

Annual Report 2012

Department of Chemistry



"Collaboration with industry is the inspiration for us to find new challenges."

Professor Erling H. Stenby,
Head of Department, DTU Chemistry



Chemistry Reaching Out

We are proud to present our Annual Report that reflects DTU Chemistry's optimism and drive. The Department's profile has become even sharper, and we have strengthened our dialogue with a wide range of collaborators in the past year. We have also taken significant steps towards creation of a stronger and more unified department. This is reflected in an increasing collaboration between our different sections.

High level of innovation

During the year, we disclosed 11 inventions for patenting, and several have been sold to companies. This is the highest number ever in the department's history. We have reached a high level of innovation which is remarkable for a department addressing more fundamental research.

The positive development is linked to the fact that we have obtained the right balance in our faculty. On one hand, DTU Chemistry is characterized by fundamental research in applied chemistry with scientific excellence as our trademark. On the other hand, researchers have also an eye on the potential use of our findings. This level of understanding is achieved through our dialogue with industry.

New talent

Our high level of ambition and high professional standards have also enabled us to recruit highly talented people in recent years. This is promising for our further development and in the past 12 months this positive trend has continued with the appointment of four new faculty.

We also welcomed a growing number of PhD students with financial support from public funds, private businesses and especially private foundations. For the third year in a row, we held a symposium where 50 PhD students

successfully presented their projects to colleagues and a growing number of external participants.

Popular with young people

During the year we made a big effort to recruit new students. Our efforts are based on the idea that it is important that the most talented young people are able to get the flavor of advanced chemistry already during their years in high school.

The result is a steady increasing interest in our study programs. The number of applicants exceeds the number of student we can accommodate. So we have been able to maintain the high level of our students.

Interdisciplinary cooperation in growth areas

Interdisciplinary research is important and exciting if it is based on core competences in several areas. We are constantly enhancing cooperation both between the experts of the Department as well as other DTU departments. A highlight has been the establishment of the interdisciplinary Centre for Nanomedicine and Theranostics in collaboration with DTU Nanotech, DTU Veterinary and DTU Nutech. It is an exciting initiative in an area of growth that we expect a lot from.

The highly multidisciplinary nature of the center allows for research in new biomedical technologies and evaluation of new treatment concepts in vitro and in vivo. The overall vision of the center is to develop advanced biomaterial technology and new medical interventions for diagnosing and treating severe diseases.

Increasing external funding

We are proud to announce that for the third year in a row one of our younger researchers succeed to compete for a

grant in the prestigious career program Sapere Aude from The Danish Council for Independent Research. Moreover, two of our PhDs obtained the attractive Sapere Aude Post Doc grants.

Our external funding comes from many sources. They include The Danish Council for Independent Research & Natural Sciences, the Danish Council for Independent Research & Technology and Production Sciences, the Danish Council for Strategic Research, the Danish National Advanced Technology Foundation, the Lundbeck Foundation, the Carlsberg Foundation, the Novo Nordisk Foundation and the Maritime Foundation. In addition, the Department's research is supported by grants from a number of companies such as DONG Energy, Haldor Topsoe, LAB, Maersk Oil, Novo Nordisk, Novozymes, Vattenfall and Wacker Chemie.

The benefits from the increasing external funding are the ability to realize more of our exciting ideas and ambitions. It is a prerequisite for success that you can test your ideas. We should like to emphasize, however, that money and funding is not a goal in itself but rather a means to carry out excellent research and give top level training to our students.

We are very conscious about the importance of a close dialogue with our partners as well as dissemination of our many achievements and activities. This is one of the motivations behind DTU Chemistry's Annual Report which I hope will inspire to further collaboration between you and us.

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CONTENT

Chemistry Reaching Out	3
1. Inorganic Chemistry	
On Course for Low Emissions	8
Smarter Large Scale Production of Acetic Acid	10
The Second Gold Rush of Catalysis	12
2. Organic Chemistry	
NMR: A Natural Choice	16
The Game of Chemical Research	18
3. Physical Chemistry	
When dreams come true	22
A New Tool in X-ray Protein Powder Diffraction	24
4. Comprehensive Chemistry	
New Frontiers are Opening in Danish Oil Recovery	27
The Inner Entrepreneur Comes Alive	28
Chemistry under the Surface	30
5. PhD Theses 2012	32
6. Master Theses 2012	48
7. Funding	49
8. Acknowledgement	50
9. Highlights at DTU Chemistry	51
10. Publications	55
11. Staff	56

1. Inorganic Chemistry

The Inorganic Chemistry section consists of the Centre for Catalysis and Sustainable Chemistry (CSC) and the research groups on Metalloprotein Chemistry and NanoChemistry. While these three areas are relatively distant in their content, a high degree of coordination is maintained through exchange of know-how and sharing of equipment.

The Centre for Catalysis and Sustainable Chemistry develops novel chemistry and improves already known industrial processes. The goal is to develop a sustainable chemical industry and thereby secure the future for coming generations in terms of energy, resources and the environment. The research has three focus areas: fuels from waste and biomass, industrial flue-gas cleaning, and sustainable production of chemicals.

The group on Metalloprotein Chemistry focuses on the role of metals in biological systems through interdisciplinary research such as design of recombinatory metalloproteins, which involves genetic engineering, fermentation and chromatography. The group also does metalloprotein characterization by mass spectroscopy, and by enzymatic, spectroscopic, and structural characterization.

The group on NanoChemistry focuses on fundamental physical and chemical understanding at the single molecule level. Further, the aim is to take this knowledge into applications, e.g. for ultra-sensitive sensors and novel catalysts. The group is currently extending its scope into the electric properties of biological molecules such as proteins and DNA-based molecules. Hybrid systems combining single biological molecules with inorganic nano-structures with relevance to biological screening, biocatalysis, and other types of nano-biotechnology are designed. Altogether, the Inorganic Chemistry section has eight faculty members and 19 PhD students, which is due to rise to 25-30 PhD students over the next few years.

The section is coordinated by Professor Rasmus Fehrmann.

On Course for Low Emissions

The shipping industry is one of the sectors which can benefit from ionic liquid cleaning of exhaust gas. The concept is being developed at DTU Chemistry.

Demands on the shipping industry to cut emissions of sulphur dioxide (SO₂), nitrogen oxides (NO_x) and carbon dioxide (CO₂) are growing steadily. And as space is a limited resource onboard a ship, the environmental equipment required for the task needs to be kept down in volume. This makes a new concept for exhaust gas cleaning by ionic liquids highly relevant to the sector, according to Professor Rasmus Fehrmann, who heads the Centre for Catalysis and Sustainable Chemistry (CSC) at DTU Chemistry:

“The technology will also be relevant to a number of on-shore applications. For instance we have dedicated research on solutions for entirely or partially biomass-fired combined heat and power stations. The cement industry is another interesting onshore application. However, ships do have extraordinarily strict demands for keeping volumes and weight of equipment down. As the new ionic liquid based solutions take up considerably less space compared to present solutions, I can very well imagine that the first breakthroughs for the technology will come in the shipping industry.”

CSC's research in the field is supported by the Danish Maritime Fund. Several companies, among them MAN Diesel and Turbo, are collaborating.

International demands change the scene

For many years, emission control was far less in focus in the shipping industry compared to onshore environmental standards. However, demands by the International Maritime Organization (IMO) are about to change the scene. As of January 1st 2013, all new ships commissioned will need to be built in accordance with criteria for maximum allowable CO₂ emissions. Further, in 2015 new regulations on SO₂ will be implemented, as will regulations on NO_x in 2016.

Also, some individual countries and local authorities choose to put environmental demands on ships. For instance, ships with high emissions of nitrogen oxides - associated with a number of health issues - may soon face restrictions in which harbours they will be able to access.

Most current systems for cleaning exhaust gas from energy production are based on heterogeneous catalysis. Several ship owners have applied or are about to apply so called scrubbers for sulphur dioxide.

Ionic liquids display high selectivity

For some years now, CSC has held a handful of patents on heterogeneous catalysis based flue gas treatment. Recently the same has become the case for the possible next generation of equipment based on ionic liquids.

An ionic liquid is defined as “a substance composed of two distinct ions that is liquid below 100°C”. In other words an ionic liquid has a very high boiling point. This is highly attractive,

because the amounts lost due to vaporization are kept close to zero, which practically eliminates the need to add new ionic liquid to the system.

A large number of ionic liquids exist. The research has shown it possible to design an ionic liquid that matches a given absorption task with high selectivity.

“Firstly, a suitable ionic liquid must allow for water, nitrogen and oxygen to pass unhindered. These are of course large components in the exhaust gas, which we do not want to capture. Secondly, the ionic liquid needs to absorb the relevant compound efficiently and with high selectivity. Thirdly, smooth desorption of the compound must be possible, thus making the ionic liquid ready for further absorption. We have several good candidates meeting these demands for capture of both sulphur dioxide and nitrogen oxides, while we are working on candidates for carbon dioxide.”

No need for supporting chemicals

The main attraction of an ionic liquid solution is the fact that it can be used in a swing-operation manner, allowing for a continuous intake of exhaust gas at one point of the installation, while the compressed end product is desorbed at the opposite point.

“For instance, the process can yield nitrogen oxide which is subsequently reacted with water to form nitric acid in a continuous process. One can even imagine the produced acid being stored in the ship's fuel containers, provided it is rinsed properly. The longer the ships sails, the more acid will be produced. As at the same time more fuel is consumed, more empty

“The research and development within totally new technologies for exhaust gas cleaning with respect to CO₂, NO_x and SO_x sounds very interesting from a shipowners' point of view, as the new environmental demands are a real challenge to our industry. The more alternatives we have with regard to technological solutions, the better. We will follow the research at DTU with interest in the coming years.”

*Hans Otto Kristensen, Senior Advisor,
Danish Shipowners' Association.*

containers will be available. Such a system would be highly attractive. Further, the ionic liquid solution doesn't need any supporting chemicals,” Rasmus Fehrmann explains.

The group is investigating several designs for the system. A promising new concept is the Supported Ionic Liquid Phase (SILP) absorber systems. The concept allows for high efficiency due to a high internal absorption surface and a fast absorption/desorption cycle. The group is an international pioneer in SILP technology.

Vision: a unified system of absorption

As the ionic liquid method is highly selective it will not be possible to capture more than one undesired compound for each ionic liquid. For instance, one needs three different subsystems to absorb sulphur dioxide, nitrogen oxides and carbon dioxide respectively. The same is the case for heterogeneous catalysis based flue gas treatment, for which the group at DTU Chemistry has by no means ceased its efforts.

“It is possible that quite different solutions can be best choice for each of the various undesired compounds. However, we do

envision such subsystems to be combined in a unified system which provides the optimal overall solution,” says Rasmus Fehrmann, noting that the performance of one subsystem may influence the performance of another:

“For example, we see problems in our preferred system for nitrogen oxide removal if the flue gas contains sulphur especially as SO₂. So the removal of nitrogen will be better, when the flue gas has first undergone sulphur absorption.”

While the individual processes have already been shown to be efficient and selective, especially for absorption of nitrogen oxides and sulphur dioxide, there is still room for investigation regarding the interdependences of the various subsystems.

“One challenge is the fact that the various processes work best at different temperatures. In the laboratory we can easily heat or cool so as to run each process at the ideal temperature, but at full scale you need to design your system very carefully. Otherwise you will lose energy and the overall solution becomes uneconomical. Dealing with this issue is especially relevant on board a ship where the flue gas temperature may vary with changes of the sailing conditions.”



Smarter Large Scale Production of Acetic Acid

Based on a DTU Chemistry patent, the chemical company Wacker Chemie AG has begun operations at a pilot plant in Munich, Germany.

Following just a few years of fruitful collaboration with DTU Chemistry, Wacker Chemie AG has invested in a pilot plant in Munich, Germany. The plant produces acetic acid (AcOH) by a novel method patented by DTU Chemistry.

Acetic acid is produced on a scale of millions of tons annually. In aqueous solution it is commonly known as vinegar. Nowadays only a small proportion is for use of acetic acid in its pure form, while the rest is used as a precursor molecule for higher value chemicals. The largest single use is for vinyl acetate monomer (VAM), which again is the precursor molecule for poly(vinyl acetate), used in a variety of fields ranging from floor

tiles to safety glass. VAM is also used as an emulsifier in water based paints, adhesives, and coatings including textile coatings.

Further, acetic acid is an important starting point for manufacture of terephthalic acid, which in turn is the precursor to polyethylene terephthalate (PET) used in the majority of plastic bottles and in various similar applications.

Continuous production replaces batch production

The standard method for production of acetic acid is by reacting methanol and carbon monoxide over a rhodium catalyst. However, in the joint project with DTU Chemistry a novel set-

up involving an ionic liquid catalyst was developed. An ionic liquid is defined as "a substance composed of two distinct ions that is liquid below 100°C". The ionic liquids were introduced in the Supported Liquid Phase (SLP) concept, thus as a Supported Ionic Liquid Phase (SILP) catalyst where the support is a mesoporous material with high surface area e.g. silica, titania, alumina or zirconia.

"The main attraction of the SILP process is that it allows for a steady production of acetic acid without having to stop and restart the reaction, and thus avoiding complex procedures between batches. Furthermore, in many cases, continuous production can be cheaper due to reduced reactor size, efficient use of precious catalysts and lower or no consumption of volatile solvents," explains Professor Rasmus Fehrmann, who together with Associate Professor Anders Riisager leads the work on SILP catalysis at DTU Chemistry and are supervisors of the project, which was carried out by PhD student Christopher Hanning.

Three patents have been generated

The project was based on a technology transfer agreement between Wacker Chemie AG and DTU.

"The financial details of the agreement are confidential. However, I can say that the agreement ranks at the very top in terms of revenue for DTU," Rasmus Fehrmann comments.

Besides the initial patent, two further patents have been applied for based on research in Christopher Hanning's PhD project. Both these patents relate to supporting technology for the main process. They have been taken out jointly by DTU and Wacker Chemie AG.

"The main attraction of the SILP process is that it allows for a steady production of acetic acid without having to stop and restart the reaction, and thus avoiding complex procedures between batches. Furthermore, in many cases, continuous production can be cheaper due to reduced reactor size, efficient use of precious catalysts and lower or no consumption of volatile solvents."

