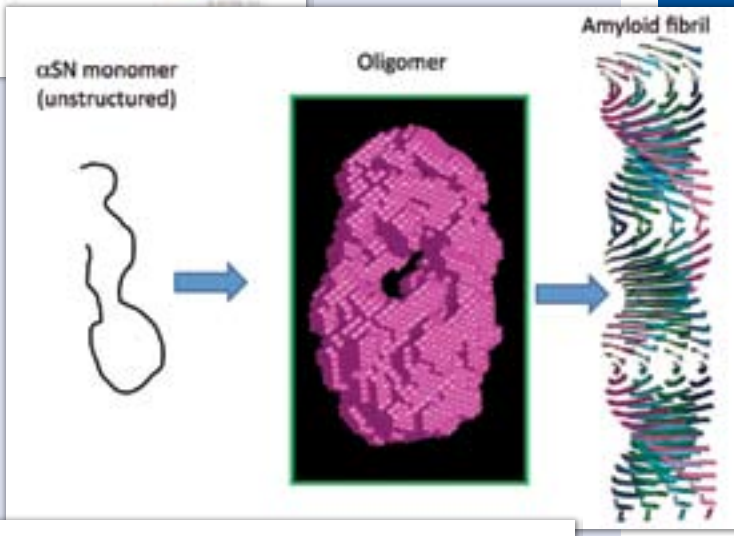



*Fig. 2. Formation of amyloid fibril from the unfolded monomer. The oligomer structure has been obtained by small-angle X-ray scattering measurements (in collaboration with Dr Bente Vestergaard, University of Copenhagen).*

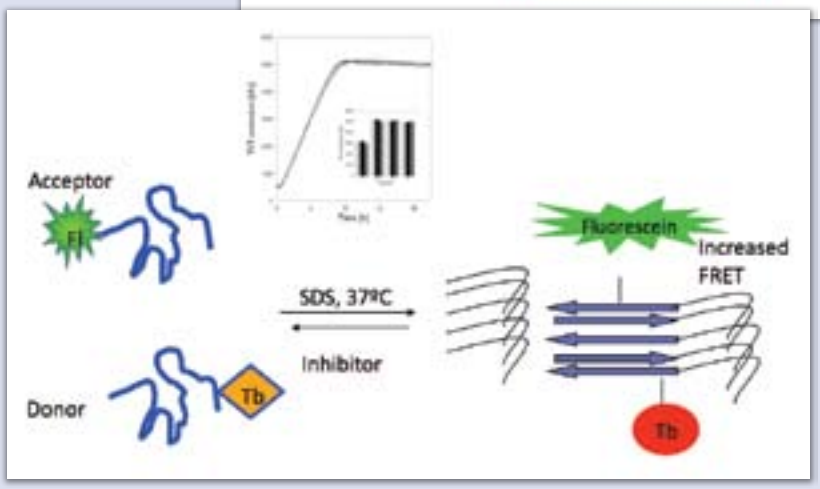



*Fig. 3. Assay developed by Wyeth Research Ltd to monitor aggregation of αSN. When two differently labeled αSN molecules join up as a result of aggregation in sodium dodecyl sulphate (SDS), the result is a change in the so-called FRET (Förster Resonance Energy Transfer) which leads to a change in the fluorescence of the solution. The inset graph demonstrates the reproducibility of the several different aggregation assays in the presence of SDS. Formation of fibrils is monitored by the dye Thioflavin T, which increases its fluorescence signal in the presence of fibrils.*

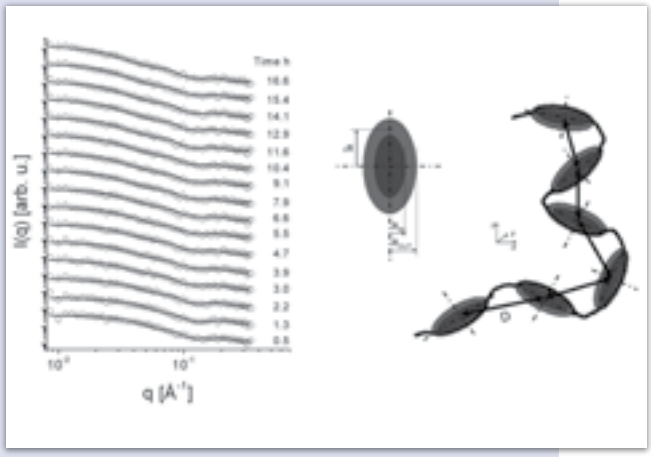



*Fig. 4. The small-angle X-ray scattering data (left) allow us to reconstruct the shape of the αSN aggregates formed in the presence of SDS (right). They appear to consist of shared micelles (inner dark ellipse) stabilized by adjoining αSN molecules (outer light ellipse shell). These are tied together by flexible linkers and grow in a simple stepwise fashion.*

# Small box with large potentials

*By Jørgen Kjems and Kurt V. Gothelf*

Building mechanical machines has fascinated humankind throughout history, and during the last century the miniaturization of machines and other devices has been a cornerstone in the technological development of our society. The approach has usually been to refine technology to manufacture very small objects in a "top-down" assembly procedure assisted by microscopes to visualize the process. Nature, on the other hand, has through evolution developed highly complex mechanical machinery that is constructed in a very different way. The highly complicated macromolecular machinery in nature is assembled and operates by means of molecular interactions. Our understanding of self-assembly processes has until recently been so limited that only a few relatively simple objects have been created by man by this means. With the invention of the DNA origami method by the American scientist Paul Rothemund it became clear that DNA, the information-carrying molecule of life, is also able to direct the assembly of highly sophisticated individual structures in 2D.The principle relies on Nature's genetic code: the pairing between DNA strands was used as a programme to direct the folding of a natural DNA strand into a predetermined shape.

When Centre for DNA Nanotechnology (CDNA) was established at iNANO in 2007 as one of the Danish National Research Foundation's Centres of Excellence, the main purpose of the centre was to explore DNA as a material for self-assembly of nanoscale structures. Now, researchers at CDNA and iNANO have taken the origami technology a big leap forward by demonstrating self-assembly of a three-dimensional nanomachine that can sense and act on external stimuli. Hundreds of small, chemically synthesized DNA molecules are used to sculpt a natural, single-stranded DNA from a bacterial phage into the shape of a hollow cube with a side length of approximately 35 nm, representing the most complex man-made nanostructure ever generated by self-assembly. Almost as if by magic, the DNAs assemble themselves into precisely the structure predesigned on a computer. One of the major challenges of making objects this small is verifying that they are actually made. Hence a number of biophysical high-resolution pictures were generated by different physical methods, including atomic force microscopy (AFM), small-angle X-ray scattering (SAXS) and cryogenic electron microscopy (see Fig. 1).

## Opening a DNA box on command

Building a small box at nanoscale was an academic achievement, but what can it be used for? Well, to make any use of a box, it is necessary to be able to open it! Therefore the DNA box was created with a lid that opens and exposes its interior when the box encounters a specific "key" – in this case a DNA or RNA molecule encompassing a specific sequence. This provides an opportunity to use the DNA box as a diagnostic sensor for revealing the presence of, for instance, viruses or cancer. In the long term, it may become possible to control the release of medicine from the DNA box in diseased cells.

An extremely useful feature of the DNA box is that the exact constitution of its approximately 500,000 atoms is known, and it is possible to attach extra components to its 250 addressable spots with e.g. molecules, proteins, etc.
This feature has been utilized to attach small molecular "lamps" to the lid. In this way it is possible to follow the opening and closing of the individual boxes solely by the fluorescent light coming from them: the lamp shines red when the box is closed and green when it is open (see Fig. 2).

## What next?

Experiments are being carried out to encapsulate biological enzymes in the DNA boxes and control the activity of the enzymes by external signals. For instance, drugs have been placed inside the boxes and the boxes are currently being tested for their ability to enter cells and release the drugs there. The ability of the DNA boxes to react to the local environment they are located in and release medicine, provides hope that they can be used to target cancer cells or cells affected by viruses. In other experiments, the researchers are trying explore the capacity of the boxes to function as small logic circuits with the long-term

*Page 22 from the left: Ebbe Sloth Andersen, Mingdong Dong, Morten Muhlig Nielsen, Kasper Jahn, Jørgen Kjems, Kurt Vesterager Gothelf, Flemming Besenbacher, Victoria Birkedal*

*Page 23 from the left: Wael Mamdouh, Christiano L. P. Oliveira, Jan Skov Pedersen, Holger Stark, Bjørn Sander, Mariola Monika Golas, Ramesh Subramani*

goal of building highly efficient DNA computers.

## National and international impact

The DNA box was described in Nature and was subsequently mentioned in hundreds of science magazines worldwide, including National Geographic and Scientific American, and in several international newspapers, including The Wall Street Journal. At the national scene it was selected as the scientific breakthrough of the year by two leading newspapers.

## Participants in the interdisciplinary project

The DNA box project was carried out by CDNA and other researchers at iNANO, but also involved a German team who performed part of the characterization of the box. The project was headed by professor Jørgen Kjems, Department of Molecular Biology, and professor Kurt Vesterager Gothelf, Department of Chemistry, both at iNANO. First author of the article in Nature, post-doctoral scholar Ebbe Sloth Andersen, played a key role in the project.

Andersen ES, Dong M, Nielsen MM, Jahn K, Subramani R, Mamdouh W, Golas MM, Sander B, Stark H, Oliveira CL, Pedersen JS, Birkedal V, Besenbacher F, Gothelf KV, Kjems J., Self-assembly of a nanoscale DNA box with a controllable lid. Nature. 2009 May 7;459(7243):73-6.

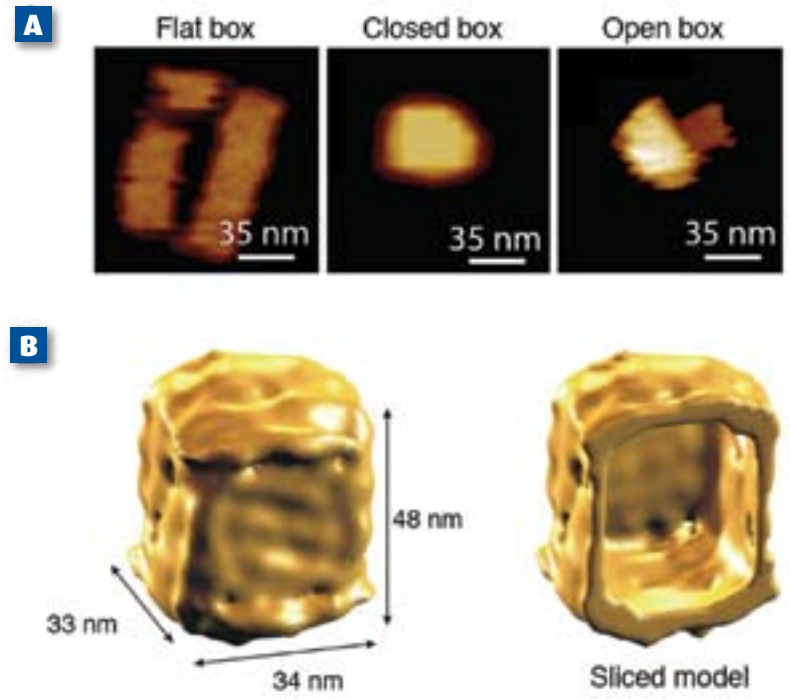



*Fig. 1. Imaging of the DNA box. (A) The DNA boxes visualized by atomic force microscopy (AFM) in flat, closed and open state. (B) Cryogenic transmission electron microscopy imaging of the DNA box with its height, width and length in nanometres. The box on the right is sliced to show the interior cavity that potentially can be used for functions such as transporting medicine into diseased cells in the body.*

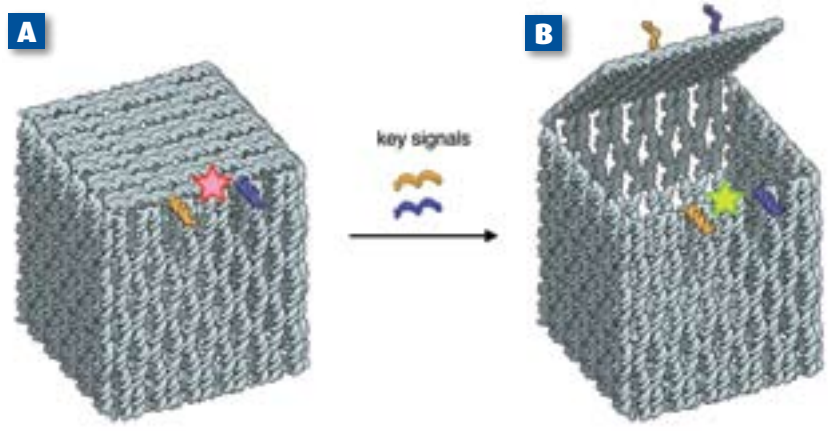



*Fig. 2. (a) Closed DNA box. The two DNA locks are shown as orange and blue, respectively, and the molecular lamp shines red, showing that the box is closed. (b) The right DNA keys have opened the DNA locks and the molecular lamp shines green, showing that the lid is open.*

# A new age of carbon electronics

*Philip Hofmann, Liv Hornekær, Thomas Garm Pedersen, Louis Nilsson, Bjørk Hammer, Richard Balog, John Thrower, Bjarke Jørgensen, Flemming Besenbacher*