Professor Rasmus Fehrmann, DTU Chemistry

Wacker Chemie AG

Wacker Chemie AG is a part of the Wacker Group with some 17,200 employees. Wacker is a globally active company with 25 production sites and 20 technical competence centres. 2011 sales reached EUR 4.9 billion. Wacker is an industrial partner to the Centre for Catalysis and Sustainable Chemistry (CSC) at DTU Chemistry.



The Second Gold Rush of Catalysis

Trapping tiny gold particles inside a solid porous structure is a promising method for improving heterogeneous catalysts. Also, such a method may bring other metals, which are currently rejected due to sintering issues, back in the game.

To the inorganic chemistry community, it is a long-standing joke to refer to the emotions following a discovery made a few decades ago as “the gold rush”. It was shown that gold-nanoparticles are surprisingly active and selective catalysts for several oxidation reactions with molecular oxygen despite the unreactive nature of pure metallic gold. This soon led to extensive efforts both in academia and industry. Now a second phase of this “rush” is beginning, according to Assistant Professor Søren Kegnæs, DTU Chemistry:

“One of the approaches towards enhanced catalytic performance is to reduce the size of the active gold nanoparticles. With smaller size follows a larger internal catalytic surface. However, the reduction of particle size increases the risk of sintering, which in turn leads to a decrease in catalytic activity.”

Thus, the development of novel sintering-stable heterogeneous nanoparticle catalysts is highly important, Søren Kegnæs emphasizes:

“Gasoline-engine cars emit pollutants such as carbon monoxide, hydrocarbons, sulphur and nitrogen oxides, leading to the formation of photochemical smog and acid rain. The number of automobiles is increasing and more than 50 million cars are manufactured every year; nearly all of them with exhaust catalysts. It is highly desirable to find improved catalysts with higher efficiency and longer duration. Obviously, the same goes for a wide range of other applications, i.e. in the energy industry and in chemical industry.”

Gold particles in a cage

By late 2011, Søren Kegnæs became a DTU Chemistry faculty member as Assistant Professor. In his new capacity, he will primarily strengthen the already wide range of activities under the Department’s Centre for Catalysis and Sustainable Chemistry (CSC). He also heads a new project on the development of sintering-stable heterogeneous nanoparticle catalysts. The project, commenced by January 2013, is financed by FTP under the Danish Council for Independent Research.

The project is based on previous discoveries, which have demonstrated that it is possible to minimize sintering by trapping gold or other metal nanoparticles inside a solid porous structure like zeolites. These are crystalline micro-porous materials with well-defined structures. When designed optimally in relation to the gold nanoparticles in question, the zeolite pore will act like a cage, allowing for the reactant to access the gold nanoparticle, but preventing the particle from engaging in sintering with other particles.

“In spite of the vast technological, environmental and economic interests, general methods for the stabilization of metal nanoparticles against sintering are lacking. A few specific catalytic systems with this focus do exist, but at present they are rather expensive, difficult to synthesize, and they cannot be produced on an industrial scale. We hope to change this scene,” says Søren Kegnæs.

Collaboration with the Max Planck Institute

The research of the project will not be limited to just gold nanoparticles. Currently, many other catalysts are in industrial use, for instance ruthenium and palladium.

“We hope to be able to suggest improved solutions for a number of existing catalysts besides gold nanoparticles. Further, one can imagine that other metals which are currently not considered applicable in catalysis may become of interest. An example could be copper. Mainly due to its low price, but possibly also for other reasons, copper would be a promising catalyst were it not for its strong tendency to sinter. If sintering can be prevented by containing the copper particles inside a zeolite cage, a new situation could exist,” Søren Kegnæs points out.

Beside Søren Kegnæs, three PhD students will work on the project, which is a joint effort with Professor Ferdi Schüth’s group at the Max Planck Institute, Mülheim, Germany.

“Professor Schüth’s group has a leading international position in the area of supported catalysis, nano-materials, design of meso- and micro-porous solids and their application in catalysis. The materials are optimally adapted to target application with respect to certain properties, such as high surface area,

“We hope to be able to suggest improved solutions for a number of existing catalysts besides gold nanoparticles. One can imagine that other metals may become of interest – for example copper, mainly due to its low price.”

Assistant Professor Søren Kegnæs, DTU Chemistry

catalytic activity or special optical characteristics. Therefore, the outcome of our collaboration will be a design protocol for preparation of noble metal nanoparticles on the supported silica oxides, which will be further used for instance in zeolite systems,” Søren Kegnæs explains.

Understanding replaces trial-and-error

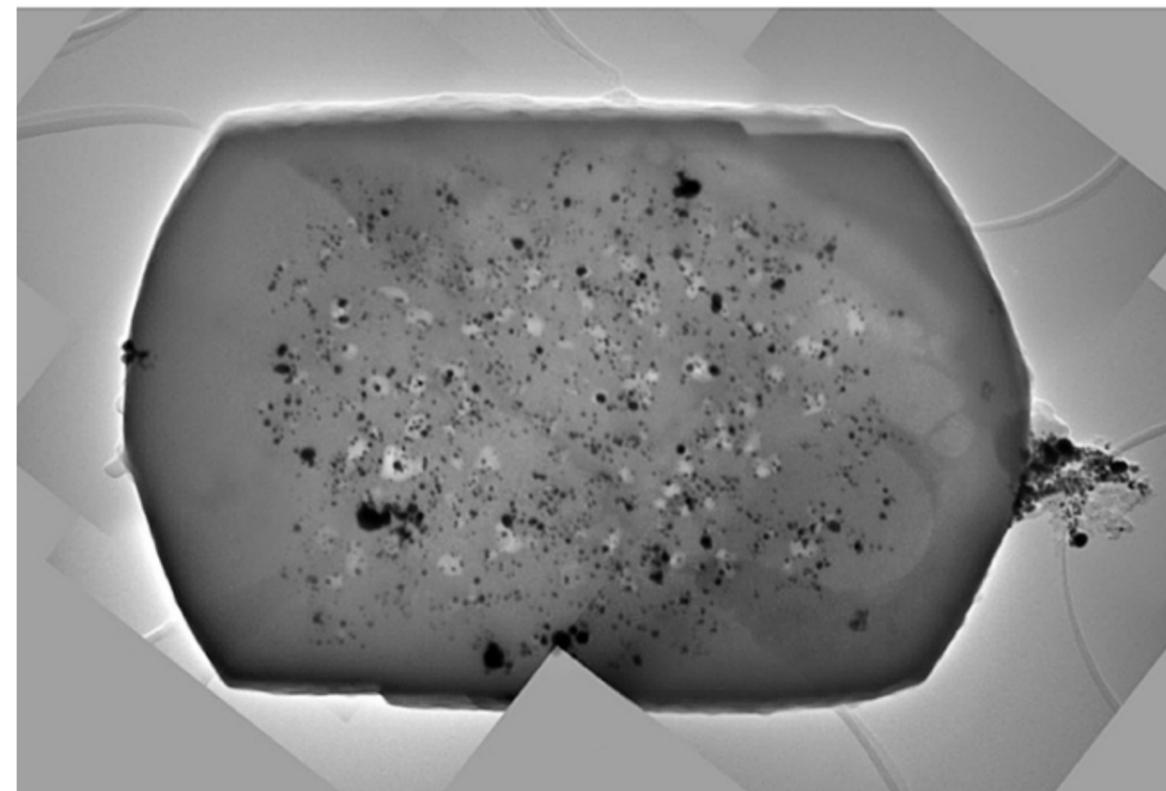
Besides making use of the equipment of DTU Chemistry, the research draws on the advanced instruments at the Centre for Electron Nanoscopy (CEN DTU).

“We are grateful to have this kind of state-of-the-art equipment nearby. Instruments such as the TEMs (Transmission Electron Microscopes, ed.) almost allow us to see the individual atoms. Catalysis has a long history of trial-and-error, but with this level of detail we are given much better chances of not only developing a functioning catalyst but also understanding the

underlying mechanism. If we understand why a given catalyst is good, we will often be able to develop an even better one,” Søren Kegnæs comments.

The obtained sintering-stable heterogeneous nanoparticle catalysts will be further investigated in different reactions like selective oxidation reaction for production of various chemicals.

“Before publication, all results will of course be evaluated for patenting and the most promising catalysts will be introduced to the industrial partners of the Centre for Catalysis and Sustainable Chemistry,” Søren Kegnæs concludes.



TEM image of gold nano particles encapsulated in a zeolite crystal. The black areas represent high density regions, and therefore correspond to the gold particles. The image and the sample were made by researchers from Haldor Topsøe in collaboration with DTU (published in *Angew. Chem. Int. Ed.* 2010, 49, 3504–3507)

2. Organic Chemistry

Research in the Organic Chemistry section is characterized by a dual approach of looking at fundamental science, while also contemplating biological and pharmaceutical applications, including biological screening, drug discovery and drug delivery systems. Organic synthesis and the design of organic molecules is the key discipline within the section, which also has high levels of expertise in spectroscopy (particularly NMR spectroscopy) and computational chemistry. The section has two interlinked main focus areas, which are catalysis and chemical biology.

Homogeneous metal catalysts are able to improve a number of chemical processes, making them more efficient, sustainable and environmentally sound. The efforts of the Organic Chemistry section on this topic focus on both experiments and simulations, which can lead to improved mechanistic understanding of the reaction pathways involved. The aim is to design even better catalysts, which are able to convert simple and easily available precursor substances into more advanced molecules.

Using organic chemistry as a tool to learn more about fundamental biology is a relatively new discipline known as Chemical Biology. With the ultimate goal of suggesting new drug candidates, the field has been a strategic focus area at DTU Chemistry in recent years. By means of organic synthesis, new molecules are designed and prepared with the aim of improving understanding of biological systems. Further, novel screening technologies are established, just as new biochemical assays and drug candidates for treatment of bacterial infections and cancer are identified. Finally, biologically active compounds found in nature, including complex oligosaccharides, are produced by stereoselective organic synthesis. The development and application of advanced NMR techniques is an important component of all these research efforts.

The work on catalysis and chemical biology is highly integrated, and several faculty members have projects in both fields. The Organic Section currently employs a total of eight faculty members and 33 PhD students.

The section is coordinated by Professor David Tanner.



NMR: A Natural Choice

What do these projects have in common: finding drugs against antibiotic-resistant bacteria, identifying toxins from mold, and probing molecules from marine microbes? These studies and more rely on DTU Chemistry experts in nuclear magnetic resonance spectroscopy (NMR).

NMR is a powerful, reproducible, and effective analytical tool for getting details about a molecule's structure. NMR aims radiofrequency pulses at a sample and monitors how they are re-emitted. Using the results, researchers identify a molecule's atoms and bonds and their overall arrangement. But interpreting NMR data takes skill, experience, and intuition. Associate Professor Charlotte Held Gotfredsen says figuring out the three-dimensional structure of a molecule from NMR data is "like assembling a three-dimensional jigsaw puzzle, without knowing what the result should look like."

The three-dimensional structure of a molecule is critical because the orientation of groups around atoms affects interactions, activity, and toxicity. This is why NMR is widely used for qualitative and quantitative measurements in drug discovery, metabolomics, material science, food quality analysis, green chemistry, and organic synthesis. DTU chemists use NMR to analyze organic molecules such as carbohydrates and peptides. They study synthetic molecules as well as natural products that are isolated or derived from plant, animal, fungal, or bacterial sources. In fact, NMR is so useful that the equipment and experts in Charlotte Held Gotfredsen's NMR group are in constant demand by national, international and DTU collaborators.

All Natural

Natural products are a major focus of the DTU Chemistry NMR group. Familiar natural products include aspirin, the anticancer drug taxol, and food coloring pigments. Commercially and medically important natural products are often secondary metabolites. They are not part of an organism's primary metabolism of breaking down sugars for energy and making basic cellular building blocks. Secondary metabolites are highly complex molecules that function in defense, symbiosis, or other activities with interesting biological effects. NMR experts from DTU Chemistry are analyzing secondary metabolites from diverse microorganisms in several ongoing projects, many in collaboration with the natural product chemistry group at DTU Systems Biology, headed by Associate Professor Thomas Ostfeld Larsen.

The collaborative projects include exploring compounds from filamentous fungi, which are a rich source of natural products including the medicines penicillin and griseofulvin and the potentially dangerous molecules aflatoxin and fumonisins. Fungal molecules might be potential scaffolds for developing drugs such as new cancer therapeutics. NMR characterization of new natural compounds is essential because their molecular structure determines their potential for future synthesis and chemical modification, for example through synthetic biology approaches. These projects align with organic chemistry activi-

ties at DTU Chemistry in the synthesis of natural products and their analogs.

"It's like assembling a three-dimensional jigsaw puzzle, without knowing what the result should look like."

Associate Professor Charlotte H. Gotfredsen, DTU Chemistry

NMR experts at DTU Chemistry also collaborate with DTU System Biology on genomic projects. Genome sequences are available for several commercially important fungi. However, knowing an organism's genes only suggests the molecules it might produce. By matching fungal genes to secondary metabolites the fungi actually produce, researchers can determine the pathways of enzymes and small molecules that eventually lead to interesting natural products. NMR analysis of a fungi's individual metabolites shows the range of molecules from a pathway, and what molecules disappear or change if a gene is mutated. NMR is also being used to analyze the collection of complex molecules made by a fungus, creating a chemical fingerprint that can be used to identify and classify fungi.

Fungi are not the only microbes that produce interesting compounds. Marine bacteria are another source of NMR samples in a project with DTU Systems Biology postdoctoral fellow Maria Månsson and Professor Lone Gram. The bacteria were collected on the 2006-2007 Galathea 3 expedition, a global research voyage sponsored by the Danish government. As researchers at DTU Systems Biology find bacteria that produce bioactive molecules, DTU chemists identify the structure of those molecules to help determine if a compound is new or has been already discovered.

Expanding to meet demand

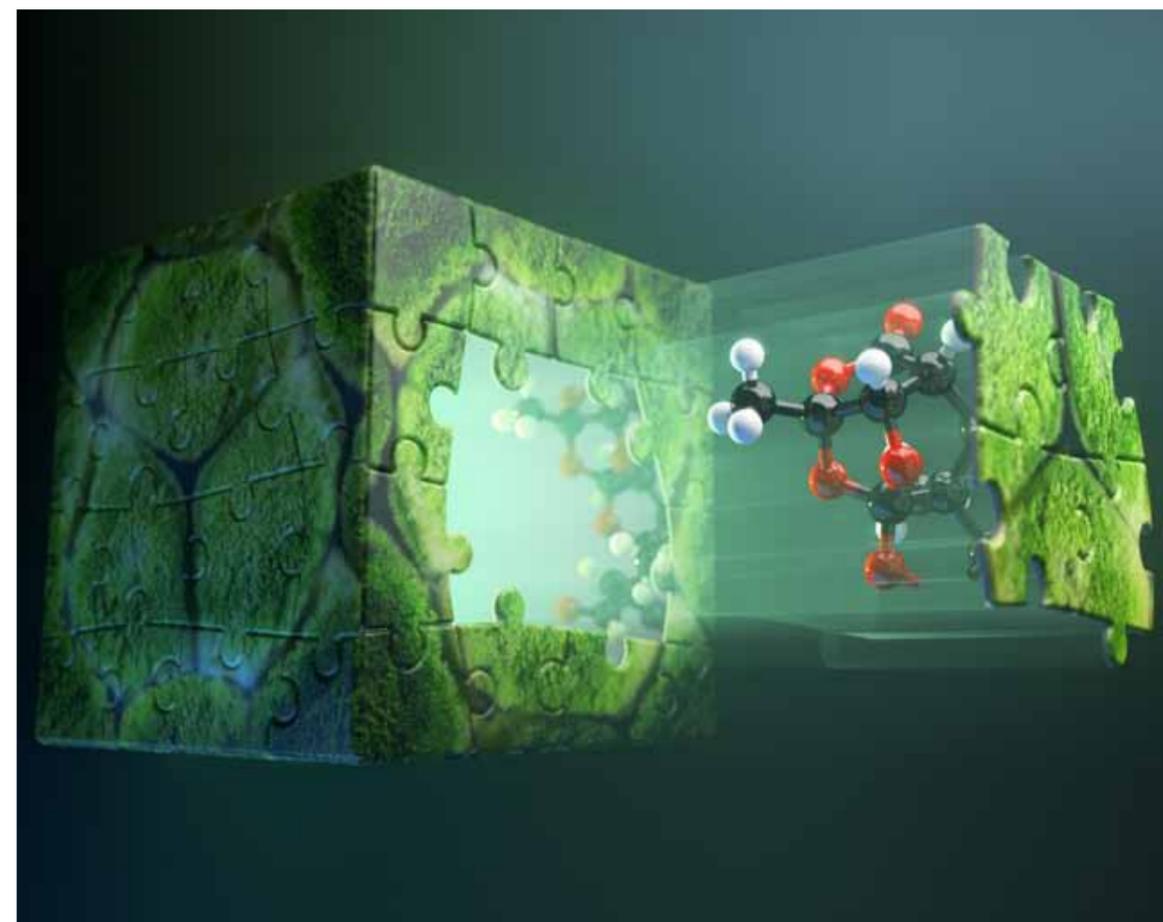
The DTU Chemistry NMR group is a place where university and industrial research intersect. With so many interdisciplinary collaborators using NMR for projects in, for example, natural product discovery, carbohydrate chemistry, and chemical biology, the potential for new partnerships is increasing. To meet the demand, DTU Chemistry is expanding its NMR capabilities. In January 2013, Jens Ø. Duus, previously director of the NMR center at Carlsberg Laboratory and a frequent collaborator with Charlotte Held Gotfredsen's group, started as a professor in NMR spectroscopy. Charlotte Held Gotfredsen and Jens Ø. Duus will be seeking internal and external support

to further build and strengthen NMR capacity at DTU Chemistry. The goal is to establish a strong NMR instrument center at DTU Chemistry. This will not only support the research and education of the Department but of many other DTU departments.

The timing is perfect for expanding NMR at DTU. Companies in the pharmaceutical and related industries are increasingly looking for complex chemical scaffolds from which to develop drugs and other useful molecules. Natural products provide a wealth of these intricate starting compounds and are expected to receive more attention from basic and applied researchers in the near future.

"Nature is better at generating these complex compounds than we are. But using NMR, we can identify the interesting compounds, characterize them, and help develop them into products that we can use," says Charlotte Held Gotfredsen.

In Nuclear Magnetic Resonance (NMR) spectroscopy, a sample is placed in a strong magnetic field and subjected to electromagnetic radiation of a specific frequency. The radiation causes the nuclei of some atoms of the sample to interact. These interactions are detected by the spectrometer as decaying electromagnetic frequencies and an NMR spectrum is generated. Based on multiple NMR spectral data the researchers are now left with elucidating the atom jigsaw puzzle.



NMR spectroscopists solve the 3D structure of fungal natural products. Illustration: Kresten Vestbjerg Andersen

The Game of Chemical Research

Professor Robert Madsen is internationally recognized in the fields of metal catalyzed organic synthesis. To him, top level science is about far more than coming up with clever ideas. The really difficult part is manoeuvring according to the changing winds of the funding regime, while constantly positioning yourself in new fields which are unnoticed by your competitors.

To Professor Robert Madsen, science is much like playing top level chess: Even when you achieve excellent results and feel on top of your game, you still need to force yourself into exploring new ideas. If you fail to do so, your competitors will soon be on to you.

“Similarly, if I have picked a research topic too late, I will find that just as my PhD student is about to publish his first results, an article covering the same content will be published by another group,” Robert Madsen illustrates.

The Danish scientist is internationally known for a series of novel processes in metal catalyzed organic synthesis. An example is the direct ruthenium-catalyzed synthesis of amides from alcohols and amines. Amides are important precursors in organic chemistry. For instance, amides can take part in peptide synthesis – perhaps the most important process in the pharmaceutical industry – or they can be the starting point for widely used synthetic materials such as nylon.

Chance favours the prepared mind

The first results on this new synthesis path were published by Robert Madsen and co-workers in 2008:

“We encountered this idea pretty much by chance. But as Louis Pasteur (French chemist and microbiologist, 1822-1895, ed.) once said: “Chance favours the prepared mind”. To me our finding emphasizes that you need to always set up your experiment in a way that allows for unexpected findings. Many groups have a tendency to work too narrowly, only setting up experiments that are practically guaranteed to yield the expected results.”

Since the first publication many more have followed from various groups, involving both ruthenium and other catalysts, resulting in improved pathways for amide synthesis.

“We entered metal catalyzed amide synthesis at a truly fortunate moment, when the entire field was just beginning to take off. And I am convinced that the possibilities are far from exhausted. Many new discoveries are waiting to be made,” Robert Madsen notes, while returning to the image of the chess player: “Still, this is not the path I am planning to continue. Right now I am in a period of transition considering what should be our next focus.”

A game you need to play

Should you, naively, ask a top chess player what his preparations are for an upcoming tournament, his answer – if any – would surely be a bluff. Similarly, Robert Madsen is not ready to disclose his specific thoughts. However, on a general level he remarks:

“Internationally, few groups are on a scale in terms of manpower and financial resources that allow them to operate only according to their own preferences. And my group is certainly not one of those. This means that I will need to pick a focus which is different from what large foreign groups are known to pursue.”

“Further, the funding system has a built-in tendency to always favour a new idea over the continuation of an existing idea. This may not be ideal from the scientist’s point of view, as often ideas which received initial funding a few years back can be really ripe for yielding results today. However, you need to understand that game, and play it well, because that is just how things are.”

Challenged with the suggestion of trying to camouflage the existing idea as a new one by adding a label which fits some current trend, he replies:

“Many scientists do just that, but in my view that is not a viable strategy. Firstly, the funding bodies know that game very well and will most often look through you. Secondly, it is actually very rewarding to constantly be involved in the early phases of scientific developments. So our strategy is to position ourselves just there.”

Everything gets published!

Obviously, constantly positioning oneself in the arenas of the upcoming breakthroughs is easier said than done.

“One implication is that every time we start on a new topic, we already need to consider how to exit it. If we maintain the individual efforts for too long, we will lose the dynamism we aim for. Still, I would like to emphasize that we are never in such a hurry to exit, that we just move on without publishing our findings. It is a core value for us to always publish our work.”

“As Louis Pasteur said: Chance favours the prepared mind. To me our finding emphasizes that you need to always set up your experiment in a way that allows for unexpected findings.”

Professor Robert Madsen, DTU Chemistry



To some people having to exit a relatively new field after, say, just four years when it is perhaps blooming internationally, may sound strange. But not to Robert Madsen:

“Well, actually the very first steps are the most interesting to take. If your ideas are good, you can be sure that others will continue in your footsteps and bring them to life. This is often a very labour-intensive process for which we wouldn’t have the resources anyway. I have grown to accept the fact that if nobody wants to take an excellent idea of mine further, it probably wasn’t that great after all!”

Projects differ, the core is constant

Robert Madsen admits that this strategy may appear to result in inconsistency:

“Maintaining the overall consistency of our work is a constant struggle. However, this is possible because all our various projects have a common core around certain aspects of organic synthesis. At some points metal catalyzed reactions may dominate, at other points it will be the chemistry of carbohydrates, bio-refining, green chemistry, or other topics. But at the end of the day, the individual projects all contribute to the same goal.”



3. Physical Chemistry

Understanding the structure and behaviour of chemical and biological systems is the main focus of the Physical Chemistry section. The research reaches from the smallest molecules up to large biological systems. Typical tools include scientific computing, X-ray scattering from conventional, synchrotron and free-electron laser sources, spectroscopy, and chemical analysis. The section has two main focus areas, which are biophysical chemistry and femtosecond chemistry.

In biophysical chemistry, the section is involved in two projects. Firstly, metalloproteins related to Alzheimer and other neurological diseases are being synthesised in collaboration with DTU Chemical Engineering and DTU Systems Biology. The role of the metal ion will be investigated using a combination of crystallography, X-ray spectroscopy (XAFS) and other techniques. The ultimate goal is to provide the basis for a new generation of drugs. Secondly, a new concept for studying the atomic architecture of protein complexes will be implemented. While NMR spectroscopy and X-ray crystallography have traditionally been the preferred methods, in this project state-of-the-art computer simulations in combination with new X-ray techniques (HXMS and SAXS) will be used to study large protein complexes. The project has a dual goal of suggesting protein-protein interactions that are potential drug targets and to suggest mutations which may produce proteins with enhanced functional properties.

Femtosecond chemistry is a field on the border between chemistry and physics. Based on applied quantum mechanics the fundamental idea is to detect – or “film” – atomic movement while it is actually happening during a chemical reaction. Further, the ambition is to be able to control these movements which happen over very short intervals of time – femtoseconds. The research is undertaken in collaboration with DTU Physics. Experiments are done at international X-ray free-electron laser facilities (XFEL).

The Physical Chemistry section presently has 11 faculty members and seven PhD students.

The section is coordinated by Associate Professor Kenny Ståhl.

When dreams come true...

Filming a chemical reaction live using bursts of X-rays

All chemists dream of being able to see molecules dance – to follow their transformation during a chemical reaction. For researchers at DTU Chemistry, the dream became a reality when they recently went to Japan to one of the world's first X-ray free-electron laser facilities. This could open the door to new and far more efficient and effective chemical processes.

It has only recently become possible to actually “film” what happens in a molecule when it changes structure. The new so-called X-ray free-electron laser facility, XFEL for short, can, with the help of X-rays, take pictures fast enough to capture the myriad processes that take place in a molecule after a chemical reaction is initiated. The molecular dynamics during the chemical reaction occurs on the femtosecond time scale, which is extremely fast. The ratio of a femtosecond to a second is the same as between a second and 32 million years! The Japanese X-ray laser system SACLA is only the second of its kind in the world – the first one opened at

Stanford University in the USA two years ago. A third, located in Hamburg, will be ready in a few years.

Associate Professors Niels Engholm Henriksen and Klaus Braagaard Møller from the research group Theoretical, Computer and Femto-Chemistry at DTU Chemistry have been involved since the very start, when the research project was started at the Centre for Molecular Movies, a centre of excellence funded by the Danish National Research Foundation. Together with DTU Physics, they have, over the past few years, been building up a body of expertise in these large high-tech X-ray facilities.

“There are endless possibilities for the new large X-ray facilities if we can achieve even a modicum of the success that traditional X-rays have had in contributing to our understanding of the molecular structures of, for example, proteins,” says Associate Professor Klaus B. Møller from DTU Chemistry.

“The ultra-short X-ray pulses make it possible for us to see still images of molecules in motion, thereby shedding light on fundamental processes in areas such as chemistry, biology and technology,” he continues.

Femtochemistry

The background for Niels Engholm Henriksen's and Klaus B. Møller's research is femtosecond chemistry, which lies somewhere on the border between chemistry and physics. The research consists of the development of concepts and ideas based on the laws of quantum mechanics translated into equations and computer programs – in order to detect (“film”) and control (“direct”) atomic motion while chemical reactions are taking place. Detection and control of atomic motion is based on the interaction between molecules and ultra-short (femtosecond) flashes of electromagnetic radiation, which can both provide the required time resolution and, through the coherent excitation of intrinsic quantum states, create

molecular states which cannot be created through conventional heating.

The Japanese Adventure

In the Japanese highlands there is a 700-metre-long tube through which compact bunches of electrons run at almost the speed of light. The electrons are exposed to undulator magnets so that they emit extremely short-lived X-ray pulses that are sent into the sample that the researchers have brought with them from Denmark.

PhD student Asmus Ougaard Dohn from DTU Chemistry got a unique chance to take part in research at the facility (SACLA) in Japan, where he and his supervisor Klaus B. Møller went recently, together with researchers from DTU Physics as well as from Sweden and Hungary. They had just 72 hours of so-called «beam time» to record how a single charge would move through the sample – in a specially designed molecule – after it had been illuminated by a laser pulse.

Time spent using an XFEL is expensive. Operating costs are high. At the facility at Stanford (LCLS), it costs approx. DKK 100,000 per hour to run an experiment – whereas the figures for SACLA in Japan are slightly lower.

«Having access to such a large and expensive facility gives us very good “value for money”. We're incredibly lucky to be able to send our PhD student Asmus Ougaard Dohn there so he can use the data for his project back here at DTU,» says Niels Engholm Henriksen, who is co-supervisor on Asmus' project, which is co-funded by DTU Chemistry and the Lundbeck Foundation.

«We have a unique opportunity to gain valuable experience which will put us in a good position in relation to the upcoming facility in Hamburg,» he continues. A facility that researchers in Denmark are very much looking forward to being able to use. When completed the expected cost will be about 1 billion euros!