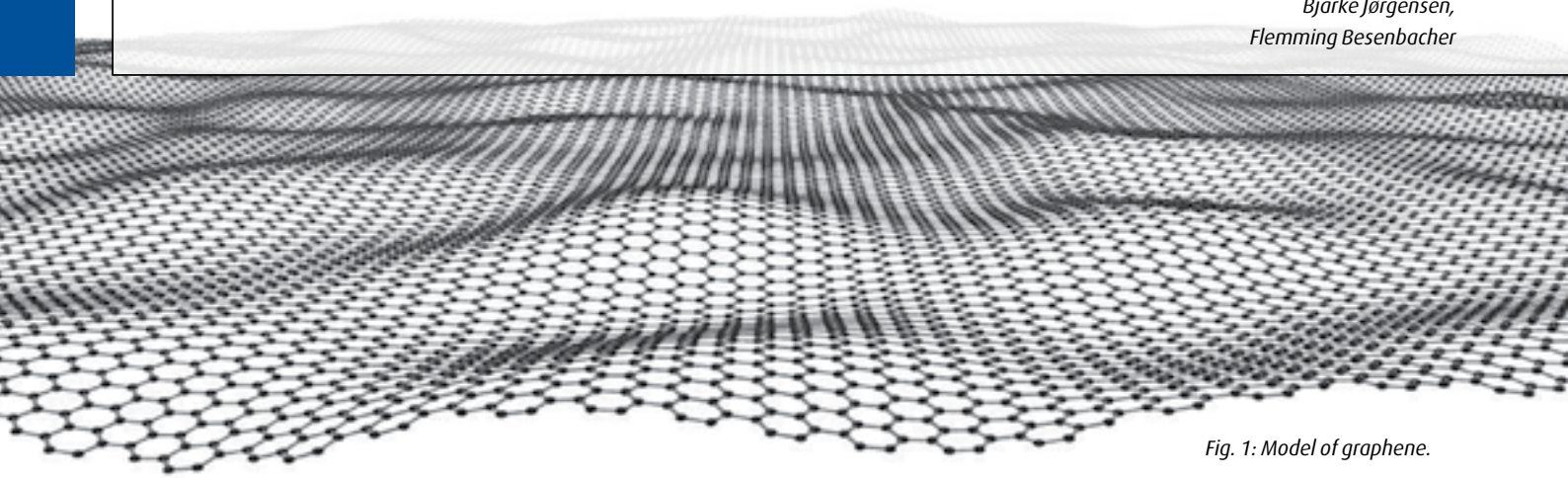


*Fig. 1: Model of graphene.*

*By Louis Nilsson, Bjarke Jørgensen, Richard Balog and Liv Hornekær*

Graphene, a one-atom-thin layer of carbon, could be the material that will one day supersede silicon as the preferred material for integrated circuit fabrication. The silicon industry has successfully developed today's microelectronic circuits during the last decades, but the industry is approaching a fundamental physical limit, where the size of the components cannot be further decreased. Also, silicon has an indirect bandgap, which impedes the production of highly efficient low-cost solar cells.

Graphene, on the other hand, has unique electronic properties, such as the highest known room-temperature conductivity, and other extreme mechanical and optical properties. Therefore, the expectations for a graphene-based electronic industry have been enormous since the first experimental demonstration of the existence of graphene in 2004.

However, the lack of a bandgap in graphene is a major challenge that must be overcome before it can be used for e.g. circuit fabrication. In a cross-institutional research project, iNANO researchers at Aarhus University and Aalborg University have combined their theoretical and experimental expertise to demonstrate how a direct bandgap with a size sufficient for real applications can be opened in graphene by adsorbing hydrogen atoms onto the surface.

To investigate the electronic effects of hydrogen adsorption on graphene, atomic hydrogen was deposited onto graphene supported on an iridium substrate. The bare and hydrogenated graphene surfaces were then investigated by scanning tunnelling microscopy (STM) and angle-resolved photoemission spectroscopy (ARPES, see inset for details).

STM images of the graphene surface after hydrogen exposure show that the hydrogen atoms arrange into clusters in an ordered pattern, see Fig. 2b. In the image, areas covered with hydrogen are depicted as bright yellow protrusions. This patterning is caused by the interaction between graphene and the iridium substrate. Theoretical calculations show that the carbon atoms in the graphene layer can rearrange so that they bind alternately to a hydrogen atom above the graphene layer and an iridium atom below the layer. This arrangement is shown in the model in Fig. 3. Due to a lattice mismatch between the graphene and the iridium substrate, only some areas of the surface can accommodate the arrangement, namely the regions where every other carbon atom is situated right above an iridium atom; hence hydrogen atoms will prefer to bind in these areas. As a result hydrogen adsorbs into the patterned structure displayed in the STM images (Fig.2b).

ARPES measurements were performed on the clean and hydrogenated graphene surfaces to investigate the effect of this patterned hydrogen adsorption on the electronic properties of graphene. The results are remarkable and are displayed on top of the STM pictures. The bright curved bands are the occupied electronic states (the valence band) as probed by ARPES. The solid red lines in the figures indicate the expected position of the unoccupied electronic states

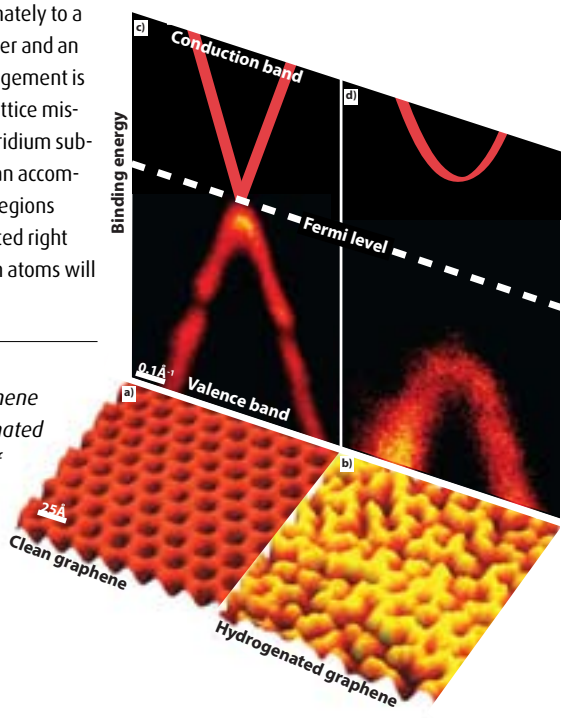



*Fig. 2: a) STM image of the clean graphene surface. b) STM image of the hydrogenated graphene surface. c) Band structure of the clean graphene surface. d) Band structure corresponding to the hydrogenated graphene surface from fig. 2b.*

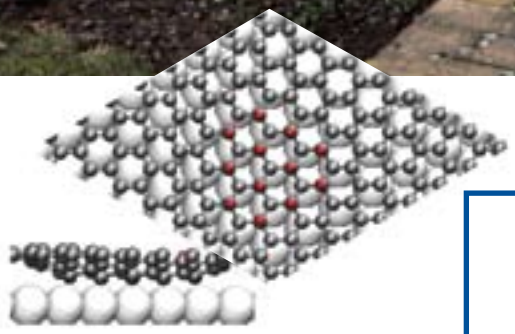


*Fig. 3: DFT calculation of a hydrogen cluster consisting of 12 hydrogen atoms (red balls) on graphene (grey balls) on iridium (white balls). Top view and side view, respectively. From the top view the arrangement of hydrogen atoms on every second carbon atom can be seen. The side view illustrates the rearrangement of the graphene.*

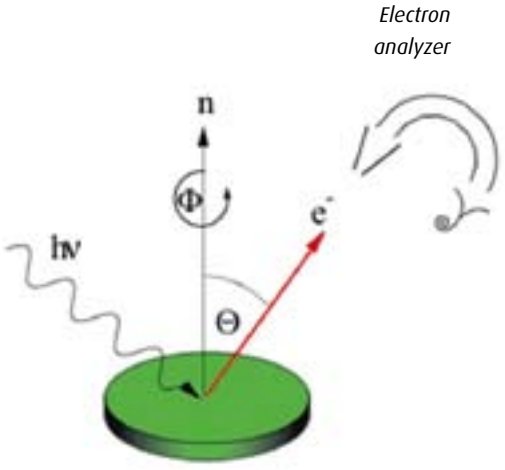
(the conduction band). While the band structure of clean graphene is well known, the exact position and shape for hydrogenated graphene is unknown.

For clean graphene, a characteristic cone-shaped band is observed and the valance band goes all the way up to the Fermi level. Free-standing graphene is a semi-metal, meaning that there is no opening between the valance band and the conduction band (which meet at the Fermi level). The band structure of graphene on iridium is very similar to the band structure of free-standing graphene; only small gaps in the valence band are seen due to the interaction with the substrate. Therefore graphene on iridium is an ideal system for studying fundamental properties of graphene.

After exposing the graphene surface to atomic hydrogen, the band structure changes drastically. The most obvious and interesting change is that a global bandgap is opened, Fig. 2d. The absolute value of the bandgap cannot be determined from the ARPES measurements since it only probes the filled states, but it can be determined that the gap is at least 0.45 eV (the energy difference between the Fermi level and the top of the valance band). A bandgap of this size is sufficient for real applications.

The physical origin of the hydrogen-induced bandgap opening in graphene is a confinement effect. In clean graphene the valence electrons are highly delocalized, but when hydrogen is adsorbed onto the surface a barrier is created for the delocalized electrons in the surrounding clean areas. Consequently, due to the wave properties of electrons, only certain energies are allowed for electrons confined in the nanosized areas without hydrogen. It is this confinement effect that leads to the observed global bandgap opening and opens up the possibility of using graphene as a new material for integrated circuit fabrication.

The presented results were published by Richard Balog, Bjarke Jørgensen, Louis Nilsson, Mie Andersen, Emile Rienks, Marco Bianchi, Mattia Fanetti, Erik Lægsgaard, Alessandro Baraldi, Silvano Lizzit, Zeljko Sljivancanin, Flemming Besenbacher, Bjørk Hammer, Thomas G. Pedersen, Philip Hofmann and Liv Hornekær in Nature Materials volume 9, 2010.




*Angle-resolved photoemission spectroscopy (ARPES) is a technique used to determine the surface electronic band structure of a crystal. Monochromatic light is incident on the surface of the sample. If the photon energy of the light source is sufficient, electrons are emitted due to the photoelectric effect. The intensity of emitted electrons (e-) is measured as a function of electron kinetic energy, emission angle (Θ), and photon energy (hν). The binding energy of the electrons can then be mapped as a function of momentum, thus revealing the so-called band structure.*

# Big opportunities in a small world

## – a new Nanomedicine centre established

*Fig.3. A nanoporous scaffold (transparent blue) for tissue engineering cultured with immortalized human stem cells (transparent red) is visualized by synchrotron generated X-rays and computed tomography at the ESRF (European Synchrotron Radiation Facility). Insight into the emerging morphology of the biological construct improves our understanding of the dynamics of growing cells in biocompatible materials. Scale bar is 10 µm.*

**In the future, nanomedicine will provide important tools for understanding, diagnosing and treating diseases. By exploiting novel physical, chemical, and biological properties of materials at the nanometer scale, nanomedicine will provide targeted, site-specific therapeutics with reduced adverse effects, novel imaging methods for the early diagnosis of diseases, and novel implant materials that support tissue regeneration processes.**

*By Jørgen Kjems and Allan Flyvbjerg*

An emerging new research field, nanomedicine, carries great promise for future understanding, diagnosis and treatment of diseases by applying nanoscience to the health area. Nanomedicine includes the areas of molecular drug design, drug delivery, in vivo bioimaging, in vitro diagnostics and novel materials including surface-functionalized implants. More than just an extension of "molecular medicine", nanomedicine will employ biomimetic nanoscale systems to address medical problems. Nanomedicine will have great impact on the medical profession, for the definition of disease, for the diagnosis and treatment of medical conditions including chronic illness, and ultimately for the improvement of general human health and well-being.

### iNANOmedicine initiative

With two major grants from the Danish Agency for Science, Technology and Innovation and the Lundbeck Foundation, iNANO is now gearing up its research efforts in the nanomedicine area. The combination of the DKK 26 million infrastructure grant "iNANO-MED Core Facility" and the DKK 30 million research project "LUNA" allows the pursuit of ambitious targets through collaborative efforts between iNANO, the Faculty of Health Sciences at Aarhus University (SUN) and Aarhus University Hospital.

The iNANO-MED Core Facility is set up to provide cutting-edge bioimaging tools for the visualization of processes and structures in unprecedented detail. A Titan cryo-electron microscope (cryo-TEM) will allow the visualization of membranes in their native environment, which will nicely complement recent structural studies that have been performed using X-ray crystallography and small-angle X-ray scattering (SAXS). These methods, although providing great detail at great resolution, rely on scattering effects from ordered assemblies of molecules in artificial settings. Cryo-TEM, in contrast, allows the study of membrane surfaces and embedded protein complexes at nanometer resolution, which potentially provides valuable additional detail on interactions and signal-receptor recognition events.

Also, an IVIS imaging system has been purchased, which facilitates non-invasive longitudinal monitoring of disease progression, cell trafficking and gene expression patterns in living animals based on fluorescent probes (see Fig. 1). The IVIS can be used for studying mouse models for oncology, inflammation, cardiovascular diseases, immunology, tissue engineering, toxicology, drug delivery and drug metabolism.

The Lundbeck Foundation Nanomedicine Centre for Individualized Management of Tissue Damage and Regeneration (LUNA) aims at developing novel, clinically relevant nano-based technologies in drug design, drug delivery, bioimaging and tissue engineering, to support individualized prevention, diagnosis and treatment of cardiovascular and musculoskeletal diseases.