The future looks bright

There is, however, no guarantee that researchers will succeed in creating their own molecular movies at these facilities; and even if they do, they may not understand what they have filmed. But in Japan, Asmus Ougaard Dohn did actually manage to create useful data to bring back for his PhD project on ultrafast molecular dynamics. In the 63rd hour, researchers broke out into ecstatic dancing, as the computer screen

showed a graph – amid the noise and mess – indicating unequivocally that this was a time-resolved scattering signal – evidence that they had captured “something moving in the molecule” that they could work on. The series of scattering patterns can be combined to form a kind of movie of how the molecule behaves as the electron moves from one end of the molecule to the other.

“Our overall goal is to develop a translation device between the data we record and images with atomic resolution in both time and space that can show molecules' structural dynamics during chemical reactions at the same moment they occur. If successful, it will give an unprecedented insight into the world of chemistry, and the results may lead to new ways to optimize chemical reactions,» says Klaus B. Møller.

“Our research is driven by pure curiosity, combined with a clear perspective on practical applications,» adds Niels Engholm Henriksen. But there is still a long way to go before using the new facilities can be considered a “routine job”. Most of the work is currently going into developing the necessary computational technology to interpret the data produced; and DTU Chemistry has been there right from the start.

FEMTO11

The Femtochemistry Conference

The 11th Edition of the International Femtochemistry Conference - Frontiers of ultrafast phenomena in Chemistry, Biology, and Physics - will take place in Denmark, from 7 to 12 July 2013. The scientific venue will be at DTU.

FEMTO11 will bring together 200-300 scientists from all over the world

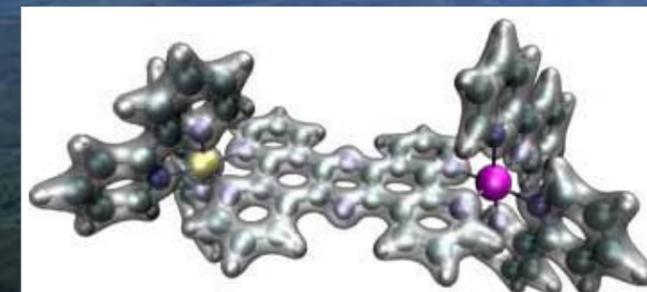
to present and discuss the most recent advances in femtosciences, including structural dynamics studied by XFEL facilities, reaction dynamics, coherent control, solvation phenomena, liquids and interfaces, fast processes in biological systems, strong field processes, attosecond electron dynamics, and aggregates, surfaces and solids with contributions from both theory and experiment.

Furthermore, the conference will open with a keynote lecture by Nobel Laureate Ahmed Zewail well known to both Associate Professors Niels

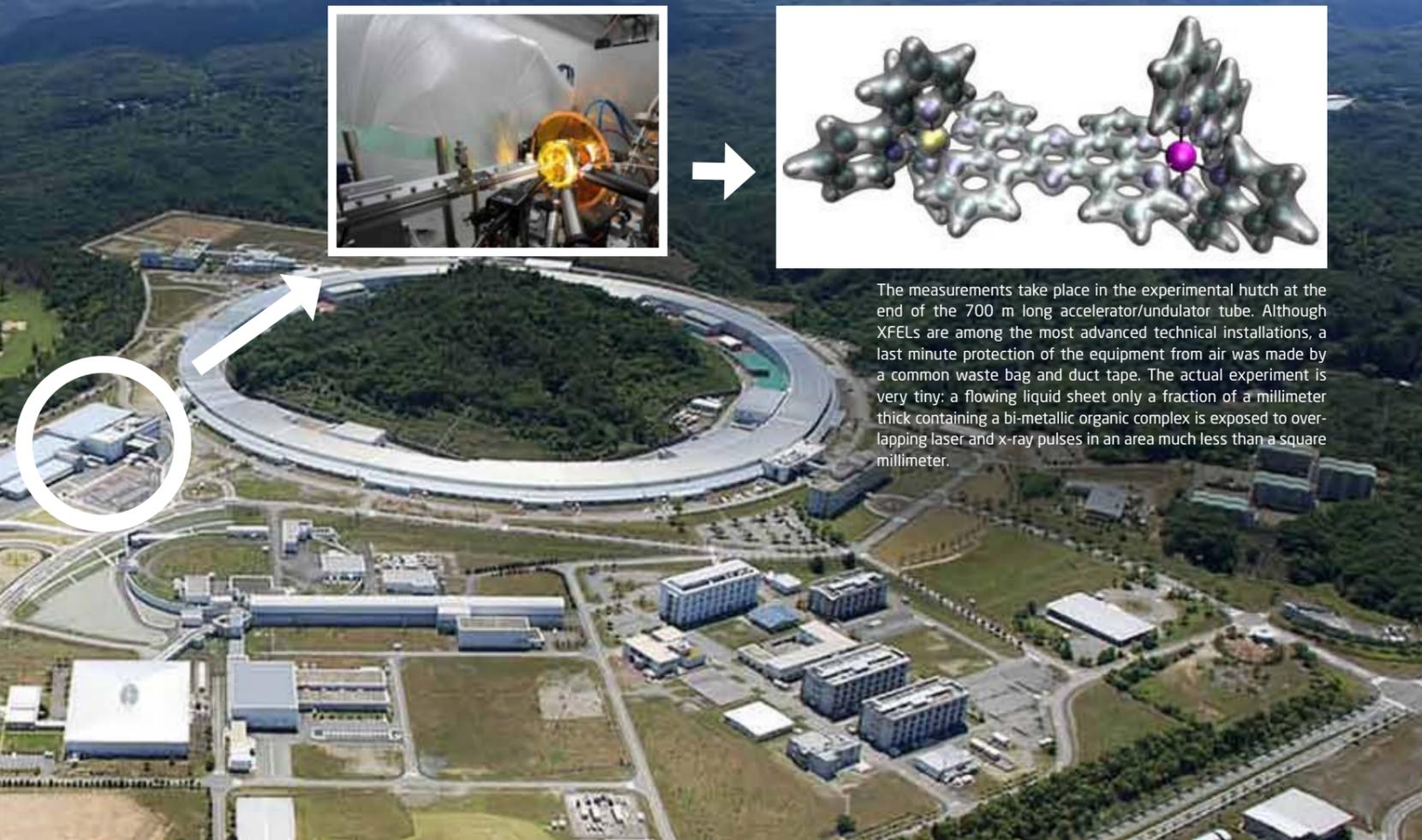
Engholm Henriksen and Klaus B. Møller from DTU Chemistry who have collaborated with the Nobel Laureate for several projects during the years. “We are very proud and happy to host this prestigious Conference here at DTU,» says Conference Chairman Niels Engholm Henriksen from DTU Chemistry. “It's a unique chance to positioning our research in Denmark as an important player on the international scene of femtosciences.”

We welcome you to participate, please learn more at the website:

www.femto11.com



The measurements take place in the experimental hutch at the end of the 700 m long accelerator/undulator tube. Although XFELs are among the most advanced technical installations, a last minute protection of the equipment from air was made by a common waste bag and duct tape. The actual experiment is very tiny: a flowing liquid sheet only a fraction of a millimeter thick containing a bi-metallic organic complex is exposed to overlapping laser and x-ray pulses in an area much less than a square millimeter.



A New Tool in X-ray Protein Powder Diffraction

Previous development by DTU Chemistry of in-house powder diffraction used on protein samples, which replaces costly and time consuming tests at synchrotron facilities, is backed by newly developed software. This makes the method easier to apply for other researchers and industry.

The use of proteins in industry is growing in importance, and so is the demand for fast characterization of protein samples and their internal structure. An alternative to growing single crystals – which is often tricky – is the use of powder probes and in-house X-ray powder diffraction (XRPD). The method utilizes equipment already available in most chemistry laboratories and will give a fast answer to which crystal form/polymorph is being studied. However, certain corrections need to be made in order to get accurate results. The X-ray and Protein Crystallography group at DTU Chemistry has developed software for the purpose.

“After we published our results, it was in principle possible for others to apply in-house XRPD, but in practice it was not that straightforward. Realizing this we have developed software tools that aid the user in making the necessary corrections,” explains Associate Professor at DTU Chemistry, Pernille Harris, co-author of the original study published by the Journal of Applied Crystallography in spring 2010. The article was written in colla-

“The collaboration between Novozymes and DTU Chemistry is truly exciting. Essential knowledge on proteins and production processes is gained, and this is likely to be of long-term value. The collaboration is organized in a manner which involves frequent meetings to evaluate the results obtained. These meetings are inspirational and provide new useful insight. We find meeting and collaborating with DTU Chemistry scientists highly inspirational on a professional as well as on a personal level. It is of direct use in our daily work”

Stein Ivar Aspmo, Recovery Scientist, and Majbritt Thymark, Research Scientist, Novozymes.

boration with PhD Christian G. Frankær, Associate Professor Kenny Ståhl (both DTU Chemistry) and Associate Professor Ole Faurskov Nielsen, University of Copenhagen.

Crucial correction for solvent

In the underlying study, in-house XRPD results for different proteins were compared with Protein Data Bank data with good agreement. However, agreement was not achieved directly, but only after including various corrections including the disordered bulk solvent and geometric factors. Another vital part of this success was improvements made in the signal/noise ratio; in other words reducing the “noise” from background sources. This increased the value of the signal of interest.

In particular the solvent correction was found crucial for a good agreement, as protein crystals contain up to 80 per cent solvent – if dried out, they will break.

“This greatly adds to the complexity of the task. In fact, we were only able to overcome these obstacles because we have both extensive X-ray powder diffraction competencies and extensive protein crystallography competencies within the group. This is quite unique, as these two fields are normally quite distant,” Pernille Harris comments.

Building an XRPD database

One perspective is that industry will be able to screen early precipitates for crystals and possible polymorphs in a way that may save large amounts of time and effort. Furthermore, as structure-based drug design is a growing field and drug candidates are often proteins themselves, there is a growing need for quick characterization of polymorphs and substrate-protein complexes.

In organic and inorganic chemistry, characterization of novel samples using powder diffraction is a routine method:

“Quite often in drug discovery one obtains unknown X-ray crystallography signals, which could lead you to think you have synthesized a novel substance. But before you get too carried away it is worth checking if the signals in question are actually just a result of for instance two well-known substances having been mixed by accident. This can be done by comparing XRPD results with a database of known powder diffractograms,” explains Pernille Harris.

While the method is standard in inorganic chemistry – where databases include hundreds of thousands substances – it is still under development in protein chemistry. Presently about

70,000 protein structures are listed in the Protein Data Base and of these only a few are present in the powder diffraction database.

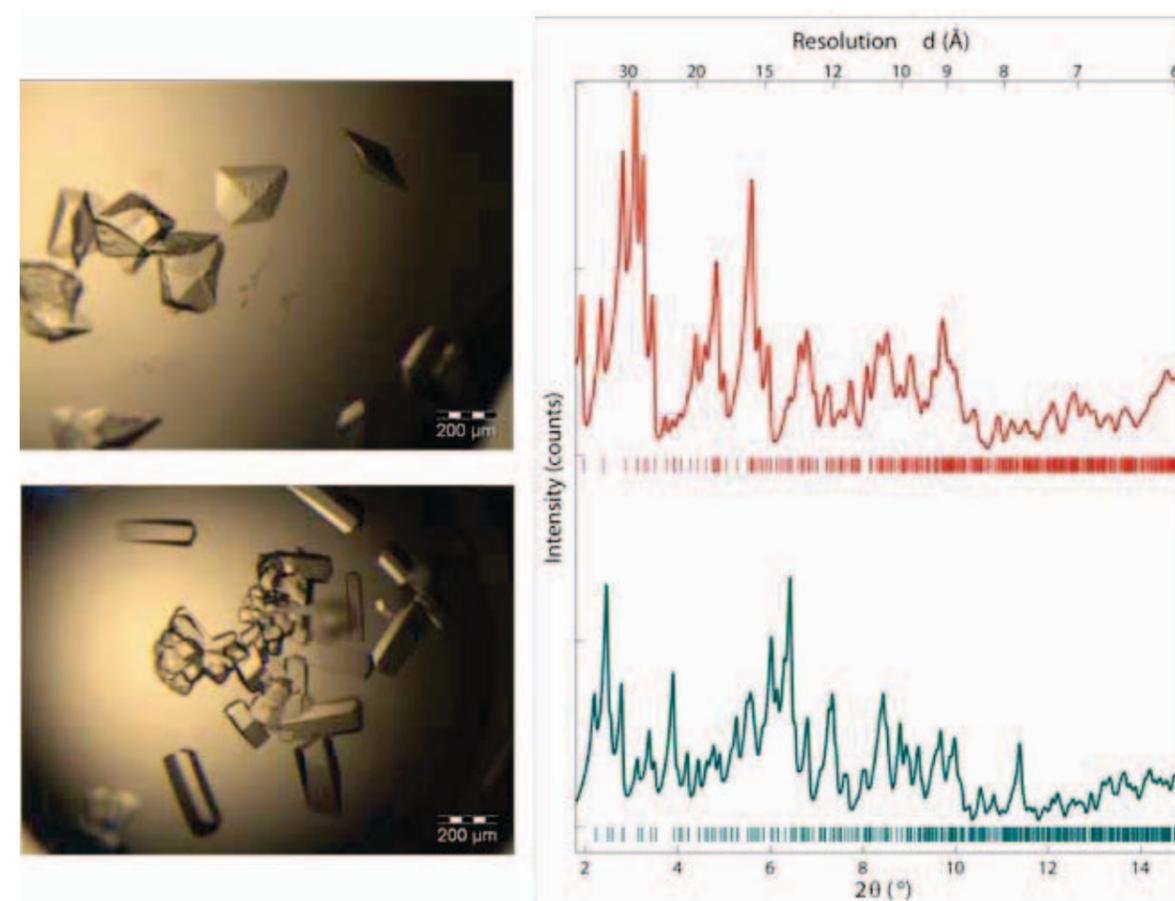
“We hope that we can contribute to the growth of a protein powder database,” Pernille Harris states.

New Industrial Post Doc project

Also, the method promises better surveillance of manufacturing processes. In production, proteins may precipitate in pipes and other production gear. Should this occur, it will be highly valuable to have a method which quickly determines the composition of the precipitate in question. This will in turn allow for quick process modifications that mitigate further problems.

Christian G. Frankær has, in his PhD project, concluded in 2012, shown that in-house XRPD is applicable for the purpose, and that it is even possible to obtain useful results when the probe has been polluted by other substances. This will often be the case in a production environment.

Christian G. Frankær will continue his research in a new Industrial Post Doc project at DTU Chemistry in collaboration with Novozymes A/S, with financial support from the Danish National Advanced Technology Foundation.



Different protein crystal forms (left) result in different fingerprints as seen by the X-ray powder diffraction patterns (right).

4. Comprehensive Chemistry

New Frontiers are Opening in Danish Oil Recovery

A scientific programme led by DTU will assist energy corporations as they drill several kilometres into the North Sea subsoil to explore virgin oil and gas reservoirs.

Oil exploration at great depth is known as HPHT – High Pressure, High Temperature. The high temperature is caused by the greater proximity to the Earth's hot core, and the high pressure by the weight of the overlying layers. While previously it was believed that oil could not be present under such conditions, research in recent years has proved that it is indeed possible. Still, the practical challenges involved are many, and the aim of a new research programme "NextOil DK" is to assist the energy sector in meeting them.

"Data from relevant experiments conducted under high temperature and pressure are scarce in the open scientific literature. We know that some companies have carried out such laboratory experiments but also that they are not always keen to share all their results with academia and competitors. The financing behind the NextOil DK program allows us to establish a strong facility dedicated to the purpose. We expect the facility to become a key player in HPHT-related research, not just in Denmark but also internationally," says Erling Stenby, Head of Department at DTU Chemistry and Chairman of the Steering Committee of NextOil DK. Erling Stenby is also Chairman of the interdisciplinary Center for Energy Resources Engineering (CERE) at DTU which will coordinate the programme.

The first deep field has been selected

Recently DONG Energy has decided to produce the Hejre field located at a depth of 5,200-6,000 metres. The company is an industrial partner to the NextOil DK programme.

"We are aware that as we move to a certain depth, and under special conditions, a number of variables are still unknown. We need to grasp every opportunity to gain knowledge of these unknown variables, in order to be able to produce even more oil and gas in a secure and responsible way in the future. Our latest North Sea investment, the Hejre field, is HPHT, and shows that we in Denmark too can gain from a better understanding of oil production in deep fields. Hopefully, this research will also come into play in other parts of the world," comments Søren Gath Hansen, Executive Vice President, responsible for Exploration and Production, DONG Energy.

The pressure in the Hejre field is 1,000 bar, while the temperature is 160°C. According to DONG Energy, the field's exploitable oil and gas reserves amount to 171 million barrel of oil equivalents. Production is scheduled to commence by the end of 2015. The even larger Svane field, located at even greater depth and likely to contain the largest gas reserves in any Danish field, has a pressure of approximately 1,500 bar and a temperature of approximately 200°C.

Maersk Oil: Safety is a top priority

Another industrial partner to NextOil DK is Maersk Oil.

"The North Sea is still rich in resources. The time has come to address oil and gas reservoirs that are less easy to produce from. The NextOil DK project will be able to provide a significant contribution to the safety of the environment, to the safety of our employees involved in production and to society as a whole, in order to ensure that the remaining amounts of oil can be produced in a safe and effective manner," says Morten Stage, Lead Geomechanical Specialist, Maersk Oil.

The scientific work of NextOil DK is organized as three work packages on rock mechanics, reservoir fluids, and scaling (precipitation of inorganic salts from oil and water present in the reservoirs) respectively. Senior Scientist Wei Yan of DTU Chemistry is coordinating the work. The other DTU participants in NextOil DK are DTU Civil Engineering and DTU Chemical Engineering. Both are very active partners in CERE.

NextOil DK

The NextOil DK programme is focused at HPHT (High Pressure, High Temperature) oil and gas exploration in the Danish sector of the North Sea. Partners are DONG Energy, Maersk Oil, GEO and DTU. The programme has a budget of EUR 4.6 million, of which EUR 2.0 million is provided by The Danish Council for Advanced Technology Research (Højteknologifonden), and the rest by the partners. The programme began November 1st 2012 and is scheduled to run for four years.

"The NextOil DK project will be able to provide a significant contribution to the safety of the environment, to the safety of our employees involved in production and to society as a whole, in order to ensure that the remaining amounts of oil can be produced in a safe and effective manner."

Lead Geomechanical Specialist, Morten Stage, Maersk Oil



The Inner Entrepreneur Comes Alive

DTU Chemistry has initiated a new type of events, the so called Idea Days, increasing the focus on innovation. During his PhD studies Andreas Kunov-Kruse developed a new analytical device for his own research. With backing from the Department and the patent office at DTU the idea is developing into a spin-out company.

When Andreas Kunov-Kruse chose to apply attenuated total reflectance infrared (ATR-IR) spectroscopy in his PhD project on bio-refining, it was by no means an exceptional idea in itself. ATR-IR characterization is recognized as a highly reliable method of establishing the location of chemical bonds in a sample. However, the young scientist found himself challenged as he wanted to use the technique in-situ – meaning under conditions which resemble the processes taking place at a real bio-refinery. ATR-IR instruments with this capacity are about five times more expensive than the regular instruments, and competition for time at the sole instrument of this kind at DTU Chemistry is fierce. His solution was to develop a device which upgrades a standard ATR-IR instrument to do the job.

“The device allowed me to do the science I wanted to do. But I also realized that the idea could have a broader commercial value. ATR-IR is a widely used technique, and it seemed obvious that many others would appreciate a device which would upgrade an ATR-IR instrument for in-situ purposes at a modest cost,” says Andreas Kunov-Kruse, adding:

“It is a part of our fundamental training here at DTU to always consider the entrepreneurial aspects of the projects, we undertake.”

The device was built and co-invented in cooperation with Assistant Engineer Jimmie Thomsen, DTU Chemistry. It is cheap to develop and easy to use and can thus reduce possible costs to perform these investigations significantly.

Bridging across DTU

When Andreas' ideas started to surface DTU Chemistry had just initiated a new type of events, the so called “Idea days”. Once every half year a whole day is devoted to development and identification of possible innovation projects. Andreas Kunov-Kruse was invited and pitched his idea to a panel of senior DTU and industry representatives with commercialization experience.

“Andreas' idea was a good match to this format and the general increased focus on innovation. The idea was untypical though, as in this case the object was not a new chemical process or application, but a device which, albeit highly relevant to chemistry, is not manufactured by chemical means,” explains special advisor Majken Overgaard, co-organizer of the match-making and co-development events.

Through the DTU Department for Private & Public Sector Services under the University Directors' office a patenting pro-

cess was initiated. At the same time Andreas Kunov-Kruse was teamed up with two students from DTU Mechanical Engineering, Jens Piltoft and Christian Petersen.

“During a course on design and innovation, Jens and Christian developed the patented ideas further. While Andreas is very skillful in developing the functionality of the device, it is of course beyond his capacity to provide a user-friendly, industrial design, market investigations etc. - not least considering that he actually has a full time occupation within his PhD project,” Majken Overgaard notes.

The interdisciplinary collaboration soon resulted in a patent application.

Birth of a new company

The initial name for the spin-out company is Specshell. The company will be owned jointly by DTU, and the inventors.

“The Department and the patent office at DTU will continue supporting the company, and the first step will be a commercial feasibility study,” says Majken Overgaard.

Jens Piltoft and Christian Petersen will continue to work with Specshell during their master studies.

On basis of the patents and the ongoing developments, several versions of the device will be built.

“It is desirable to have separate solutions for characterization of liquid and solid probes respectively. Focus in my PhD project is on liquid probes, so this version of the device is the most mature in terms of the scientific content. But in terms of industrial design, the version for analysis of solid probes is more mature. Eventually we hope to market both, and possibly even in different versions depending on the context. A portfolio of products will make a better business case than a single product,” Andreas Kunov-Kruse comments.

“It is a part of our fundamental training here at DTU to always consider the entrepreneurial aspects of the projects, we undertake.”

PhD Andreas Kunov-Kruse, DTU Chemistry

Venture Cup finalists

The entrepreneur team can already note their first success, as the project has been selected for the final round of this year's Venture Cup.

Andreas Kunov-Kruse cannot, however, imagine a future as a full-time entrepreneur:

“I look forward to following the future development closely in a consultancy role. However, I still consider myself to be a chemistry researcher. I have a mind for this kind of inventions but it will take a lot of labor to develop these ideas into products and market them. Also several IPR and other juridical issues had to be resolved. This is not my game, and I am grateful for Majken Overgaard and her colleagues for bridging the cooperation with others that are better suited for the task. In this way I have been able to concentrate on what I do best.”



The device built and co-invented by Andreas Kunov-Kruse and Jimmie Thomsen, DTU Chemistry.

The invention

In the attenuated total reflection infrared (ATR-IR) technique a crystal is located in contact with the probe, which is to be characterized. A beam of infrared light is passed through the ATR crystal in such a way that it reflects off the internal surface in contact with the sample. The reflection forms an evanescent wave which extends a short distance - depending on the circumstances typically between 0.5 and 2.0 micrometers - into the sample. The beam is collected by a

detector as it exits the crystal. Analysis of the collected signal will reveal increased energy in positions where chemical bonds are located in the sample. While commercially available ATR-IR instruments for in-situ experiments are generally priced at around 150,000 EUR, PhD Student at DTU Chemistry Andreas Kunov-Kruse has developed a device which can upgrade much cheaper regular ATR-IR instruments to perform in-situ experiments.



It's important to fertilize sprouting ideas by giving researchers coaching and inspiration, says Special Advisor at DTU Chemistry Majken Overgaard and Associate Professor Anders Riisager who is the responsible for innovation at DTU Chemistry.

Chemistry under the Surface

Innovating research, teaching, communication and consulting require the support of professional services.



Name:
Charlotte Mondrup
Position:
Deputy Head of Department,
DTU Chemistry

For two years now Charlotte Mondrup has been the Deputy Head of Department for DTU Chemistry. Here she reflects on how she has seen an increased cooperation unfold at the department between the different units.

“Skills and talent are a prerequisite for an excellent result. Over the last years we have worked on establishing the mutual picture at DTU Chemistry that our skilled and talented researchers are matched by skilled and talented staff providing strong administrative and technical support and guidance.”

In all support units the aim is to add value to the supply chain by offering the right support and/or complementary skills to the researchers in scientific and educational matters. We have the same common goal: together we shall provide sublime research and teaching results.

You can find an excellent example of taking the research a step further by providing administrative and technical support in the article *The Inner Entrepreneur Comes Alive*. During his PhD studies Andreas Kunov-Kruse developed a new analytical device for his research. This device was built and co-invented in cooperation with Assistant Engineer Jimmie Thomsen from DTU Chemistry’s Machine Center. And with administrative support from the Department and the patent office at DTU the idea has spurred a start-up company in the near future.

It’s a great pleasure to see that we have a whole chain of specialists at the Department of Chemistry. We’re cooperating both within the Department and with several other departments and functions at DTU, as well as with external partners. We see cooperation with external partners and other departments at

DTU as a great opportunity to work with other disciplines of projects which can develop our competencies. In 2014 we’re moving into our new state-of-the-art building with new laboratories and classrooms. Moreover, our two existing buildings have gone through a nice make-over.

I see a Department ready to cooperate with current and new partners as well as meeting the challenges to contribute to excellent research and teaching in the future at the Department of Chemistry.

“Skills and talent are a prerequisite for an excellent result. Over the last years we have worked on establishing the mutual picture at DTU Chemistry that our skilled and talented researchers are matched by skilled and talented staff providing strong administrative and technical support and guidance.”

*Deputy Head of Department, Charlotte Mondrup,
DTU Chemistry*



1. The Reception have physically been transformed so the surroundings are bright, modern and friendly. New services has been introduced so both our staff, students and especially our guests can get the help they need. The reception provides direct support for diverse administration systems on the PC placed in the reception.
2. The administrative staff has various roles from PhD- and Studyadministration to fundraising and communication.
3. The Departments laboratorians are a valuable resource in the labs for both students and researchers.
4. The Service Center ensures that the daily operation of rooms and equipment work perfectly at the Department. Using LEAN, the group has reduced the operational economic costs substantially.
5. The IT-unit at DTU Chemistry supports the whole Department within research and teaching and are a very active partner in various projects across the university. For example, in collaboration with other IT executives at DTU, the IT-unit helped to introduce DTUPC, which is a tool to automatically install operating systems and software. In the coming years focus will be on IT in research laboratories.
6. The Machine Center and the glass blower have a close cooperation with the researchers offering a varied range of difficult technical tasks. Innovative thinking is a daily routine. Over the years many research-projects have been discussed and tested in cooperation with the Machine Center.

4. PhD Defences 2012

A new approach to cancer and diabetes treatment



Name: Anders Emil Cohrt, PhD
Full title: "Solid-Phase Synthesis of Modified Peptides as Putative Inhibitors of Histone Modifying Enzymes"
Supervisor: Thomas E. Nielsen

The project was supported by The Danish Council for Independent Research

Histones are alkaline proteins found in cell nuclei, where they package and order the DNA into structural units called nucleosomes. The role of histone modifications in the tight regulation of gene expression is emerging as a new area in drug discovery. Malfunctioning regulation of histone modification levels has been linked with several life-threatening diseases, including cancer and diabetes. Reversing these irregularities may improve the diagnosis of patients suffering from these diseases.

One possible way of controlling histone modifications may be offered by peptides. Peptides are organic compounds in which multiple amino acids are linked via amide bonds (peptide bonds). Peptides are synthesized by coupling the carboxyl (C-) group of one amino acid to the amino (N-) group of another. In this project, the development of methodologies to modify peptides for use as peptide-based inhibitors of histone modifying enzymes is presented. Several different approaches for both N- and C-terminal modifications have been developed.

In the first approach, two broadly useful acid-labile traceless azido handles for the solid-phase synthesis of NH-1,2,3-triazoles were developed. A variety of alkynes were efficiently immobilized on a range of polymeric supports by Cu(I)-mediated azide-alkyne cyclo-additions. Supported triazoles showed excellent compatibility with subsequent peptide chemistry. Release of pure material from solid support was readily achieved by treatment with aqueous TFA (CH_2Cl_2). In parallel, an azido donor protection group for the synthesis of NH-1,2,3-triazoles was developed for use in both solid-phase and solution-phase chemistry. The NH-1,2,3-triazoles were cleanly deprotected by treatment with TFA.