Cardiovascular diseases (CVDs) and musculoskeletal diseases (MSDs) are two of the most abundant classes of chronic conditions in Western societies, putting a major toll on healthcare budgets. Present limited success in the management of CVDs and MSDs is a likely consequence of their multifactorial pathogenesis, where disease development is determined by environmental factors as well as individual susceptibility. Consequently, there are great expectations to novel approaches to tailored treatment forms. A

**Nanomedicine initiative**
The Lundbeck Foundation Nanomedicine Centre for Individualized Management of Tissue Damage and Regeneration (LUNA) has united and vastly expanded the nanomedicine research at iNANO, Aarhus University Hospital (AUH) and the Faculty of Health Sciences at Aarhus University (SUN). The centre, which is headed jointly by professor Allan Flyvbjerg (AUH) and professor Jørgen Kjems (iNANO), aims at improving the prevention, diagnostic and treatment of cardiovascular and musculoskeletal diseases through the development and implementation of novel nano-based techniques.

*Jørgen Kjems*
*Allan Flyvbjerg*

promising approach to meeting these expectations is the joining of forces with backgrounds in nanoscience and translational medicine to perform cross-disciplinary research collaborations.

## Restoring balance

Central to the research in the LUNA centre is the hypothesis that cardiovascular and musculoskeletal diseases are caused by an imbalance in tissue damage and the body's natural ability to repair or rebuild damaged tissues. Thus, an important part of the centre's work is focused on determining the underlying mechanisms causing these diseases, and, furthermore, the development of nano-based techniques to monitor and restore balance and stimulate tissue regeneration. The central hypothesis is that a group of newly discovered molecules ('pattern recognition molecules') plays a central role in the imbalance between tissue damage and the capacity for regeneration and in part explains differences in individual susceptibility to disease development (see Fig. 2). The projects are closely coordinated along four central themes: 1) Drug design and target validation, aiming at identifying key molecular mechanisms in pattern recognition and the functional states of complement proteins; 2) New bioimaging and drug delivery technologies, which will combine discoveries from theme 1) with the development of ligands and ligand-bound nano-carriers allowing in vivo detection by advanced molecular imaging techniques to provide improved diagnosis and drug targeting; 3) Cell-based therapy and 3D scaffold-based tissue engineering aimed at finding means of restoring tissue function after irreversible damage by controlling stem cell differentiation through specially designed nanoparticles and scaffolds (see Fig. 3); and 4) Translational research in animal models ensuring the parallel testing of promising antagonist/agonist, bioimaging and drug-delivery strategies and tissue engineering in relevant animal models to provide initial proof-of-concept for the development of novel therapies in humans. While the first two themes are headed by scientists at iNANO and themes three and four by scientist at AUH and SUN, six scientific meetings each year will ensure transparent and straightforward communications and exchanges of ideas contributing to the interrelationship of the themes.

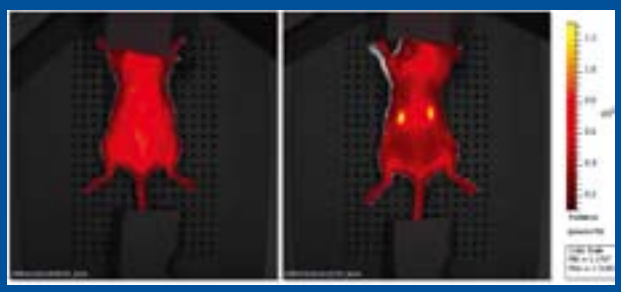
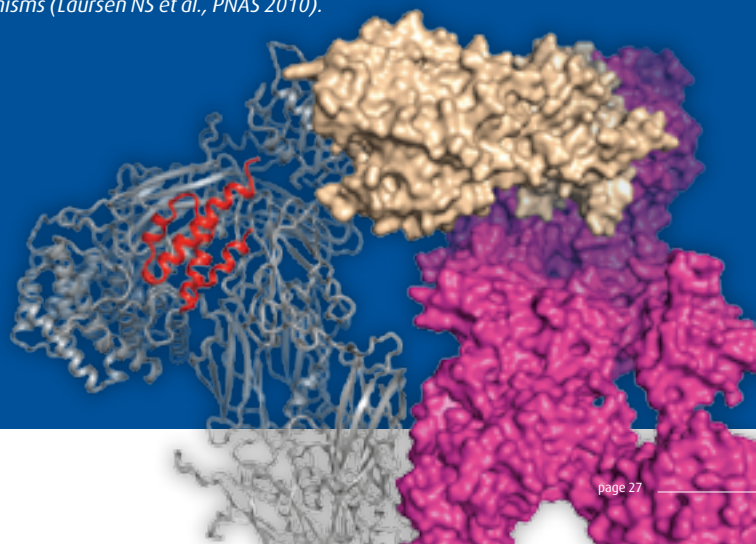


*Fig. 1. Fluorescence-labeled siRNA was encapsulated in nanoparticles and injected into the tail vein of mice. The mice were scanned by an IVIS 3D fluorescence bioimaging system at different time points after administration. The siRNA accumulated in the kidney 48 h post-injection as indicated by a strong fluorescence signal (right).*

*Fig. 2. Model representation of complement C5 (cartoon) being recognised by a proteolytic enzyme (lilac and sand colour surface) called C5 convertase, which is expressed upon stimulation of the complement system by foreign organisms (Laursen NS et al., PNAS 2010).*



# Nanomaterials for hydrogen storage

*Torben R. Jensen*

*By Torben R. Jensen*

The world is facing increasing energy demands, which may double within 25 years, and the present major energy source, fossil fuels, is a limited resource. Simultaneously, the atmospheric concentration of carbon dioxide is incontrovertibly increasing by as much as 2 ppm per year due to human energy production and may reach 550 ppm already in year 2030 (the level was 280 in 1970). Fossil fuels represent solar energy stored in the earth's crust for several hundred millions of years and all this will be burnt within ca. 200 years. Sequestration of $CO_2$ is simply impossible due to the huge amounts of $CO_2$ produced yearly, 21 gigatons in 2006 and possibly 40 gigatons in 2030. The environmental response to increasing levels of $CO_2$ remains uncertain; however, once released to the atmosphere there is no way to reduce the atmospheric levels of $CO_2$.

Renewable energy in the form of solar, wind, or wave energy is an alternative inexhaustible resource, but its utilization is hampered by its fluctuation in time and non-uniform geographical distribution. Hydrogen is an appealing solution as a safe, cheap and efficient energy carrier, and is receiving increasing political and scientific interest worldwide. Unfortunately, safe, efficient and economic storage of hydrogen, which would allow it to become the successor of gasoline, is still lacking. The aim of our research efforts is to find materials with the right combination of a high gravimetric hydrogen density, adequate hydrogen-dissociation energetic, reliability, and the low cost required for commercial vehicular application.

## Nanoporous materials

Nanomaterials science is expected to be a major future contributor of novel, clean and environmentally friendly energy technologies. Hydrogen is recognized as an ideal energy carrier, but its large-scale utilization is mainly hampered by the lack of materials with sufficient hydrogen storage properties. Therefore, we have introduced nano-confined reversible chemical reactions in order to improve the reversibility, stability and kinetics, and possibly also the thermodynamic properties, of the chemical reactions involved in the reversible release and uptake of hydrogen.

Nano-confinement is a new bottom-up approach, where hydride nanoparticles are synthesized or melt-infiltrated into an inert nanoporous scaffold material. This design has several benefits: (i) increased reactant surface area, (ii) nanoscale diffusion distances, and (iii) increased amount of grain boundaries, which facilitate the release and uptake of hydrogen and enhance the release and uptake kinetics.

## Synthesis and characterization of novel materials

Most of the known borohydrides have extreme hydrogen storage capacities, but unfortunately they also have limited reversibility and poor thermodynamic properties. In order to utilize the large storage capacity, we have prepared and characterized a wide range of novel metal borohydrides consisting of the less electropositive *d*-block metals and the more ionic

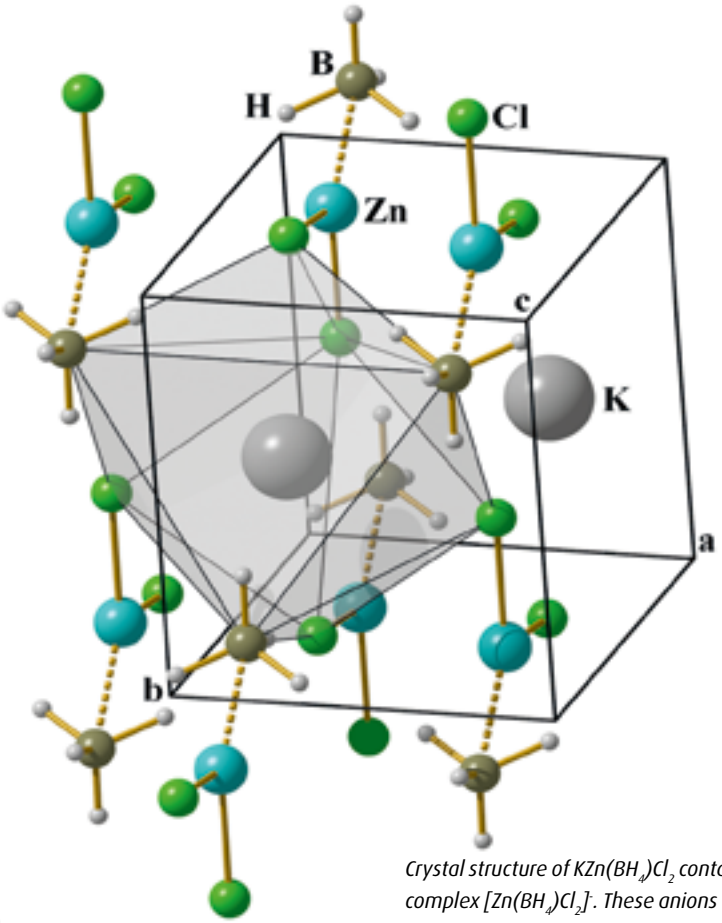

*Nanoparticles of $MgH_2$ and $LiBH_4$ are prepared in a nanoporous scaffold material, which can react and form LiH and $MgB_2$ and release hydrogen.*

A hydrogen society is often mentioned as a vision for the future. This is in fact a Danish idea and the first 'hydrogen society' was established at the Askov Folk High School (Askov Højskole) in 1895 by Poul la Cour. The basic idea is that hydrogen can store renewable energy chemically and facilitate integration of a range of different energy sources, such as wind, wave, water or solar energy. Secondly, hydrogen may allow renewable energy to be used for mobile applications. Note that transportation accounts for two-thirds and 20% of the total energy consumption in USA and Denmark, respectively. Hydrogen is up to now the only material with an energy storage potential and possible performance that may become similar to gasoline.

alkali borohydrides. Introduction of more covalent bonding into the ionic borohydrides strongly facilitates the release of hydrogen at lower temperatures. Furthermore, significant changes in the structures of the materials are observed, since the directionality of the bonding results in formation of more open and complex structures. For example, we have discovered a novel structure built from two interpenetrated 3D frameworks (see Fig. 1). This type of structural topology is normally only observed in metal-organic frameworks. Up to 30% of the structure in other novel structures is open space.

## Modification of physical and chemical properties by anion substitution

Modification of known materials is another promising approach. We have shown that the larger halides, $Cl^-$, $Br^-$, and $I^-$, readily substitute for the $BH_4^-$ complex anion, in contrast to fluorine, $F^-$, which can substitute for the hydride ion, $H^-$. Anion substitution clearly facilitates rehydrogenation of borohydride materials.




*Crystal structure of $KZn(BH_4)Cl_2$ containing the complex $[Zn(BH_4)Cl_2]^-$. These anions and an eight-fold coordination polyhedron for K atom are highlighted.*

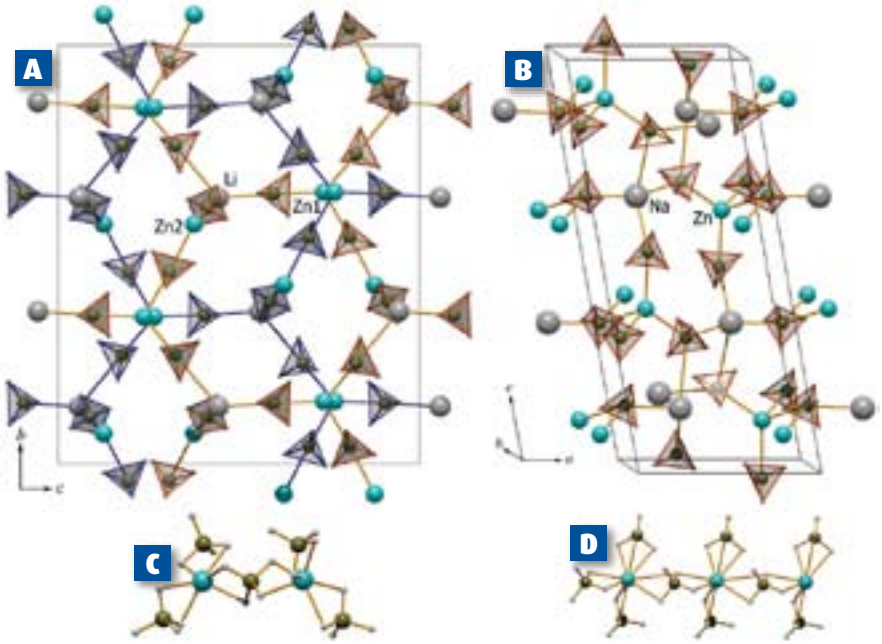



*Fig. 1. Crystal structures of (A) $LiZn_2(BH_4)_5$ and (B) $NaZn(BH_4)_3$. The doubly interpenetrated three-dimensional framework is highlighted in magenta and light brown. (C) $Zn^{2+}$ and $BH_4$ units are strongly associated into the isolated $[Zn_2(BH_4)_5]^-$ anions of trigonal planar coordinated Zn in the Zn-rich $MZn_2(BH_4)_5$ compounds. (D) The more alkaline metal-rich $NaZn(BH_4)_3$ contains 1D anionic $[Zn(BH_4)_3]_n^{n-}$ chains, with tetrahedrally coordinated Zn atoms. These structure types have not previously been observed for borohydrides.*

## References

*A Series of Mixed-Metal Borohydrides, D. Ravnsbæk, Y. Filinchuk, Y. Cerenius, H. J. Jakobsen, F. Besenbacher, J. Skibsted and T. R. Jensen, Angew. Chem. Int. Ed., 2009, 48, 6659–6663.*

*Confinement of MgH2 nanoclusters within nanoporous aerogel scaffold materials. T. K. Nielsen, K. Manickam, M. Hirscher, F. Besenbacher, T. R. Jensen. ACS nano, 2009, 3, 3521–3528.*

Materials of biology:

# Puzzles and inspiration

*Cross-section through the adhesion plug of the mussel Anomia showing a part of the complex three-dimensional arrangement of calcium carbonate crystals.*


*Crystals of calcium carbonate found in the adhesion plug of the mussel Anomia. The crystals are interconnected by a spider's web of organic material (e.g. seen just below the middle of the figure) that glues them together.*


*Through the looking glass: a view of bone showing bundles of mineralized collagen fibrils arranged around a 0.1 mm hole in this porous bone from chicken legs.*


*By Henrik Birkedal*

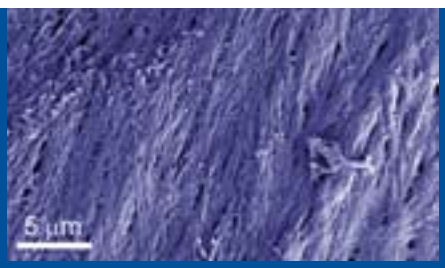
When you walk on the beach and see mussel shells on the sand you are in fact looking at an advanced nanotechnological material. As protection from predators, the mussel is encased in a shell of chalk and minute quantities of biological molecules that combine forces to yield a nano-structured, highly effective armour. Such biological materials are of immense interest because they represent solutions to important scientific and technological problems and because they are advanced nanomaterials made at room temperature and pressure – in stark contrast to our traditional energy intensive materials manufacturing methods. Motivated by these facts, we undertake research in biological materials and derive inspiration from these in order to develop new ways of making advanced nanomaterials.

## Staying put

Gluing different materials such as plastic and metal together is a difficult task, and doing it under water is even harder. However, several marine organisms have solved this technological challenge. One of them is the mussel Anomia. It stays put on pebbles or sea shells via a plug that extends out from a hole in the shell. The plug is made from inorganic crystals of calcium carbonate, the stuff of chalk, and organic material. The mussel controls the crystals' size, shape and position in three dimensions. It also controls the chemical composition of the crystals and which crystal type is formed: many substances occur in different crystal forms that are the same chemically, but have different arrangements of the constituent ions. In the plug, two calcium carbonate crystal forms - calcite and aragonite - are present, and their distribution is fully controlled by the mussel. This exquisite control over inorganic matter serves as inspiration for development of new functional nanomaterials. The animal uses the crystals to control the mechanical properties of the plug. Therefore, we measure the local hardness so that we can begin to understand how the different building blocks contribute to the mechanical performance of the plug. The next step in our research is to learn more about the organic components of the plug - the components involved in the actual glue. This will allow us to develop new synthetic glues that will contribute to solving the underwater adhesion problem.

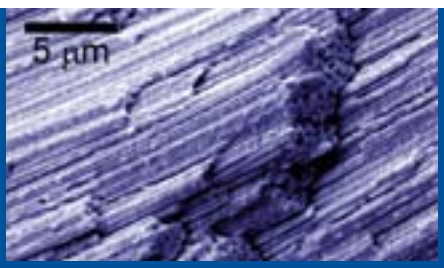
## Bones: we're all nanotechnologists!

Bone is the most keenly studied of the mineralized biological materials due to its medical importance. As people, fortunately, live longer and longer, diseases of the skeletal system will influence the quality of life to an ever-increasing degree. It is therefore necessary to understand how bone structure and properties are related to disease. Bone is essentially made from nanocrystals of a calcium phosphate mineral and collagen, the protein of skin and eyeballs. It also contains water and additional proteins, whose roles are not well understood. The nanocrystals decorate collagen




*Bone is a living tissue that is constantly being broken down and remade by specialized cells. In this close-up electron micrograph of a chicken bone, collagen fibres have been laid bare by the bone-breaking cells.*


*The sucker discs, marked in blue, of squid tentacles are teethed rings that display a tubular interior nanostructure.*




*The sucker discs of squid tentacles are teethed rings that display a tubular interior nanostructure, as shown in this image. Each tube is around 200 nm in diameter, and local modifications of the tube diameter are used to alter the local mechanical properties of the material.*

*Henrik Birkedal*

nanofibres to constitute the building blocks of bone which, in turn, are put together into structures at larger length scales, thus forming a hierarchy of structures – very much like how the Eiffel Tower is constructed from metal bars. We make experiments to understand bone nanostructure and mechanical properties. The former is done using advanced X-ray scattering techniques and electron microscopy. Much of this work is in interdisciplinary collaboration with medical doctors and other iNANO researchers, where we use state-of-the-art nanotechnological methods to shed new light on the influence of disease, fracture and drugs on bone structure and mechanics. This information will contribute towards the development of better bone treatments and thus increase the quality of life of the ageing population.

## Teethed suckers

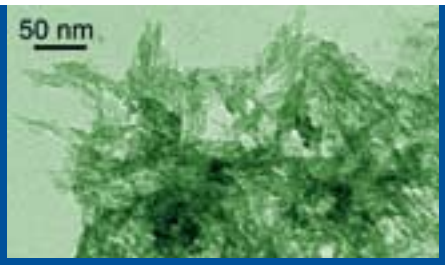
Some animals, such as insects, marine worms and squids, contain mineral-free hard parts. These biological materials illustrate how polymers can be used to make very advanced nanomaterials. We have recently discovered that squids use unique nanotubular structures to control the local stiffness of their sucker discs – the part of their suckers that penetrates into the skin of prey. Sucker discs are a bit like a bunch of garden hoses bunched together, just on a much smaller scale – the tubes are only about 200 nm in diameter. Sucker discs are made from protein and, most puzzling, do not contain chitin, the polysaccharide material used by, for example, crabs and even by the squid in its beak. The reason for this choice of construction material is at present unclear, but evidently this material shows us new ways of making advanced materials.

## Into the chemistry lab

The lessons we learn from the biological materials can be used to design and synthesize novel functional materials: the so-called bio-inspired materials. In our laboratory we are currently mostly focusing on controlling the size, shape and functionalization of calcium phosphate nanoparticles and how they can be assembled into hierarchical structures – that is how to make miniature Eiffel Towers. To excel at making new nanoparticles, we need to understand which parameters control their growth. To this end we used intense synchrotron X-rays to probe their growth process while it takes place.

To be able to make materials for e.g. bone replacement, we need to combine the nanoparticles with organic macromolecules. By controlling how the organic and inorganic components interact, we can now e.g. make very complex tubular structures composed of 95% inorganic minerals. These methods will pave the way to new functional materials of use in biomedical applications and, in the future, allow us to make many other functional nanomaterials by low-energy processes.


*In the laboratory, we can make synthetic components, which self-organize into hierarchical macroscopic structures with highly complex morphology.*




*Apatite nanocrystals synthesized in our laboratory are analogues to the nanocrystals found in bone. Here they are seen in the transmission electron microscope.*


*By controlling synthesis conditions, we can manipulate the size and shape of nanoparticles. The image is of apatite nanocrystals taken with the transmission electron microscope. The striations seen within the crystals reveal the underlying crystal lattice.*

Digestive enzymes from neglected species:

# Useful for food applications?

*Jan Johannes Enghild,*
*Tobias Wang,*
*Kristian Wejse Sangaard*

## Proteases – essential nanomachines

Proteases or proteolytic enzymes are essential components of the protein nanomachine toolbox. They are found in all living organisms and function by hydrolyzing peptide bonds. Proteases are involved in the life of other proteins all the way from synthesis to their demise, when they are degraded and recycled. Proteases thus have a cradle-to-grave relationship with all other proteins. Some proteases cleave, in a very specific manner, a single protein (substrate), while others degrade proteins in a more unspecific manner. Proteases are vital for the food and biotech industries and are used in a broad range of applications. The development of new and optimized protease properties for the different applications are achieved either by i) protein engineering based on known proteases or ii) the identification of completely new proteases. In this project we will focus on the last approach. Instead of building our own nanomachines we will take advantaged of nature, where evolution has optimized proteases for millions of years for particular tasks. The approach will be interdisciplinary and include state-of-the-art nanotechnology.

**Protein-degrading enzymes are among the best-selling industrial enzymes worldwide, with applications ranging from washing powder additives to cheese production. "Neglected species" refers to the vast majority of species that, so far, have not been characterized at any molecular level, let alone with regard to their protein degrading capabilities. Hence, there is great industrial interest in the identification of protein-degrading enzymes with unusual properties.**

*By Kristian Wejse Sangaard, Tobias Wang and Jan Johannes Enghild*

While spending a weekend at the North Carolina coastline in 1995, Jan Johannes Enghild, at that time a protein chemist at Duke University, found some unusual plants that resemble miniature "fox traps", designed to entrap insects, which are then slowly digested. This carnivorous lifestyle provides the plant with precious nitrogenous compounds, which is in shortage in many ecosystems.

Jan had studied protein-degrading enzymes, proteases, for several years, and the plants' interesting ability to kill and digest insects triggered his curiosity: Which enzymes could be involved? Would they resemble human digestive enzymes, such as trypsin or pepsin? Or, could new and undiscovered mechanisms be at stake? Jan decided to pursue these questions as a small research project in his laboratory at Duke, where he maintained a few plants in a terrarium. It was not straightforward, however, because the tools available at the time were not sufficiently sensitive to detect the minute amounts of enzyme in the precious few droplets of digestive fluid secreted by the leaves when digesting a fly. Moreover, proteins originating from the fly contaminated the digestive enzymes produced by the plant, making the identification of the plant-derived enzymes very difficult.

When Jan returned to Aarhus University (AU) as a professor at the Department of Molecular Biology and the Interdisciplinary Nanoscience Center (iNANO), de novo mass-spectrometry-based protein sequence analysis had become sufficiently sensitive to detect minute amounts of individual proteins even in complex mixtures. Jan devised a technique to stimulate secretion of digestion fluid through prey lookalikes. The breakthrough for the Venus Flytrap was a minute magnetic sphere, which moves continuously under the influence of a moving magnet field, a standard piece of equipment in all wet-labs. This tricks the plant into responding as if it had caught an animal and it begins to secrete digestive fluid. In the meantime, Jan had started to collaborate on similar topics with professor Tobias Wang, a zoophysiologist at the Department of Biology, AU, studying digestive physiologies of python snakes and spiders. These animals clearly possess an impressive ability to dismantle their prey.

The Danish Council for Strategic Research (DSF) has now elected this project for funding. DKK 24 million have been granted to a strategic alliance between Aarhus University, the University of Copenhagen and the Technical University of Denmark, and with partners Danisco A/S and Novozymes A/S, two of the world's largest enzyme producers, the food company Arla Foods amba, and research institutions in Finland, Poland, Brazil and China. The interdisciplinary research consortium carries the title "Novel enzymes of industrial relevance: specialised proteolytic enzymes for release of new bioactive peptides (NOVENIA)" and will be headed by Jan Johannes Enghild. Its aim is to identify new enzymes from snakes, spiders, carnivorous plants and cold-adapted microbiological communities for use in food applications, such as dairy processes in cheese-making and yogurt production, animal feed preparation, and production of bioactive peptides. Very little is known about enzymes in these diverse and specialized systems, and enzymatic solutions, adapted to these unusual environments, will hopefully allow the protein chemists to deduce general strategies for designing enzymes with relevant profiles.

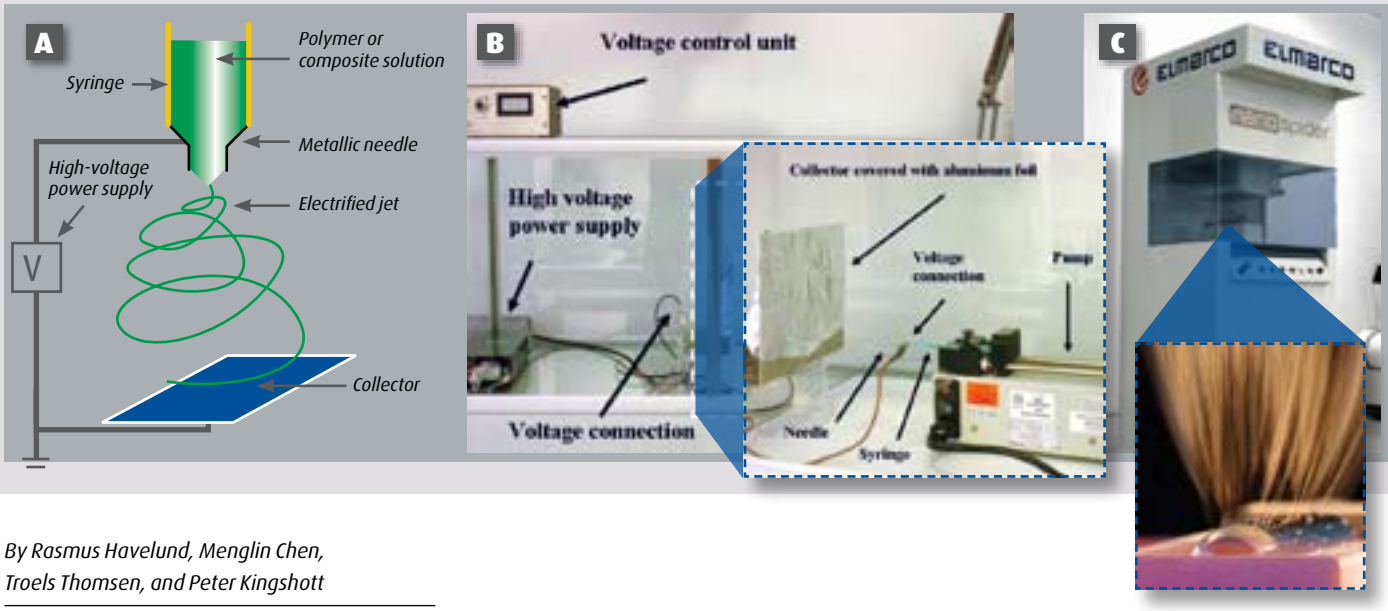
NOVENIA will use a wide range of modern discovery tools, including metagenomics, bioinformatics and proteomics. One of the project partners, associate professor Peter Stougaard, a microbiologist at the University of Copenhagen, is planning to sequence the "metagenome" of microbial communities from the Ikka Fjord in Greenland in the laboratory of another project partner, professor Søren Sørensen of the University of Copenhagen. This sequencing, combined with supercomputer-based predictive models developed by a third project partner, associate professor Thomas Sicheritz-Ponten of the Technical University of Denmark, will enable the hunt for "cold zymes", enzymes adapted to permanently low temperatures.