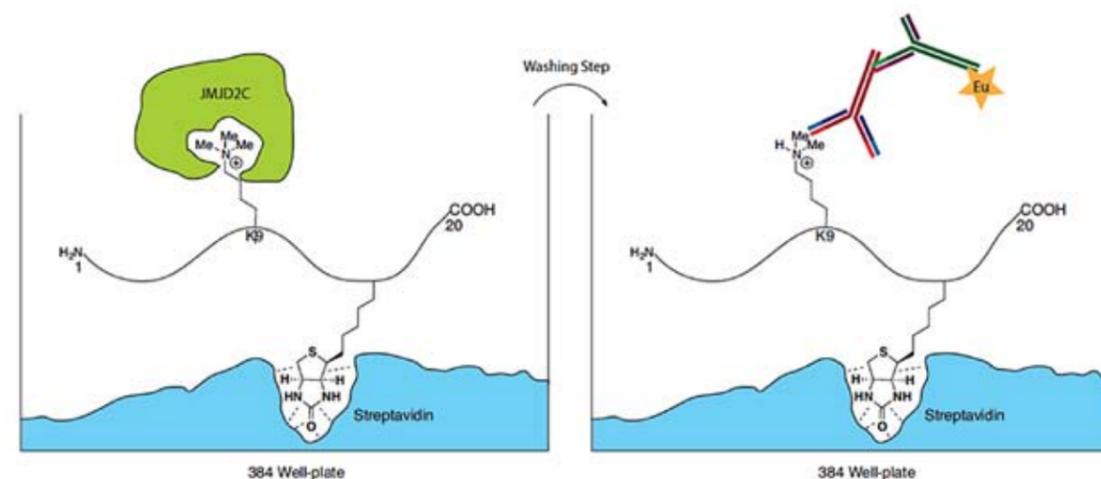
In the second approach, four different libraries of histone demethylase inhibitor candidates were synthesized based on metal chelation, cofactor mimicking and radial

Malfunctioning regulation of histone modification levels has been linked with several life-threatening diseases, including cancer and diabetes.

stabilizing inhibition strategies. The libraries were all synthesized on solid-phase using various handle strategies for the clean release of products. Two cofactor mimicking inhibitor candidates were found to inhibit the histone demethylase JMJD2C.

In the third approach, two mild and selective methods for solid-phase synthesis of thiourea- and guanidine-modified peptides were developed. By activating N,N'-di-Boc-thiourea with Mukaiyama's reagent for HgCl_2 , the N-terminal of solid-supported peptides could be cleanly converted into the corresponding thiourea or guanidine derivative. The reactions were found to be compatible with all 20 naturally occurring amino acids. N-modified peptides were cleanly obtained in excellent yields and purities.

Finally, libraries of histone H2B tail pieces were synthesized using both parallel and split-pool synthesis protocols.

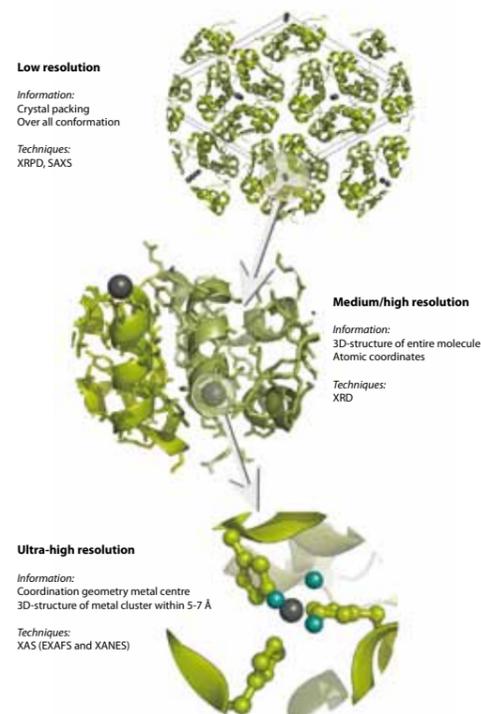


An X-ray tool box for biological studies



Name: Christian Grundahl Frankær, PhD
Full title: "Characterization of Metalloproteins and Biomaterials by X-ray Absorption Spectroscopy and X-ray Diffraction"
Supervisor: Kenny Ståhl, Pernille Harris

The project was funded by DTU



X-ray techniques constitute tools by which 3D structures of matter can be obtained on many different levels of resolution. As new synchrotron facilities are built with more advanced X-ray equipment the need for pushing the existing methods forward and combine them is important in order to study even more complex samples and see more details. As seen from a structural point of view, biological matter such as macromolecules, tissue and cells are often highly complex and inhomogeneous materials and the strategy for successful structural characterization is combination of techniques. This project focuses on the combination and complementarity of three different X-ray methods for studying biological and pharmaceutical samples: X-ray powder diffraction (XRPD), single crystal X-ray diffraction (XRD), and X-ray absorption spectroscopy (XAS).

XRPD operates at the lower end of the resolution scale, and has been demonstrated in this project to be a well-suited technique for characterizing protein precipitates, which can be carried out on in-house X-ray equipment. Crystalline precipitate can thus rapidly be distinguished from amorphous, and a procedure for fast identification of different crystal forms was

developed and tested on micro-crystals of lysozyme and insulin.

Combination of XRD and XAS was used on hexameric insulin. The 3D crystal structures of three different conformations of hexameric bovine zinc insulin (T_6 , T_3R_3 , and R_6) were solved by XRD to resolutions where the individual atoms were traced. Going from high resolution to ultra-high resolution the coordination of zinc in each conformation was studied by XAS including both EXAFS (extended X-ray absorption fine structure) and XANES (X-ray absorption near edge structure) spectroscopy. XAS is a local method meaning that only a cluster with 5-7 Å from the metal atom is studied. In this project distances between zinc and its ligands were very accurately determined from XAS with standard deviations down to 0.005 Å. A combination of XRD and XRPD was used for mapping the polymorphism of strontium ranelate, which is used in the treatment of osteoporosis. It has been known for long that the chemical similarity between strontium and calcium allows for strontium to replace calcium in bones, thus contributing to strengthening bones in patients with the disease. The compound was synthesized and crystallized and the crystal structure of the nonhydrate was

solved. The crystals were highly sensitive to humidity and temperature and easily deteriorate upon dehydration, which is often seen for pharmaceutical compounds. XRPD is a suitable method to characterize the microcrystalline powder remaining from the deteriorated crystals. An in situ XRPD study performed upon dehydration revealed the structures of four other hydrates. Using a combination of XRPD and XAS bone tissue from dogs treated with strontium malonate – a new drug used in osteoporosis treatment – was studied. The hierarchical structure of bone tissue and its many different composites makes the material highly inhomogeneous and provides many different coordination sites for strontium. A new approach for analyzing the X-ray absorption spectra resulted in a compositional model, from which the relative distribution of strontium in the different bone composites was estimated. Approximately 35-45 % of the strontium present was incorporated into calcium hydroxyapatite by substitution of some of the calcium ions, and at least 30 % was located at sites with a high structural disorder similar to Sr^{2+} in solution. The remaining strontium was absorbed in collagen or located on the surface of the hydroxyapatite nano-crystals.

New technology to produce acetic acid



Name: Christopher W. Hanning, PhD
Full title: "Supported Ionic Liquid Phase (SILP) Catalysis for the Production of Acetic Acid by Methanol Carbonylation"
Supervisor: Rasmus Fehrmann, Anders Riisager

The project was funded by Wacker Chemie AG

investigated. It is a standard method to produce acetic acid by reacting methanol and carbon monoxide over a rhodium catalyst. However, in the project a novel set-up involving an ionic liquid (IL) catalyst was developed. An ionic liquid is defined as "a substance composed of two distinct ions that is liquid below 100°C".

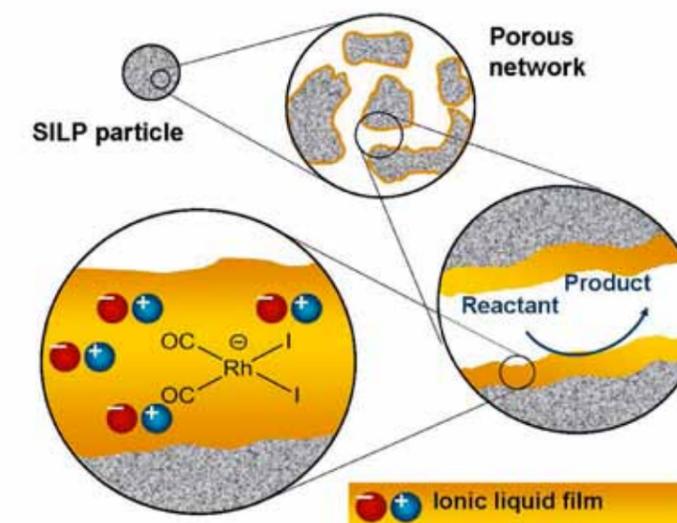
The ionic liquids were introduced in the Supported Liquid Phase (SLP) concept, thus as a Supported Ionic Liquid Phase (SILP) catalyst.

The investigated process is industrially viable for the manufacture of acetic acid. Following these results, Wacker Chemie AG has constructed a pilot plant in Munich.

Acetic acid ($AcOH$) is produced on a scale of millions of tons annually. In aqueous solution it is commonly known as vinegar, coming from the French "vinaigre", meaning "sour wine". As the common name implies, acetic acid is a result of spontaneous fermentation of alcohols. However, nowadays the vast majority of the demand is met by synthetic production. Only a small proportion is for use of acetic acid in its pure form, while the rest is as a precursor molecule for higher value chemicals. The largest single use is for vinyl acetate monomer (VAM), which again is the precursor molecule for poly(vinyl acetate), used in a variety of fields ranging from floor tiles to safety glass. VAM is also used as an emulsifier in water based paints, adhesives, textile coatings and other coatings.

Further, acetic acid is an important material for manufacture of terephthalic acid, which in turn is the precursor to polyethylene terephthalate (PET) used in the majority of plastic bottles and in various similar applications.

In the project, which was carried out in collaboration with Wacker Chemie AG a new catalytic process for acetic acid was



The main attraction of the SILP process is that it allows for a steady production of acetic acid without having to stop and restart the reaction. Continuous flow production is attractive for a number of reasons. One of them is smoother quality assurance compared with traditional batch production, which often involves complex procedures between batches. Also, in some cases continuous production can be cheaper.

A variety of nitrogen based ionic liquids were initially tested, giving good results and system stability. Later a number of phosphonium based salts were tested.

While their properties in the given context largely resemble ionic liquids, these are not classified as ionic liquids because their melting points are above 100°C. The phosphonium based salts showed even better activity in the system compared to ionic liquids.

Overall the work has shown that the investigated process is industrially viable for the manufacture of acetic acid. Following these results, Wacker Chemie AG has constructed a pilot plant in Munich, with the aim of developing the process further towards full scale implementation.

Smart detection of illegal food additives and oil components



Name: Chuan Liu, PhD

Full title: "Deep Ultraviolet Raman Spectroscopy Applied to Chemical Analysis"

Supervisor: Rolf W. Berg

The project was funded by DTU and by The Danish Council for Independent Research

Raman spectroscopy is a well-established method used in chemical analysis to observe vibrational, rotational and other low-frequency modes in a system. Its basis is laser light interacting with molecular vibrations or other excitations in the system, resulting in the energy of the laser photons being shifted up or down. The technique has benefitted strongly from the development of improved laser types over the years. However, the method still encounters challenges at certain wavelengths. For instance, light in the visible range can be disturbed by fluorescence interference. This limitation can be overcome by switching to a light source in the deep ultraviolet (DUV) range. DUV Raman spectroscopy expands the application field, especially in catalysis, life sciences, food and petroleum analysis.

The present project has examined various DUV laser types (semiconductor, solid-state and gas lasers). The considerations included safety issues since DUV light, while invisible, is potentially a very dangerous kind of radiation. Finally, a frequency-doubled Argon ion laser (95-SHG-QS) produced by LEXEL-lasers, Inc. was selected for further adaptation.

Using petroleum analysis as a model for DUV Raman spectroscopy application, several oil and gasoline types were characterized. Fluorescence interference in Raman spectroscopy is a persistent problem for wavelengths in the visible range in e.g. petroleum analysis. This problem generally disappeared when using DUV Raman spectroscopy.

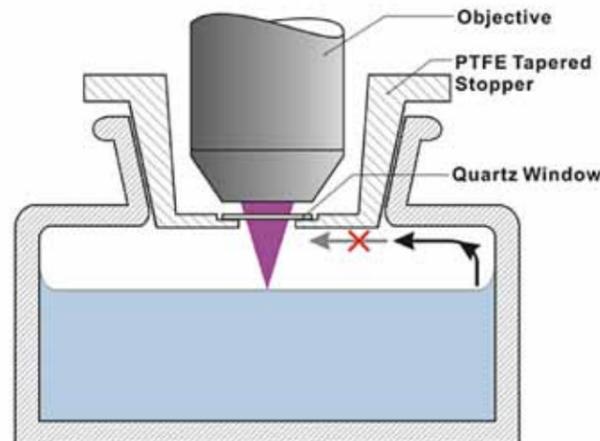
In the project, a special gas gap cell was designed for implementation of DUV Raman spectroscopy. The DUV Raman spectra of gasoline excited by three different wavelengths, 257.3, 244.0 and 229.0 nm were measured. The results show that the spectra obtained by the 257.3 nm excitation line are useless for gasoline samples because of strong fluorescent interferences. The spectrum of the 244.0 nm excitation line contains less fluorescent background and it is possible to obtain clear Raman bands. Finally, by use of the 229.0 nm excitation line, the fluorescent interference is completely eliminated.

More specifically, mixtures of toluene/pentane and toluene/naphthalene were studied using both the 229.0 nm and the 244.0 nm excitation lines. It was shown that the Raman spectrum produced by the 229.0 nm excitation line for home-made artificial gasoline mixtures – with gradually increasing naphthalene contents – can be used to determine the concentration of naphthalene. The intensity of the respec-

tive characteristic bands at 1004 cm^{-1} and 1381 cm^{-1} indicated the relative concentrations of the aromatics, toluene and naphthalene, in the gasoline.

The project also applied DUV Raman spectroscopy to the detection of Sudan I red colorant or dye in food. Although banned as a food additive, it is sometimes seen that Sudan I is added to food to give it a red appearance – an example is red chili pepper. It is known that detection of Sudan I cannot be obtained with green or blue laser line excitation because of the fluorescence interference. It was shown in this project that Raman spectra of Sudan I – without fluorescence interference – can be achieved with the 244.0 nm excitation line. Thus, DUV Raman spectroscopy is a potential detection method for this illegal food colorant.

Deep ultraviolet Raman spectroscopy is a potential detection method for Sudan I red, which is sometimes illegally added to food to give it a red appearance.