In addition to the isolation of new enzymes, substantial efforts will be devoted to characterizing the bioactive peptides released by these enzymes. Such peptides often have beneficial health effects such as hypotensive, antioxidant, antimicrobial, and immune-stimulating bioactivities. Project partners associate professor Jeanette Otte, a food scientist from the University of Copenhagen, and Finnish MTT Biotechnology will document these effects.

Further down the line, nanotechnology-based encapsulation and immobilization techniques will optimize the stability of enzymes, ensuring their behaviour as renewable catalysts. These initiatives will provide the grounds for new generations of enzymes.

New spin on nano:

# From the nanoscience lab to market in four years




*By Rasmus Havelund, Menglin Chen, Troels Thomsen, and Peter Kingshott*

One of the most magnificent things in the natural world is the ability of spiders to spin webs made of fibres just a few micrometers thick. The variations in design and functionality are mind-boggling. We at iNANO are in the middle of a project that utilizes a very simple method for spinning our own fibres. We wish we could do it as perfectly as our eight-legged friends, but instead we have our own version, which is called electrospinning (Fig. 1A), and the fibres have nanometer dimensions.

Electrospinning uses an electric field to draw fibres from a liquid reservoir containing material (typically a polymer) that you wish to make the fibres from (Fig. 1A). The fibres accumulate on a collector a few centimetres away from the syringe holding the polymer reservoir (Fig. 1B). The textile material produced consists of fibres with diameters tunable from 10 µm to 10 nm, depending on the conditions of the spinning. The advantages of nano-fibres are the extremely large surface area achieved (several orders of magnitude higher than conventional non-woven textiles), low volumes of material used, barrier properties and all-round versatility with many polymers that can be spun. There are many different structures that can be made by electrospinning, including porous fibres, aligned fibres, fibres with functional additives, new surfaces, hollow and core-shell fibres, multi-layer fibres; the list goes on, all with different features suiting your intended function.

The project is funded by the Danish National Advanced Technology Foundation and has Fibretex A/S as the industry partner, with iNANO and Aalborg University as the academic and educational partners. The main research interest of Fibretex A/S in nano-fibres is filtration, in particular air and noise filtration; however, liquid filtration is also on the R&D agenda. They utilize the commercial Nanospider (Fig. 1C) to produce semi-large-scale nano-fibres ($m^2$) from new functionalized nano-fibre recipes developed at iNANO using our lab-scale spinning apparatus. Fibretex A/S is now already selling new nano-fibre products to a few customers in Denmark and globally: what a success!

The success is not only commercial. We have managed to publish more than 20 articles in high-ranking international journals, generated a handful of patents, and educated several graduate and numerous undergraduate students, as well as given postdocs the opportunity to develop their careers.

Our ambitions at iNANO with nano-fibres are visionary on account of the huge number of potential application areas for nano-fibres. We see opportunities for commercial success beyond the current project in the energy, environment and medical sectors. For example, we see liquid filtration as an opportunity in waste-water treatment and in the biotechnology sector; there are possibilities for using nano-fibres in fuel cells; antibacterial and anti-inflammatory nano-fibres could be alternative wound dressings or coatings for medical prostheses; nano-fibres can be used as scaffolds for tissue-engineering applications or even vehicles for drug delivery; and we are even considering using them for chemical sensors and biosensors.

One of the keys to our success is exploitation of the state-of-the-art analytical instrumentation available at iNANO. We are interested in incorporating functional additives into the surface of nano-fibres to filter organic molecules from solutions, for example. The efficiency of nano-fibres at removing molecules is heavily dependent on the presence of capturing molecules at the surface. The only way of seeing these molecules, quantifying how many are present at the surface and determining their distribution is to use highly surface-sensitive and specific nano characterization tools. We use X-ray photoelectron spectroscopy (XPS) and time-of-flight secondary ion mass spectrometry (ToF-SIMS). Funding for these instruments came from Aarhus University to support this project. XPS tells us how many molecules are present by determining the elemental composition, and ToF-SIMS identifies them from their molecular structures and can be used to map their distribution on the surface of individual fibres.

Examples of our results are shown in Fig. 2. We take pictures using scanning electron microscopy (SEM) to verify that we actually have nano-fibres, since they are too small to see in a normal micro-

*Rasmus Havelund,*
*Peter Kingshott,*
*Menglin Chen,*
*Troels Thomsen*

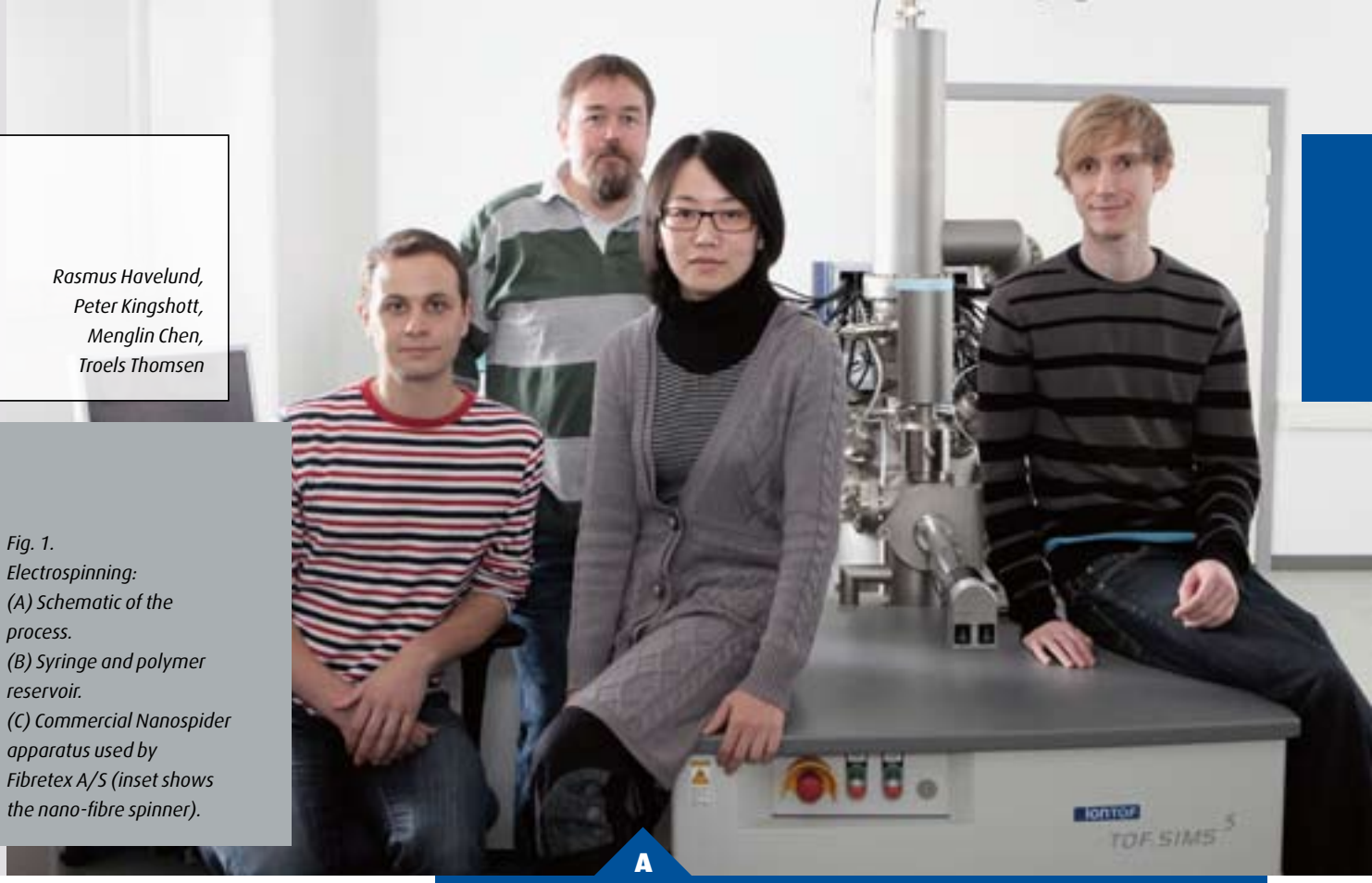
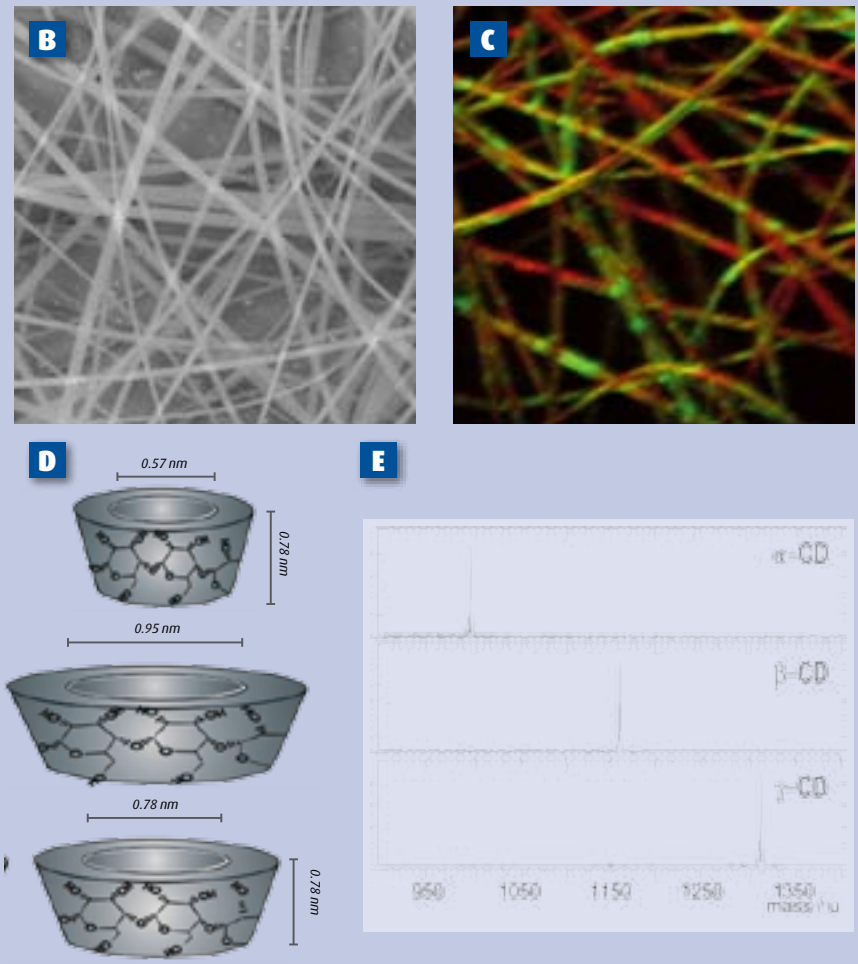



*Fig. 1.*
*Electrospinning:*
*(A) Schematic of the process.*
*(B) Syringe and polymer reservoir.*
*(C) Commercial Nanospider apparatus used by Fibretex A/S (inset shows the nano-fibre spinner).*

A

*Fig. 2. Surface analysis of nano-fibres: A) The ToF-SIMS instrument and the group who use it. B) SEM image of a typical mat of fibres. C) Corresponding ToF-SIMS chemical maps. D) Structures of the cyclodextrin (CD) molecules used as functional additives. E) Mass spectra showing the detection of the chemical structures on the fibre surfaces.*




scope (Fig. 2B). The fibres are then analysed using the powerful ToF-SIMS instrument (Fig. 2A), which generates chemical maps of the individual fibres and provides information about the distribution of chemical species in the outer 1-2 nm of the fibre surface (Fig. 2C). The red colour represents the polymer (in this case polystyrene) and the green shows where the functional molecules are located. The molecules we use are different types of cyclodextrins (CDs) (Fig. 2C). CDs bind to small molecules that get trapped in their hydrophobic core when exposed to aqueous solutions. Prior to chemical mapping we identify their presence from individual mass spectra (Fig. 2E).

The combination of simple fabrication methods and advanced surface nano-tools helps us fast-track the development of nano-fibres: an approach that is beneficial to all parties in the project. We envisage maintaining this approach in future nano-fibre projects.

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T. Uyar, P. Kingshott, F. Besenbacher (2008): Electrospinning of Cyclodextrin Pseudopolyrotaxane Nanofibres, Angew. Chem. Int. Ed. 47, 9108-9111.

# Intervening with cancer metastasis

*Jørgen Kjems,*
*Peter Andreasen,*
*Niels Christian Nielsen*

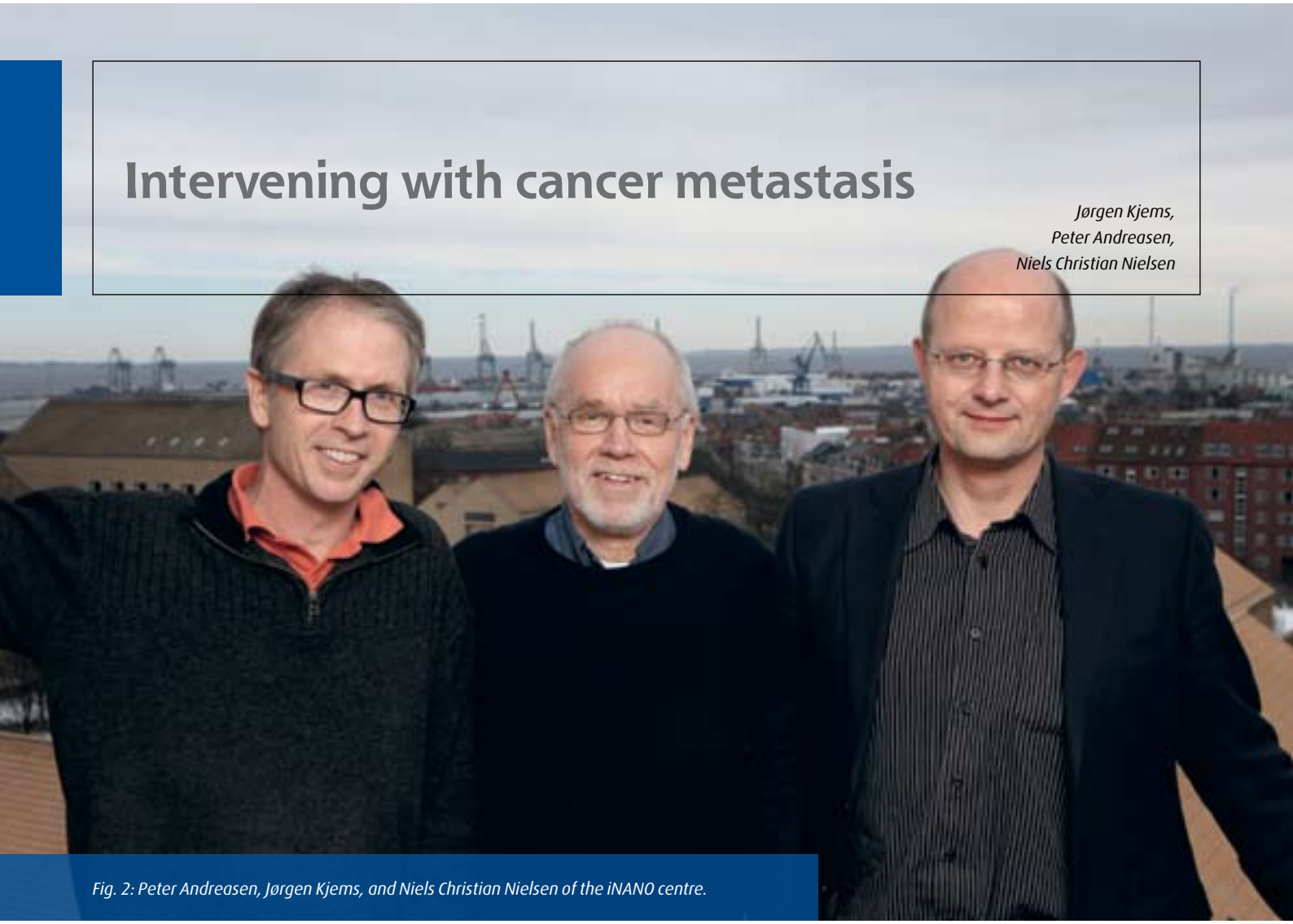


*Fig. 2: Peter Andreasen, Jørgen Kjems, and Niels Christian Nielsen of the iNANO centre.*

**Researchers from the Interdisciplinary Nanoscience Center (iNANO) contribute strongly to a new Danish-Chinese cancer research collaboration. The aim of the Danish-Chinese Centre for Proteases and Cancer is to establish new methods for predicting the prognosis of cancers and to provide new treatment possibilities, among others things by using new methods in molecular imaging.**

*By Peter A. Andreasen*

For the foreseeable future, patients will continue coming to hospital with cancerous tumours, which will be removed surgically. In some cases, the surgery will have cured the patient. In other cases, the cancer cells will have spread in the body of the patient and formed metastases already at the time of diagnosis. It is the metastases that may eventually kill the patient. Patients at risk of having metastases at the time of surgery should therefore be given adjuvant treatment to prevent growth and further spread of the cancer cells. The problem is that the metastases are most often not detectable at the time of diagnosis. How does one distinguish between cured patients and patients at risk of recurrence of the disease? Planning post-surgery treatment is currently a major challenge in oncology. And if metastases do eventually become clinically manifest later, how are they best treated?

The iNANO centre provides an excellent environment for contributing to solving these problems. Ideally, the prediction of the need for adjuvant therapy should be based on molecular analysis of the primary tumour and/or blood samples. A variety of molecules has been found to be of interest as prognostic markers. Of particular interest are enzymes catalyzing the degradation of proteins, the so-called proteases. Proteases, together with various co-operating factors, cause degradation of the normal tissue surrounding the cancer cells and enable them to invade normal tissue and spread in the body. About twenty years ago, Joe Duffy (St. Vincent's University Hospital, Dublin) and Peter Andreasen (Aarhus University) discovered that high tumour levels of components of one such protease system, the plasminogen activation system, are strong markers for a poor prognosis and can be used to select patients for adjuvant therapy (Fig. 1). This important finding has later been documented by research in many laboratories around the world. In fact, the American Society for Clinical Oncology now recommends measurements of this protease system for evaluating prognosis and treatment possibilities for breast cancer patients. Moreover, much evidence supports the idea that inhibition of proteases can be used to inhibit growth and spread of cancer cells. An important aspect is to develop methods for characterizing metastases with respect to their content of specific protein-degrading proteases. The availability of specific inhibitors will then allow intervention with exactly the proteases present in the metastases of individual patients, thus making

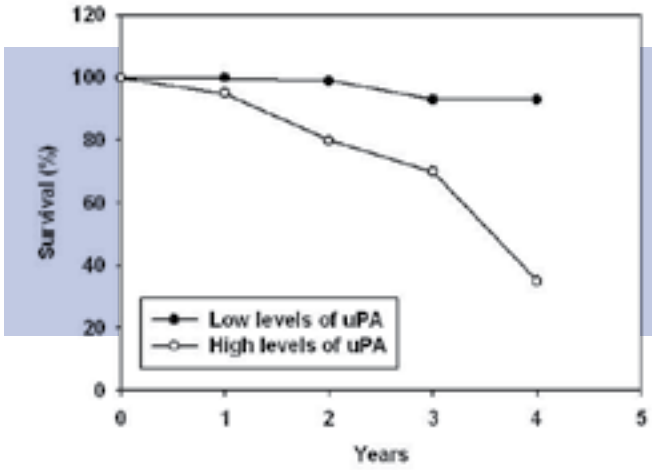



*Fig. 1. The level of a protease, urokinase-type plasminogen activator (uPA), in breast tumours as a prognostic marker. Patients were divided into two groups according to the level of uPA in their tumour. Survival was plotted against time since diagnosis for each group.*

*Fig. 3: Henrik Gardsvoll, Michael Ploug, Mingdong Huang and Benedikte Jacobsen discuss X-ray crystal structure analysis results.*

an important contribution to an optimal individualized treatment.

This is exactly where the instrumentation and expertises of the iNANO centre come in. With the purpose of promoting such research, the Danish National Research Foundation and the National Natural Science Foundation of China have decided to support a virtual research centre formed by the research groups of Mingdong Huang, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, Fuzhou; Dongxu Liu, Faculty of Life Sciences, Hubei University, Wuhan; Michael Ploug, Niels Behrendt, and Andreas Kjær, Copenhagen University Hospital; Peter Andreasen, Jørgen Kjems, and Niels Christian Nielsen, members of the iNANO centre at Aarhus (Fig. 2 and Fig. 3). The work of the Danish-Chinese Centre for Proteases and Cancer focuses on finding new types of protease inhibitors based on the three-dimensional structure of the protease-inhibitor complexes (see Fig. 3), and testing the inhibitors in animal tumour models. The researchers at Aarhus have strong expertise in isolating new types of inhibitors, including peptides and RNA aptamers, by a molecular biological strategy called "directed evolution". The Chinese researchers have a strong expertise in characterizing protease-inhibitor complexes using X-ray crystal structure determination. And the iNANO centre has the potential to make a particularly strong contribution to the development of non-invasive imaging techniques for detecting specific proteases in metastases. The idea is to couple specific protease inhibitors to probes that can be visualized by magnetic resonance imaging (MRI), positron-emission tomography (PET), or optical methods. Binding inhibitors to the proteases will thereby direct the probes to cancerous tissue containing the proteases in question. The challenge is to achieve sufficient specificity, sensitivity, and resolution. The 16-Tesla magnet of Niels Christian Nielsen's research group provides the maximal sensitivity for MRI and can be used for visualizing ferric oxide nanoparticles and 19F-labelled RNA aptamers and peptides. A newly acquired IVIS spectrum instrument will allow imaging of fluorescent or bioluminescent probes. These imaging methods are currently being tested on animals with experimental tumours. Overall, the combination of basic molecular characterization of these protease systems with modern methods of molecular imaging may eventually result in improved treatment possibilities for cancer patients.

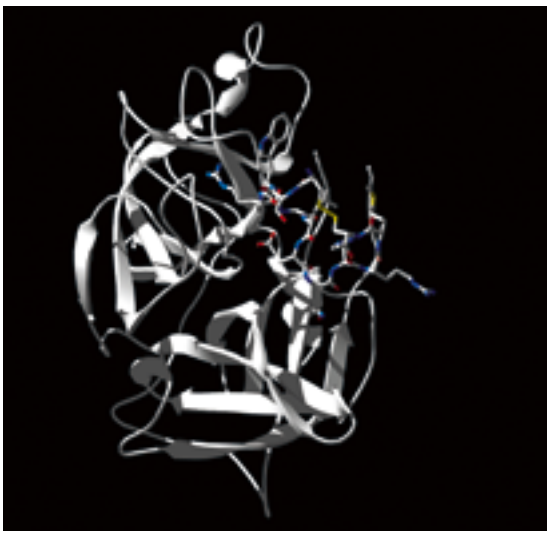


*Fig. 4: The three-dimensional structure of of an inhibitor (shown as sticks) bound to the active site of a proteolytic enzyme (urokinase-type plasminogen activator; shown as ribbons). The structure was determined by the laboratory of Mingdong Huang at the Chinese Academy of Sciences, Fujian Institute of Research on the Structure of Matter, Fuzhou, China, by X-ray crystal structure analysis.*

# Sino-Danish collaboration on molecular self-assembly


*Kurt Vesterager Gothelf, Flemming Besenbacher, Mingdong Dong, Trolle Linderoth, Bjørk Hammer, Peter Thostrup, Jørgen Kjems, Christian Bombis*

**iNANO now houses a new Sino-Danish National Research Foundation centre, "Self-assembly and Function of Molecular Nanostructures on Surfaces". The centre explores and exploits interactions at the molecular level to provide insight into molecular mechanisms of self-assembly and chemical reactions at surfaces, thereby enabling the design of artificial self-assembled structures with desired properties and functions.**

*By Peter Thostrup and Trolle R. Linderoth*

The joint Sino-Danish effort was kick-started in September 2009 with a mini-symposium held in beautiful Fragrant Hills, a short drive from Beijing. The symposium was graced by the presence of an internationally renowned personality in the field of self-assembly, Paul Weiss, new director of UCLA California NanoSystems Institute.

The Sino-Danish Research Center is a collaboration between iNANO and three Chinese elite research institutions: the National Center for Nanoscience and Technology (NCNST), Peking University and Tsinghua University, all located in Beijing.

Self-assembly is a crucial concept in nanoscience and nanotechnology, where functional nanostructures in one, two and three dimensions are formed cheaply and effectively by taking inspiration from nature's ability to build in a "bottom-up" fashion by exploiting recognition forces between specially designed molecular building blocks.

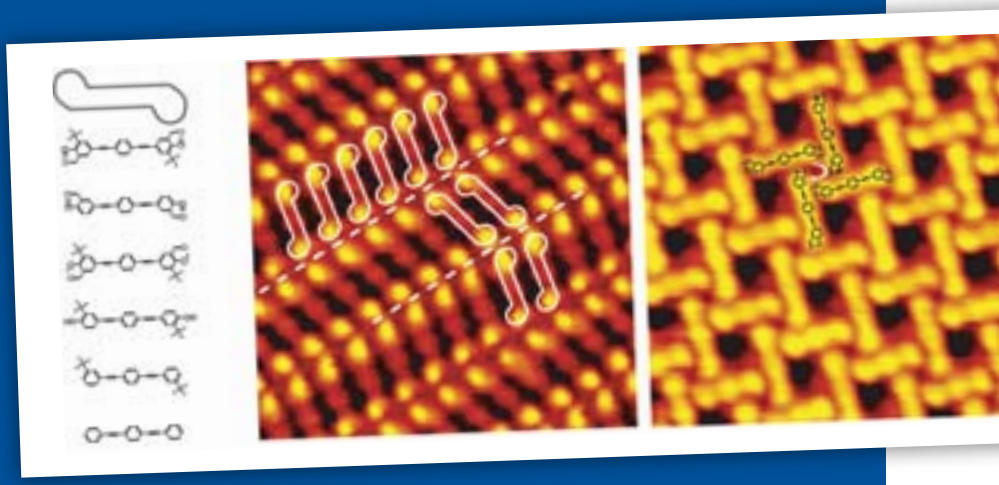
The activities at the centre will focus on synthesis and characterization of molecular nanostructures on surfaces, and the Chinese and Danish research groups involved have complementary competences within this area of research. In particular, groups with world-leading expertise in the use of special and advanced scanning probe microscopes will work at the centre. The scanning probe instruments make it possible to image surfaces by scanning over them with a sharp needle, and a remarkable resolution can be attained, allowing individual atoms and molecules to be observed. Additionally, the centre encompasses world-leading experts in chemical synthesis of new molecular building blocks, molecular biology and computer modelling. The projects at the centre will lead to new fundamental insights regarding molecular self-assembly and provide new principles for the formation of robust molecular nanostructures on surfaces. Molecular nanostructures with advanced functions will be developed, for instance within areas such as chemical recognition, chirality, and magnetism, and their properties will be exploited in a number of potential application areas, such as biochemical sensors.