Novel strategies for designing small molecules



Name: Erhad Ascic, PhD

Full title: "Build/Couple/Pair and Multi-functional Catalysis Strategies for the Synthesis of Heterocycles from Simple Starting Materials"

Supervisor: Thomas E. Nielsen

The project was financed by the DSF Center for Antimicrobial Research (CAR)

In a biological context molecules with one hundred atoms or less are considered small. In the body, small molecules are active in numerous functions, for instance in the regulation of cellular processes and as messengers, moving information between cells. Small molecules are of interest to all areas of the life sciences, e.g. as drug candidates or as tools for obtaining fundamen-

tal insight into key biological processes. In both cases it is not likely that even the best intellectually conceived idea for a molecule will prove ideal for the given purpose. Rather, it is a well-established method to create a molecular library consisting of many molecules which are then screened in biological assays. But what is the best strategy for generating a library with as many relevant molecules as possible?

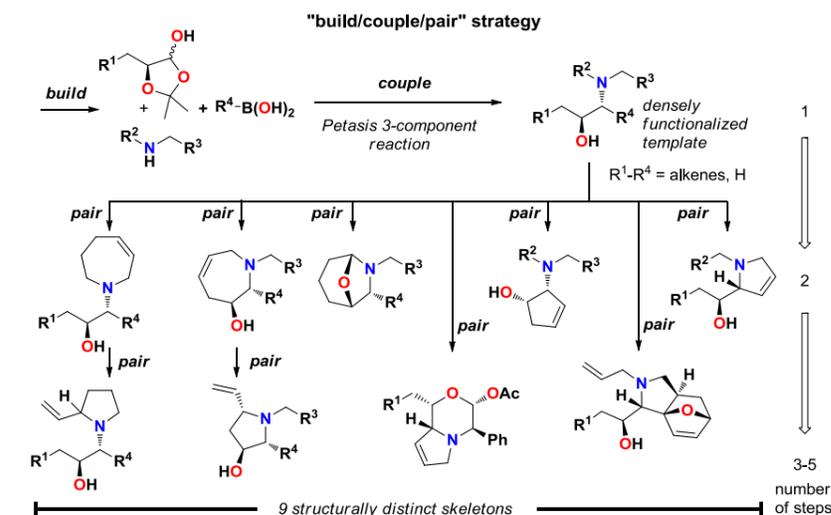
This project investigates two different approaches to meet this challenge.

The first approach is a "build/couple/pair" strategy for the synthesis of structurally distinct skeletons. The strategy is efficient and concise as it involves just two-five steps. A Petasis 3-component reaction is used to synthesize anti-amino alcohols displaying pairwise reactive combinations of alkene moieties. Upon treatment with a ruthenium alkylidene catalyst, these dienes selectively undergo ring-closing metathesis reactions to form skeletally distinct heterocycles. In addition, a ruthenium-catalyzed tandem RCM/isomerization/N-alkyliminium cyclization sequence to hitherto unknown oxazabicyclooctane derivatives is developed which grants an extra element of skeletal diversity. Further skeletal diversification reactions utilizing palladium-catalyzed ring-contraction and intramolecular Diels-Alder reactions are also demonstrated.

Small molecules are of interest as drug candidates or as tools for fundamental insight into key biological processes.

The second approach involves a ruthenium-catalyzed tandem ring-closing metathesis/isomerization/N-acyliminium cyclization sequence. Double bonds created during ring-closing metathesis isomerize to generate reactive N-acyliminium intermediates which undergo intramolecular cyclization reactions with tethered heteroatom and carbon nucleophiles. In the tandem process, two new rings are formed, where a single metal catalyzes two mechanistically distinct reactions in one chemical operation. In this way, a series of interesting indolizidinones are formed in good yields with excellent dia-sterioselectivities, including a formal total synthesis of the antiparasitic natural product harmicine and the first total synthesis of mescalotam. Furthermore, preliminary asymmetric variants of the tandem process have been identified, affording indolizinoindoles in up to 60 % ee.

In addition, a novel palladium-catalyzed tandem Tsuji-Trost/isomerization/N-alkyliminium cyclization has been developed. In this tandem process various THBC ring systems have been formed in good yields from readily available tryptamines.

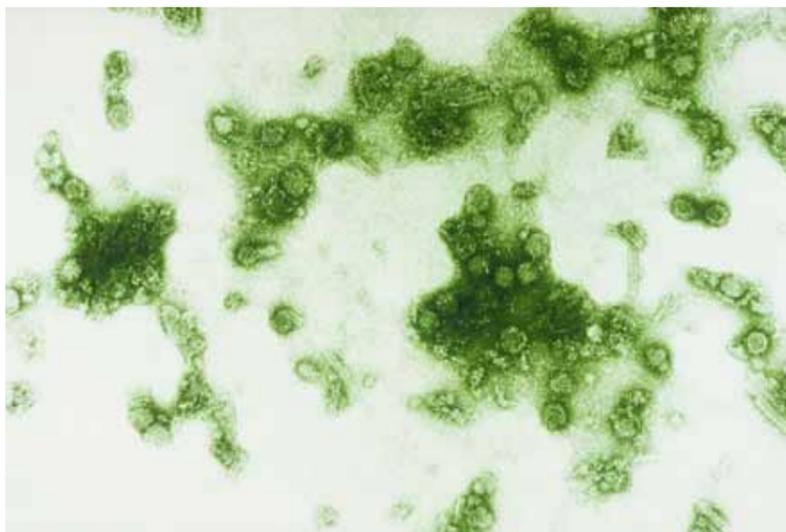


A possible drug design against dengue virus



Name: Györgyi Osztrovszky, PhD
Full title: "Studies and Applications of Metals for the Synthesis of Carbinols, Amides and Carbohydrates"
Supervisor: Robert Madsen

The project was financed by DTU and by the Torkil Holm Foundation



Dengue virus (DENV) is a mosquito-borne virus, which causes flu-like illness. It may occasionally develop into a potentially lethal complication, severe dengue fever. While the global incidence of dengue fever has grown significantly in recent decades, neither a treatment nor a vaccine is presently at hand.

In this project, a tri-saccharide probe has been efficiently synthesized as a putative DENV receptor. More specifically, the GlcNAc β 1-3Gal β 1-4GlcNAc tri-saccharide was considered based on previous studies. The synthesis of the tri-saccharide probe was achieved by coupling of the corresponding D-glucosamine donor and the lactosamine acceptor, followed by deprotection. The tri-saccharide is now under biological investigation and may provide valuable information for a successful structure-based drug design against DENV. In addition, a D-glucuronic acid thioglycoside building block has been successfully prepared for the synthesis of H/HS oligosaccharides, which can also inhibit DENV infection. Both results were obtained during an eight month external stay at the Institute for Glycomics, Griffith University, Australia.

The DENV-related research was one of four different projects which jointly constitute the thesis. The four topics are not interlinked, but all are related to organo-metallic and carbohydrate chemistry.

In one project, the addition of allylmagnesium bromide and benzylmagnesium chloride to carbonyl compounds was studied in the presence of protic agents (e.g. water, methanol, ethanol, phenol). In a number of cases, especially with the use of allylmagnesium bromide, the carbonyl addition was found to be faster or comparable to the protonation by the reagent.

Another project related to the direct synthesis of amides from alcohols and amines with the simultaneous liberation of dihydrogen. This synthesis path had previously been discovered in the Madsen group at DTU Chemistry. Further development of the reaction conditions was investigated, in which stoichiometric additives or hydrogen acceptors were not required and the reactions were catalyzed by ruthenium N-heterocyclic carbene complexes. Two catalyst systems were found to be effective promoters for the amidation. These two systems do not show any significant differences in reactivity. This indicates that the same catalytically active species are operating.

Finally, regio-selective Koenigs-Knorr glycosylation was studied with a num-

ber of unprotected acceptors by means of organo-boron derivatives, which can either activate or block cis-diols via ester formation. By means of phenyl-boronic acid high regio-selective and stereospecific glycosidic bond formations were achieved.

Dengue virus (DENV) is a mosquito-borne virus, which causes flu-like illness. While the global incidence of dengue fever has grown significantly in recent decades, neither a treatment nor a vaccine is presently at hand. In this project, a tri-saccharide probe has been efficiently synthesized as a putative DENV receptor.

Biological and inorganic hybrid materials



Name: Hideki Ikemoto, PhD
Full title: "Catalytic Activity and Photo-physical Properties of Biomolecules Immobilized on Mesoporous Silica"
Supervisor: Jens Ulstrup, Qijin Chi

The project was supported by the Danish Research Council for Technology and Production Sciences

Hybrid materials that combine biological and inorganic materials offer new perspectives in pure and applied biophysics. The inorganic component may for instance enhance the stability of the biological component towards temperature and other environmental changes. In this project three different biological molecules were combined with (inorganic) mesoporous silica (Santa Barbara Amorphous-15 (SBA-15) in particular). The resulting hybrid materials were studied with emphasis on both their stability and the preservation of the biological activity of the biological substance.

The first hybrid material was formed by immobilizing the metallo-enzyme horseradish peroxidase (HRP) on rod-shaped SBA-15 by physical adsorption. It was shown that the thermal stability of the immobilized enzyme was significantly improved in comparison with free HRP. The catalytic activity was slowed down markedly, but the maximum rate (V_{max}) was much more robust to heat than for the free enzyme. The immobilized enzyme was also much more resistant to urea - a strong denaturing agent - than the free enzyme.

However, exposure to another denaturing agent, guanidinium chloride, caused no difference between immobilized and free enzyme. The different behaviour in the two cases is due to differences in hydrogen bonding of water and the increased hydration strength of the protein inside the nanopores.

The second hybrid material was formed by immobilizing the copper-containing enzyme galactose oxidase (GAOX) on SBA-15 with a hexagonally ordered pore structure. It was shown that catalysis by the immobilized enzyme was approximately 30 % lower than for the free enzyme. No improved thermal stability was seen. A similar hybrid material was formed by immobilizing GAOX on mesoporous foam mesoporous silica with a cage-like pore structure. Here significant leaching of enzyme was observed. Covalent attachment of GAOX was found to prevent leaching.

The third hybrid material was formed by immobilizing the light harvesting complex 2 (LH2) from purple photosynthetic bacteria on SBA-15 with hexagonally ordered cylindrical pores or on mesoporous silica with disordered cage-like structures. The studies showed that LH2 is adsorbed into the pores of mesoporous SBA-15. Fluorescence spectra similar to those of free LH2 could be recorded, indicating that the LH2 molecular structure is largely

In this project three different biological molecules were combined with (inorganic) mesoporous silica (Santa Barbara Amorphous-15 (SBA-15) in particular).

preserved inside the pores. But the temperature dependence of the spectra in the range 77-298 K combined with spectral band-shape analysis pointed to small but systematic differences between free and pore-confined LH2. Lifetime measurements of free and pore-confined LH2 in the nano- to picosecond time range yielded other intriguing results. Free LH2 in solution and LH2 confined in a disordered pore structure with large spherical pores showed mono-exponential fluorescence decay, while LH2 confined in hexagonally ordered pores showed bi-exponential fluorescence decay. Further investigations are needed, but as a temporary interpretation, the faster decay time for the conjugates of LH2 and SBA-15 is caused by fluorescence decay channels specific to the molecular scale in the solid state confinement.



Femtosecond energy transfer processes in liquids



Name: *Jacob Petersen, PhD*

Full title: "Vibrational and Rotational Energy Relaxation in Liquids"

Supervisor: *Klaus B. Møller, Niels E. Henriksen*

The project was supported by The Danish National Research Foundation and by the Niels Bohr Foundation

In a typical chemical reaction some kind of energy redistribution will take place. In particular, when a chemical bond is formed in a molecule, a transfer of excess energy out of the molecule's vibrational mode associated with the newly formed bond often follows.

While in a low-pressure gas, the vibrational energy redistribution can be assumed to be collision-free, this is not the case in solutions. Due to the many-body effects present in a dense fluid, the non-equilibrium

vibrational energy distribution for a solute molecule, in which a chemical bond is formed, can decay to equilibrium by a transfer of energy to the various degrees of freedom of the solvent – with a possible energy flow "through" the solute's rotational degrees of freedom. In this case the vibrational energy redistribution is referred to as vibrational and rotational energy relaxation, i.e. a dissipative process that dampens the intra-molecular motion of the solute molecule by transferring excess energy to the surrounding solvent.

Traditionally, it was not possible to follow these processes in real-time experimentally, as the time scales are often in the femtosecond or picosecond domains. Due to continued experimental developments in time-resolved optical spectroscopy and x-ray diffraction, however, it is possible to carry out real-time measurements of relaxation processes.

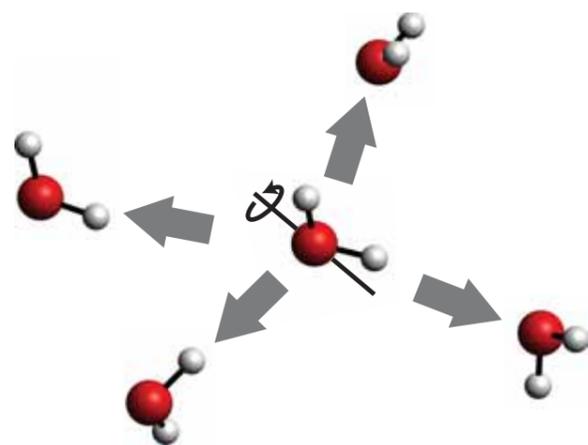
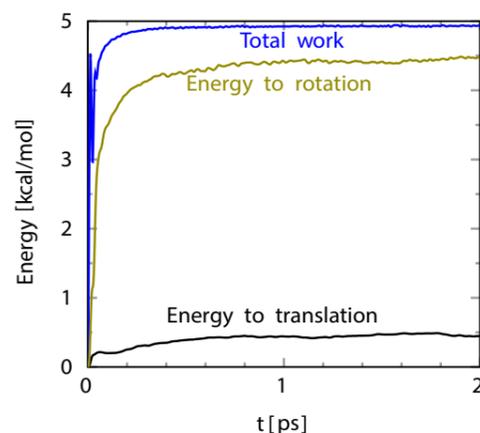
These developments have also caused changes on the theoretical side, where the choice of description has moved from purely analytical calculations to more realistic modelling of interactions and dynamics in the liquid phase. In computer simulations an atomistic description of the system is possible, which permits serious testing of theoretical results.