The centre will be a facilitator for valuable transfer of knowledge and exchange of talented younger researchers between the Danish and Chinese research environments. In a wider perspective, the centre's research will form a central part of the research themes that will constitute the core activity of the Sino-Danish Center for Education and Research (SDC), which is presently being planned in collaboration between the Danish Ministry of Science, Technology and Innovation, Danish Universities and the Graduate

The new centre has also sparked the interest of the Chinese Ambassador to Denmark, His Excellency Hangsheng Xie, who paid a visit to iNANO at the beginning of 2010. On the programme was a videoconference with the Chinese partners who gave a presentation of the centre.

## What is self-assembly?

*Self-assembly is the process by which complex objects form by spontaneous association of their constituent parts. Self-assembly is of central importance to the "bottom-up" approach, which promises a cheap and efficient route to synthesizing functional nanostructures from fundamental building blocks, in contrast to the more expensive and technologically demanding "top-down" approach applied for instance in today's semiconductor industry. Understanding and exploiting the principles of self-assembly is therefore one of the key challenges within the area of nanoscience and nanotechnology. Molecular self-assembly is controlled by specific interactions such as hydrogen bonding, van der Waals forces, or coordination between molecular species that lead to supra-molecular aggregates with a well-defined architecture determined by the functional properties of the molecular building blocks. The concepts of molecular self-assembly and molecular self-organization are central in the realms of biophysics and biochemistry, and the ultimate source of inspiration towards formation of artificial self-assembled structures is the way living matter is organized at the nanometre scale, where biomolecular building blocks such as proteins or DNA strands are formed and function through intermolecular recognition events.*



Self-assembled molecular structures on a gold surface observed by scanning tunneling microscopy. The images show examples of structures that differ with respect to chirality or "handedness". While the structure to the left is highly symmetric, exhibiting the indicated mirror planes, the structure to the right has a chiral organization of the molecular backbones and would differ from its mirror image. The images are taken from a paper, published in ACS NANO by Kurt Gothelf, Trolle Linderoth and co-workers, in which chemical synthesis of the family of molecules shown is combined with in situ surface self-assembly and STM characterization to show how organizational and conformational surface chirality can be steered by controlling molecular chemical functionality. Elucidation and control of chiral adsorption phenomena is one of the targets of the joint Sino-Danish Center on Molecular Self-assembly.

University of Chinese Academy of Sciences (GUCAS).

iNANO researchers include Bjørk Hammer, Flemming Besenbacher, Trolle Linderoth, Jørgen Kjems and Kurt Vestager Gothelf. The Chinese researchers come from the Chinese National Centre for Nanoscience and Technology (http://english.nanoctr.cas.cn) (Chen Wang), Peking University (Kai Wu) and Tsinghua University (Yan-Mei Li).

The website of the joint Sino-Danish Research Center is: http://www.inano.au.dk/research/research-areas/sino-danish-research-center

*Danish and Chinese researchers attending the inauguration symposium in front of a Buddhist temple in beautiful Fragrant Hills, Beijing.*

# iNANO and industry

## Message from the Chairman

This will be my last message as chairman of the iNANO board because the chairmanship was transferred to Bjerne Clausen, director of the Technology Division of Haldor Topsøe A/S, on 6 January 2010. I have been chairman of the iNANO board since 2004 and this is a good time to see a change of leadership and the introduction of fresh ideas.

## The evolution of iNANO

I would like to use this opportunity to express my admiration for the iNANO organization and especially the way in which it has continually developed over the years. In fact, I have been on the board since the very beginning in 2002, so I can safely say that iNANO from its inauguration has developed into a global player and is recognized worldwide for its eminent science.

At the same time, excellent programmes in undergraduate and postgraduate education have been established and the number of students has been consolidated at a satisfactory high level. Furthermore, the drop-out rate has been kept low thanks to focused follow-up measures.
I attribute these successes, first of all, to the skills of the people involved, but also to iNANO's loyalty towards its stated mission of promoting excellent interdisciplinary education, research, and innovation. The interdisciplinary aspect is an integral part of all nanoscience and nanotechnology, and Aarhus University happens to be the perfect venue in which such collaborative ambition can to come to fruition. Visionary leadership, flat hierarchy, open dialogue and sympathetic department heads and deans have come together to break down barriers and help iNANO reach its current status.

## Research and innovation

Ever since its pioneering days in 2002, iNANO has been particularly successful in attracting research grants from many sources: the EU, the Danish Strategic Research Council, the Danish National Advanced Technology Foundation, and from private donors. Most of these donors require their funded projects to have real and direct involvement from industrial companies. Research and education have always been strongholds at iNANO so, as chairman of the board and coming from Danish industry, I have seen it as one of my most important jobs to encourage and help build up innovation and technology transfer mechanisms at iNANO. This has been a few years in the making, since there was little tradition at Aarhus University for bringing innovation into focus.

With the help of experienced players in the field, such as organizations in the local innovation environment, and to my great pleasure, recent years have seen growth in the number of iNANO patents and the creation of start-up companies with an iNANO research and patent portfolio. As examples, I need only mention the two new companies created in 2009: CABRA A/S and Nanoference.

Congratulations on the results so far and good luck to you all going forward!

Hans Jørgen Pedersen
Chairman of the iNANO board


MERCK SERONO
fertin
Fresenius Kabi
H2 Logic
WIDEX
Roche
iPHT Jena
malegra
qsense
oticon
ALFA LAVAL
AstraZeneca
Elkem
Danfoss BIONICS
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Ibsen
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TEKNOLOGISK INSTITUT
Arla FOODS
AAK
Vipergen
SYSTEMATIC
NKT Photonics
RiNA
DANISCO
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chewtech
Danfoss
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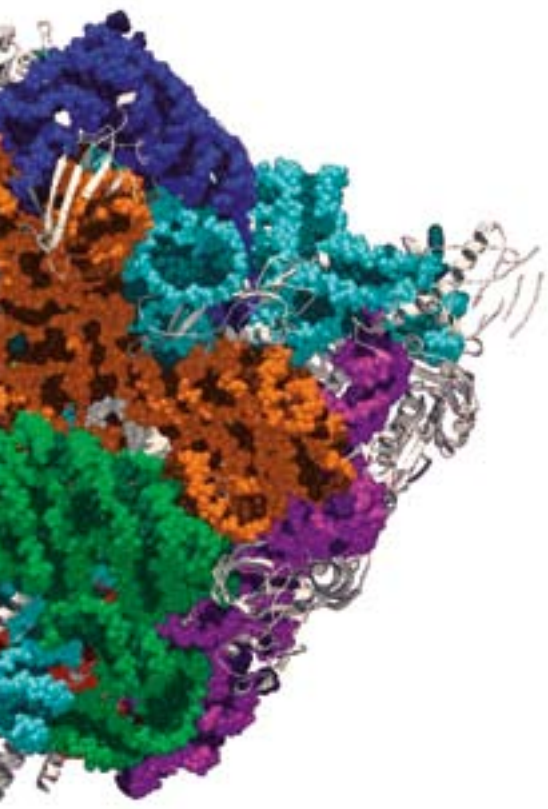
BILWINCO
Gerstenberg Schröder
FERRING PHARMACEUTICALS
Novosense
sanofi aventis
VARIAN
Vestas

# 2009 Highlights

## Awards and recognitions

**Again in 2009, iNANO scientists were the recipients of an impressive number of awards and appointments due to their spectacular research results, which also created widespread interest and exposure in the media.**



### DNA nano-box named research breakthrough of the year

The Danish magazine Året Rundt (The Year Round), published each year with the year-end edition of Ingeniøren (the Danish engineering journal), elected the DNA nano-box (detailed elsewhere in this report) as "2009 research breakthrough of the year" in science and technology. The scientists behind the DNA nano-box are from the Danish National Research Foundation's Centre for DNA Nanotechnology (CDNA), which is managed under iNANO. The DNA nano-box was described in a May issue of the journal Nature.

### Professor Bo Brummerstedt Iversen awarded the Danish Academy of Sciences' Industry Prize

The Danish Academy of Sciences and Letters' Industry Prize is awarded to a scientist who has made a special effort in facilitating collaboration between academia and Danish industry. The 2009 prize was awarded to iNANO professor Bo Brummerstedt Iversen, who is the director of the Centre for Energy Materials, funded by the Danish National Research Foundation, and of the Center for Materials Crystallography, funded by the Danish Strategic Research Council. Both centres are located at Aarhus University and managed under iNANO.

### Jørgen Kjems, professor and iNANO vice-director, receives the Danish Association of Masters and PhDs' Research Award

On 24 November, the Danish Association of Masters and PhDs' Research Award 2009 was given to professor Jørgen Kjems of iNANO Center and Department of Molecular Biology at Aarhus University. Jørgen Kjems was awarded the prize for his outstanding basic research and his ability to communicate complicated scientific concepts to the public.

### iNANO professor Daniel Otzen receives the Alzheimer Award

Professor Daniel Otzen from iNANO and the Center of Insoluble Proteins (inSPIN), also funded by the Danish National Research Foundation, received the 2009 Alzheimer Award in recognition of his research efforts on protein structure and on the causes of protein misfolding, when proteins do not fold correctly, with serious consequences, including potential development of many well known diseases.

### iNANO professor Bjørk Hammer wins elite-researcher award

One of the five 2009 EliteForsk (elite researcher) awards was won by Bjørk Hammer, iNANO professor in theoretical solid-state physics. The EliteForsk Prize is awarded to support and strengthen Denmark's very best and most talented researchers.

### Flemming Besenbacher receives local industry award

In recognition of Flemming Besenbacher's strong commitment to industry-university collaboration in the area of nanotechnology, the trade association "Erhverv Aarhus" awarded its prestigious 2009 Industry prize to the iNANO director.

### iNANO senior researcher Jeppe Vang Lauritsen receives ERC Award

In 2009 iNANO scientist Jeppe Vang Lauritsen was awarded one of the highly prestigious European Research Council awards. The European Research Council awarded Jeppe Vang Lauritsen a research grant with the title "Understanding the Atomic Scale Synergies of Catalytically Active Metal Nanoclusters on Oxide Surfaces". The five-year ERC grant is a recognition of and support for Europe's best young researchers, allowing them to start their own independent research group.

# Appointments

In 2009, several iNANO PhD students were recognized with important prizes. This underscores the high level of iNANO students. Among the awards were:

## EliteForsk travel award to Kasper Jahn

Kasper Jahn has won the EliteForsk travel award for his research on the application of DNA self-assembly chemistry for bringing together proteins and metal particles at the nano-scale.

## Professor Wei Xu awarded the PhD Prize of the Danish Academy of Natural Sciences

In recognition of his outstanding PhD thesis, the Danish Academy of Natural Sciences awarded the Academy's PhD prize to professor Wei Xu. Wei Xu has a PhD from iNANO and is now professor at the College of Materials Science and Engineering, Tongji University, China.

## iNANO students win Grundfos Challenge Engineering Prize

Three iNANO PhD students, Louis Nilsson, Marie Østergaard Pedersen and Rasmus Schöler, won the Grundfos Challenge Engineering Prize. They received the award for their innovative "WaterWindows" idea, where the vision is to collect solar energy and reduce air condition costs by circulating water in windows. This is the third year in a row that the participating iNANO team won a prize at the Grundfos Challenge.

## iNANO director Flemming Besenbacher appointed Einstein professor of Chinese Academy of Sciences

As the first Dane, professor Flemming Besenbacher has been appointed as "Einstein professor" of the Chinese Academy of Sciences. Since 2005 the Einstein professorship has been annually awarded to 10-15 internationally recognized scientists, including several Nobel Laureates. The purpose of the award is to strengthen the cooperation between Chinese research institutions and internationally recognized scientists.

## Professor Flemming Besenbacher appointed Fellow and elected member of the board of directors of the Materials Research Society

The title of Fellow is given to researchers who have published outstanding research results within materials research. Each year the title is bestowed upon the 0.2% of the best members of the Materials Research Society (MRS). One of only three Europeans, Besenbacher was also elected member of the MRS board of directors. American MRS is the world's prime society for materials research with more than 16,000 members.

## Dr Martin Kussmann appointed adjunct honorary professor in interdisciplinary nano and nutritional science

In October 2009 Dr Martin Kussmann, group leader of functional genomics, Nestlé Research Center, Switzerland, was appointed adjunct professor in interdisciplinary nano and nutritional science at Aarhus University. Martin Kussmann's research at the Nestlé Research Center integrates genomics, transcriptomics, proteomics, genetics and bioinformatics applied on nutritional sciences. The appointment of Martin Kussmann strengthens the relations of iNANO to industry and iNANO's profile in nutritional science.

# Colloquia

**This year we have chosen not to include the lists of iNANO publications and specialized iNANO lectures.**

**Both lists can be found at our homepage:**

**Pulications 2009:**

**http://www.inano.au.dk/research/publications/2009/**

**Specialized lectures 2009:**

**http://www.inano.au.dk/news-events/specialized-inano-lectures/previous-specialized-lectures-2009/**

## iNANO Annual Meeting 2009

**January 21,** Professor, Dr. Jean Marie Lehn, Collège de France,Laboratoire de Chimie Supramoléculaire, ISIS, Strasbourg, France, "Nanoscience and nanotechnology - the self-organization approach"

**January 21,** Professor, Dr. Zhong Lin Wang, Center for Nanostructure Characterization (CNC), School of Materials Science and Engineering, Georgia Institute of Technology, Atlanta, GA, USA, "Nanoenable energy harvesting technology – from nanogenerators to nanopiezotronics"

**January 21,** Professor, Dr. Simon Billinge, Department of Applied Physics & Applied Mathematics, Columbia University and Condensed Matter and Materials Science Department, Brookhaven National Laboratory, NY, USA, "Material structure in the nano-world: the nanostructure problem and our efforts at solving it"

**January 21,** Professor, PhD Tejal Desai, Laboratory of Therapeutic Micro and Nanotechnology, Department of Physiology and Division of Bioengineering, University of California, San Francisco, CA, USA, "Nanostructured interfaces for therapeutic delivery"

**January 21,** Professor, PhD Richard P. Van Duyne, Department of Chemistry, Northwestern University, Evanston, Illinois, USA, "Molecular plasmonics: nanoscale sensing and spectroscopy"

**January 21,** Professor Hagan Bayley, Department of Chemistry, University of Oxford, Oxford, GB, "Building and controlling networks of droplet interface bilayers"

## iNANO colloquia, Aarhus

**January 30,** Dr. Ali Khademhosseini, Harvard-MIT Division of Health Sciences and Technology, Department of Medicine, Brigham and Women's Hospital Harvard Medical School, Cambridge, MA, USA, "Microengineered hydrogels for stem cell bioengineering and tissue regeneration"

**February 20,** Professor Hicham Idriss, Aberdeen Chair Energy Futures and Professor of Chemistry, Scotland, UK, "The Surface Reactions and Photoreactions of TiO2 single crystals"

**March 13,** Professor Jørgen Kjems, Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Denmark, "How to make nano-scale dolphins, boxes and other (hopefully) useful things in DNA"

**March 20,** Professor H.-G. Rubahn, NanoSYD, University of Southern Denmark, Denmark, "Nano at Alsion – new visions for functional nanofibres"

**March 27,** Associate Professor Duncan Sutherland, Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Denmark, "Engineering at the nanoscale to study plasmonics and stem cells"

**April 17,** Assistant Professor Rikke Meyer, Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Denmark, "Formation of catalytically active Palladium nanoparticles on the surface of bacteria"

**April 24,** Professor Enrico Traversa, NAST Center & Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma Tor Vergata, Roma, Italy & International Research Center for Materials Nanoarchitectonics (MANA), National Institute for Materials Science (NIMS), Tsukuba, Ibaraki, Japan, "Tuning hierarchical architectures of 3D polymeric scaffolds for cardiac tissue engineering"

**May 1,** Professor Bruce German, Department of Food Science & Technology, University of California, California, USA, "The nanoscience of diet and health: Where size matters!"

**May 15,** Professor and Dr. Sanjay Mathur, Institue of Inorganic Chemistry, University of Cologne, Germany, "Chemically engineered nanoparticles, nanowires and nanocomposites: Processing, applications and devices"

**May 22,** Professor Miquel Salmeron, Materials Science and Engineering Department University of California, Berkeley, California, USA, "Water at interfaces: adsorption, reactions, wetting"

**May 29,** Dr. Samir Kumar Pal, Department of Chemical, Biological & macromolecular Sciences, Unit for nanoscience & Technology, S. N. Bose national Centre for Basic Sciences, Calcutta, India, "Use of fluorescent quantum dots in ultrafast biophysical studies"

**June 12,** Associate Professor and director of Studies at Aarhus School of Engineering Thomas Vosegaard, Center for Insoluble Protein structures (inSPIN), Department of Chemistry and Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Denmark, "Solid-state NMR techniques for studies of membrane protein structure and dynamics"

**June 19,** Chief Technology Officer & vice President of R&D Michael Egholm, 454 Life Sciences Corporation a Roche company, Branford, Connecticut, USA, "Ultra high throughput sequencing: Technology and applications"

**June 26,** Professor Richard D. Ludescher, Department of Food Science, Rutgers University, New Brunswick, NJ, USA, "Photophysical probes of the amorphous solid state of biomaterials"

**August 21,** Senior Scientist Peter Kingshott, Interdisciplinary Nanoscience Center (iNANO), Aarhus University, Denmark, "Towards the development of new material surfaces based on colloid crystals and polymer nanofibres"

**August 28,** Professor Bjørn Torger Stokke, Biophysics and Medical Technology, Department of Physics, The Norwegian University of Science and Technology, Trondheim, Norway, "Swelling of biospecific hydrogel materials with nanometer precision"

**September 18,** Professor and Chairman John Jansen, Department of Biomaterials, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands, "Nanotechnology for regenerative medicine"

**September 25,** Associate Professor Kim Daasbjerg, Interdiciplinary Nanoscience Center, iNANO, Aarhus University, "Radical ways of modifying surfaces"

**October 2,** Associate Professor Elena E. Ferapontova, Interdisciplinary Nanoscience Center, iNANO, Aarhus University, "Behind the biosensor development: Electrochemistry of enzymes and nucleic acids"

**October 9,** Professor Ned Seeman, Department of Chemistry, New York University, New York, USA, "DNA: Not Merely the Secret of Life"

**October 16,** Professor Mark A. Spackman, School of Biomedical, Biomolecular and Chemical Sciences, University of Western Australia, Crawley, Australia, "Hirshfeld surface analysis – A novel tool for visualization of intermolecular interactions"

**October 23,** Project Director Claus Hviid Christensen, Research and Development, Haldor Topsøe A/S, Kgs. Lyngby, Denmark, "Design of new catalysts of energy and environmental challenges"

**November 6,** Professor and Doktor rerum naturalium Klaus D. Jandt, Friedrich-Schiller-University Jena, Jena, Germany, "Functional biomaterials and biointerfaces on the nanometre scale"

**November 13,** Senior Lecturer Dan Peer, Laboratory for Nanomedicine, Department of Cell Research and Immunology, Tel Aviv University, Tel Aviv, Israel, "Immune targeting nanoparticles containing siRNAs to curtail leukocyteimplicated diseases"

**November 20,** Professor Kristian Strømgaard, Department og Medicinal Chemistry, Faculty of Pharmaceutical Sciences, University of Copenhagen, Copenhagen, Denmark, "Combining chemistry and biology in studies of receptor proteins in the brain"

**November 27,** Professor Bengt Nordén, Fysikalisk kemi, Chalmers University of Technology, Göteborg, Sweden, "Use of polarized light (linear dichroism) for studying structure of bio- macromolecules, in solution at membranes and in complexes"

**December 4,** Professor Clemens A. van Blitterswijk Department of Tissue Regeneration, Twente University, Enschede, Netherlands, "Materiomics: Dealing with complexity in tissue engineering"

**December 11**, Professor Ian Richardson, School of Civil Engineering, University of Leeds, Leeds, United Kingdom, "A close look at the built environments glue"

**December 18,** Project Scientist Jonathan Trent, Global Research into Energy and the Environment at NASA (GREEN) Lead, Protein Nanotechnology Group Bioengineering Branch, NASA Ames Research Center Moffett Field, California, USA, "Nine billion, Nanotech, climate change, peak oil, and your future..."

# PhD theses and Patents

## PhD theses

**Andersen, Morten Østergaard,** Delivery of RNA interference therapeutics from scaffolds. Modulation of inflammation and stem cell differentiation for tissue engineering applications

**Bremholm, Martin,** In situ X-ray scattering studies of nanoparticles in supercritical water

**Bäverbäck, Petra Margareta,** A scattering study of structural properties of mixed self-assembling systems

**Dolatshahi-Pirouz,** Alireza, Development of nano-structures biointerfaces by Glancing Angle Deposition (GLAD)

**Glud, Sys Zoffmann,** In vivo small interfering RNA delivery to lung and brain by nasal administration

**Hald, Peter,** Supercritical synthesis of complex nano materials

**Jensen, Lea Bjerre,** Multifunctional 3D scaffolds for musculoskeletal reconstruction - Scaffold production and in vitro performance test

**Jensen, Maria Fuglsang,** Many-body interactions investigated with Angle-Resolved Photoemission Spectroscopy

**Jensen, Mona Christine Robenhagen,** Atomic-scale characterization of $Al_2O_3$, ZNO and $TiO_2$ surfaces: A scanning probe microscopy study

**Jensen, Stig Mølgaard Rask,** Investigations via FRET on interactions within the RNAi-machinery & Establishing a FRET assay for detection of DSB-repair activity

**Jensen, Thomas Hartvig Lindkjær,** Development of a novel biomaterial: A nanotechnological approach

**Kalashnyk, Nataliya,** Self-assembly of organic molecules on metals and thin insulating films: Hydrigen-bonded systems, chiral induction and peptide aggregation

**Knudsen, Martin Markvad,** Design and synthesis of organic modules used for the formation of self-assembled nanostructures

**Kristensen, Jacob Broberg,** Development of antifouling enzyme solutions for marine coatings

**Nielsen, Lone,** New synthetic methods for introducing silicon into peptides and alkaloids

**Pedersen, Marie Østergaard,** Solution and solid-state NMR of insoluble proteins. Amyloid in Alzheimer's disease and the antenna protein CsmA

**Poulsen, Søren Lundsted,** Methodologis for measuring the degree of reaction in Portland cement blends with supplementary cementitious materials by 29Si and27A1 MAS NMR spectroscopy

**Sørensen, Suzette,** Characterisation and redirection of MCAD exon 5 splicing"

## Patents

**D.Q.S. Le, J.V. Nygaard, M. Foss, F. Besenbacher, C.E. Bünger,** Submerged perfusion bioreactor, priority application PA 2009 00692.

**J. Kjems, J. Overgaard, K.A. Howard, F. Besenbacher, I. Nawroth, J. Alsner,** Treatment of radiation-induced fibrosis, priority application PA 2009 00132.

**L. Bjerre, J.V. Nygaard, C.E. Bünger, F. Besenbacher,** Three-dimensional nanostructured hybrid scaffold and manufacture thereof, priority application EP 09163896.5.

**S. Shipovskov, D.S. Sutherland, P.A. Levashov, F. Besenbacher,** Active protein compositions and coatings, and methods for producing the same, priority application PA 2009 70179.

**L. Aagaard, F.S. Pedersen, B. Bjerregaard, L. Larsson, J.F. Talts, A.L. Kjeldbjerg,** Methods and compounds for regulation and detection of human endogenous retroviral envelope polypeptide, priority application PA 2009 70044

**M.R. Duch, F.S. Pedersen, S. Bahrami, L.J. Østergaard, M. Tolstrup, L. Iversen, C. Johansen, A.T. Funding,** Compositions comprising immunosuppressive peptides, priority application PA 2009 70005

**S. Bahrami, M. Tolstrup, M.R. Duch, F.S. Pedersen, L.J. Østergaard,** Bivalent molecules for HIV entry inhibition, priority application PA 2009 70296

**T. Broch-Nielsen, J. Bondergaard, P. Kingshott, F. Besenbacher,** Permanent hydrophilic nonwovens, European Patent Application No. 09 008 335.3.

# Staff

*iNANO administration: Annette Wandahl, Peter Thostrup, Tina Fredsted, Trine Møller Hansen, Leif Schauser, Sys Zoffmann Glud*

## Appointments of staff associated with iNANO in 2009

Bjørk Hammer was appointed Professor at Department of Physics and Astronomy and iNANO

Liv Hornekær was appointed Associate Professor at Department of Physics and Astronomy and iNANO

Birgit Schiøtt was appointed Professor at Department of Chemistry and iNANO

Henrik Stapelfeldt was appointed Professor at Department of Chemistry and iNANO

## Senior staff

Andreasen, Peter
Baatrup, Erik
Balling, Peter
Besenbacher, Flemming
Birkedal, Henrik
Birkedal, Victoria
Bøttiger, Jørgen
Christensen, Niels Egede
Daasbjerg, Kim
Duch, Mogens
Dong, Mingdong
Enghild, Jan Johannes
Fago, Angela
Ferapontova, Elena
Foss, Morten
Gao, Shan
Gothelf, Kurt Vesterager
Hammer, Bjørk
Hofmann, Philip
Hornekær, Liv
Howard, Ken
Iversen, Bo Brummerstedt
Jakobsen, Hans Jørgen
Jensen, Jan Egebjerg
Jensen, Torben René
Keiding, Søren
Kingshott, Peter
Kjems, Jørgen
Knudsen, Birgitta
Knudsen, Charlotte Rohde
Kristensen, Martin
Larsen, Arne Nylandsted
Lauritsen, Jeppe Vang
Linderoth, Trolle René
Lægsgaard, Erik
Malmendal, Anders
Mamdouh, Wael
Meyer, Rikke L.
Nielsen, Brian Bech
Nielsen, Niels Chr.
Nissen, Poul
Ogilby, Peter Remsen
Olsen, Jeppe
Otzen, Daniel
Pedersen, Finn Skou
Pedersen, Jan Skov
Pedersen, Steen Uttrup
Revsbech, Niels Peter
Schiøtt, Birgit
Skibsted, Jørgen
Skrydstrup, Troels
Sørensen, Esben Skipper
Stapelfeldt, Henrik
Stensgaard, Ivan
Sutherland, Duncan
Svaneborg, Carsten
Vosegaard, Thomas
Xu, Xuebing
Zelikin, Alexander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