In the project, the time-evolution of vibrational and rotational energy relaxation in liquids is followed via classical MD (Molecular Dynamics) simulations. It was found that the classical BZ (Bersohn-

When a chemical bond is formed in a molecule, a transfer of excess energy out of the molecule's vibrational mode associated with the newly formed bond often follows.

Zewail) model is in good agreement with quantum mechanics wave packet calculations in terms of the time-evolution of the expectation value of the nuclear position in the anti-bonding state.

Further, the vibrational energy relaxation of I_2 subsequent to photo-dissociation and recombination in CCl_4 was studied using classical MD simulations. The vibrational relaxation times and the time-dependent I-I pair distribution function was compared to new experimental results, and a qualitative agreement was found in both cases. The rotational energy relaxation of H_2O in liquid water was studied via simulations and a power-and-work analysis. The mechanism of the energy transfer from the rotationally excited H_2O molecule to its water neighbours was elucidated, i.e. the energy-accepting degrees of freedom of the surrounding solvent water molecules were identified.



Improved understanding of a crucial brain enzyme



Name: *Lærke Tvedebrink Haahr, PhD*

Full title: "Purification and Characterization of Tryptophan Hydroxylase"

Supervisor: *Hans E. M. Christensen*

The project was funded by DTU

Metal-containing proteins, metalloproteins, are involved in a variety of important biological processes. The iron-containing enzyme tryptophan hydroxylase (TPH) has attracted strong interest in recent years, as it plays a key role in the body's production of serotonin. Serotonin is an important neurotransmitter involved in several psychological functions such as appetite and body temperature regulation. Malfunctioning serotonin production can lead to various psychiatric disorders, including depression and obsessive-compulsive disorders (OCD). Further, serotonin is a precursor for the hormone melatonin, which

is involved in regulation of the sleep-wake cycle. It is likely that more knowledge on TPH may aid in developing improved treatments for serotonin-related disorders.

TPH exists in two isoforms, called TPH1 and TPH2. TPH1 is expressed in peripheral parts of the body, while TPH2 is primarily expressed in the central nervous system.

In the project, a successful purification method for full-length human TPH1 (hTPH1) was developed, which resulted in pure, active and stable protein. The method includes affinity-purification using a maltose binding protein (MBP) tag and high salt concentration in all buffers. It is the first time that a successful purification method for hTPH1 has been presented, which also yields stable protein after cleavage from the affinity tag.

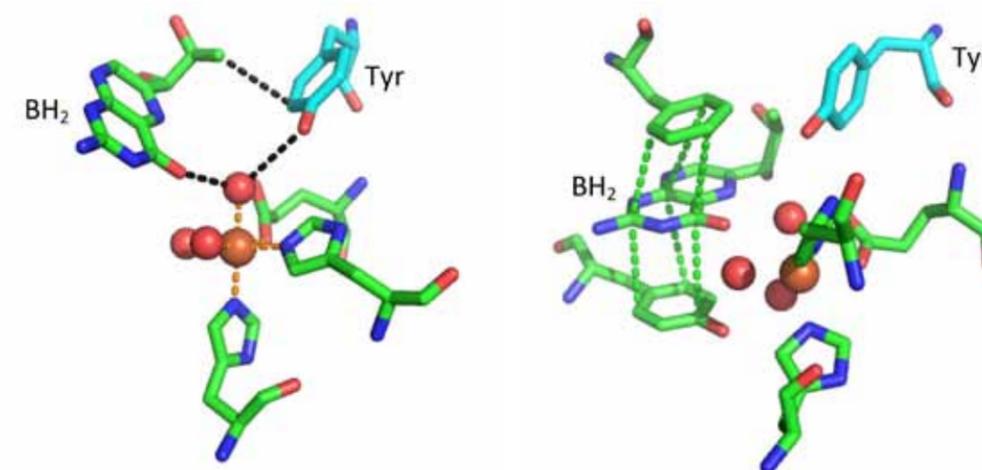
Furthermore, successful purification procedures were developed for a number of other TPH variants. A purification method for the regulatory and catalytic domains of human TPH1 (rchTPH1) using a MBP affinity tag was developed, and revealed that the regulatory domain causes dimerization. Also, a new purification method for the catalytic domain of human TPH1 (chTPH1) using a glutathione S-transferase (GST) tag was developed.

Attempts to purify two human TPH2 variants were made using the same general methods as for hTPH1, but the yields were low, and the products were unstable and could not be concentrated.

Four mutants of the catalytic domain of human TPH2 (chTPH2) were made, and it can be concluded that Glu363, which is an iron ligand, is essential for activity, while Tyr358 affects the activity, but is not absolutely required. Circular dichroism and magnetic circular dichroism results on chTPH2 clearly demonstrated that the active site iron changes conformation from 6C to 5C only when both substrate and cofactor bind. A difference between samples made in glycerol and sucrose was observed. Addition of glycerol to chTPH2 in the Fe(III) form gave a yellow colour indicative of interaction. DSF measurements demonstrated that chTPH2 is significantly more stable in the Fe(II) form compared to the Fe(III) form. Furthermore, the addition of substrates and cofactor only stabilizes chTPH2 when Fe(II) is present.

Isothermal titration calorimetry measurements on chTPH2 determined the dissociation constant of BH_2 to $5 \mu M$, while the dissociation constant for tryptophan is somewhat higher. Tryptophan and BH_2 bind independently of each other.

Malfunctioning serotonin production can lead to various psychiatric disorders including depression.



Green chemistry for manufacturing of pharmaceuticals



Name: Linda Luise Reeh Lorentz-Petersen, PhD

Full title: "Iridium- and Ruthenium-Catalyzed N-alkylation of Amines with Alcohols and Amines"

Supervisor: Robert Madsen

The project was funded by the Danish National Research Foundation

While consumers ever more frequently are given a choice between more or less environmentally harmful products and solutions – for instance when purchasing washing powder or deciding on their means of transportation – this is not yet the case with pharmaceuticals. Still, in anticipation of future consumer demands and in accordance with its own environmental policies, the pharmaceutical industry is already taking an interest in "green" manufacturing.

In this context, both high purity – minimizing by-products – and avoidance of environmentally harmful waste are important criteria when developing green chemistry.

In this project, pharmaceutical manufacturing which involves "amine" functions has been selected as the focus point, as this is the case in no less than 12 of the 20 top-selling drugs in the US (in 2010). More specifically, iridium and ruthenium catalysts have been employed for the N-alkylation of amines with either alcohols or amines.

Three approaches have been considered.

Firstly, self-condensation of primary amines afforded secondary amines in good to high yields. The reaction is catalyzed by the commercially available $[\text{Cp}^*\text{IrCl}_2]_2$ complex. The procedure is environmentally benign as it is performed in the absence of both solvent and additives and the only by-product is ammonia.

Secondly, it has previously been demonstrated by the Madsen group at DTU Chemistry that condensation of diamines and diols catalyzed by $[\text{Cp}^*\text{IrCl}_2]_2$ furnishes the piperazine skeleton. The only by-product of the reaction is water. The substrate scope was extended and the limitations of the reaction were studied. Introduction of a C-substituent on one or both of the starting materials gave C-substituted piperazines in high yields. Synthesis of N-benzylpiperazine from ethylene-glycol and N-benzylethylenediamine was also successful.

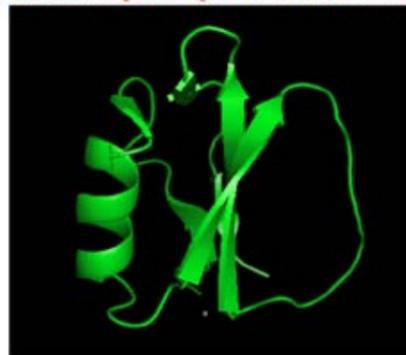
Thirdly, anilines and vicinal diols were reacted in the presence of a ruthenium complex (RuCl_3 with PPh_3 or xantphos) to give indoles in good yields. In this case water and dihydrogen are the only by-products. When unsymmetrical diols were employed the corresponding indole with the largest substituent in the 2-position was favoured.

Finally, during an external stay at The Scripps Research Institute, San Diego, California, USA, folding of the well-

known protein Cl2 was studied. The goal was to synthesize more stable mutants compared to the wild type protein and to measure the difference in energy of the transition state upon mutation. Several mutants were synthetically prepared via folding assisted ligation and studied.

The pharmaceutical industry is taking an interest in "green" manufacturing. In this project, pharmaceutical manufacturing involving amine functions has been selected as focus point, as this is the case in no less than 12 of the 20 top-selling drugs in the US.

1 5 10 15 20 25 30 35 40 45 50 55 60 64
LKTEWPELVGKSVAAAKKVLQDKPEAQHVLVPGTIVDMEYRIDRVRLFVDFKLDNIAQVPRVG



Amino acid sequence and 3D structure of Cl2

DNA as conductors in miniaturized electronic devices



Name: Princia Salvatore, PhD

Full title: "Electronic Properties and Assembly of DNA-based Molecules on Gold Surfaces"

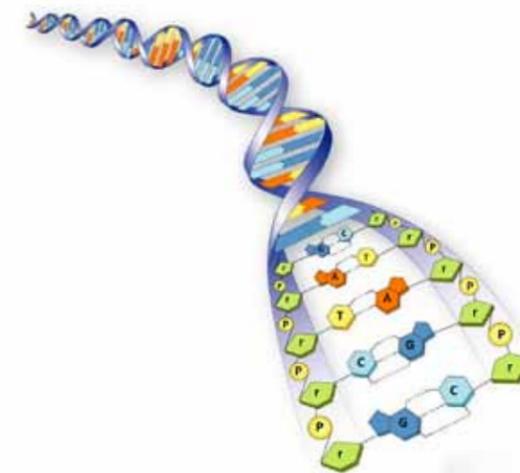
Supervisor: Jens Ulstrup, Allan Glargaard Hansen

The project received financial support from the Villum Kann Rasmussen Foundation

DNA (deoxyribonucleic acid) is the large organic polymer composed of nucleobases holding all the genetic information. Aside from this crucial role, DNA has attracted attention because of its electrical properties. It has been suggested that DNA can be prepared with pre-designed nucleobase sequences and/or functional ligands to form electrically conductive molecular structures ideal for miniaturized devices such as biosensors and integrated circuits, operating under physiological conditions.

The use of DNA as a conductive wire is rooted in the well-stacked array of aromatic base pairs along the DNA double helix, forming a charge conduction pathway. However, several challenges have to be overcome. These include the need to establish well-characterized electrical connections to the DNA molecules without damaging the bases and duplex conformation, and the complexity of dealing with a fragile and dynamic structure in a buffer solution.

The project is a multifaceted study of DNA based on strands and individual components, attached or adsorbed on single-crystal Au(111) and Au(110) gold



surfaces, and on citrate-reduced gold nanoparticles (NP).

Pure and new synthetic oligonucleotides (ONs) were functionalized with terminating alkanethiols and attached to the gold surfaces via their terminal thiol groups, with subsequent formation of self-assembled monolayers grafted to the substrate through the strong gold-sulphur bond. Mercaptohexanol treatment embedding the thiolated ONs in a matrix of smaller thiol-based molecules was exploited to form dilute, more open ON structures favourable for binding of redox molecules at the gold/electrolyte surface. Voltammetric analysis proved the efficiency of the approach. Voltammetry and in situ scanning tunneling microscopy directly in the biological media (in situ STM) offered powerful tools to address structural changes induced by polycation binding where an unexpected, highly base specific voltammetric peak in the presence of spermidine ions was disclosed. The peak is of capacitive origin and offers a novel route to detection of hybridization and base pair mismatches on the basis of the high sensitivity to base pair mismatches showed by such ON-based monolayers.

A "terpy" (terpyridine) redox unit was shown to be a suitable template for in situ preparation of several DNA-bound transition metal complexes (Os, Fe, and Ru). Composite voltammetric behaviour for each of the metal-functionalized

DNA as a conductive wire is rooted in the stacked array of aromatic base pairs along the DNA double helix, forming a charge conduction pathway.

ON-based monolayers was observed and supported by in situ STM/STS, but interestingly, strong in situ STM contrasts induced by metal coordination of terpy-functionalized ONs were disclosed. This may be a novel way to explore the conductivity mechanism in ON strands under mild reaction conditions.

Finally, unmodified moieties (i.e. DNA constituents and pure ONs) on the open Au(110)-electrode surface and on citrate-reduced NP surfaces were addressed by cyclic voltammetry and in situ STM, and by surface-enhanced Raman spectroscopy (SERS). The studies proved adsorption of DNA bases on the gold substrate, disclosing distinct adsorption patterns for each base, with new insight into nucleobase assembly on a freshly cleaned Au(110) surface. In particular, SERS offered a valuable and rapid way of characterizing interactions between the DNA-based molecules and the NP surface, with no need for complex sample preparation.

Novel approaches to the synthesis of peptide mimetics



Name: Rico Petersen, PhD

Full title: "Solid-Phase Iminium Cyclization Reactions for the Synthesis of Natural Product-Like Diketopiperazines"
Supervisor: Thomas E. Nielsen

The project was funded by DTU

Peptides are organic compounds in which multiple amino acids are linked via amide bonds (peptide bonds). Production of peptides – or peptide synthesis – is a key process in organic chemistry. Peptides are synthesized by coupling the carboxyl group of one amino acid to the amino group of another. As the technique normally requires a large number of steps, each adding a new amino acid, it is important to keep purity in each step high, as the eventual losses will be multiplied during the process, leading to a low efficiency of the total synthesis. Also, structural and stereo-chemical control is essential.

In the project a methodology for solid-phase synthesis of peptide-derived fused

2,5-diketopiperazines with an emphasis on structural and stereo-chemical control was developed, while applying two different approaches.

The first approach was based on a highly trans-stereo-selective intramolecular N-acyliminium ion cyclization of N-terminal peptide glyoxylamides, assembling the complete molecular skeleton in a single step. The scope of the methodology was found to be broad, allowing for numerous variations in the "western" amino acid part, including components such as proline, homoproline and N-methylated amino acids, delivering products in moderate to excellent purities (52 to 93 %). The methodology also allowed for modifications in the "eastern" nucleophilic part, including components such as neutral or electron rich phenyl-derivatives, 2-substituted furans and thiophenes, olefins, alcohols and sulphides, generating products in good to excellent purities (61 to >95 %). Furthermore a proton exchange pathway, active under basic conditions and showing convergence towards the trans-product was identified.

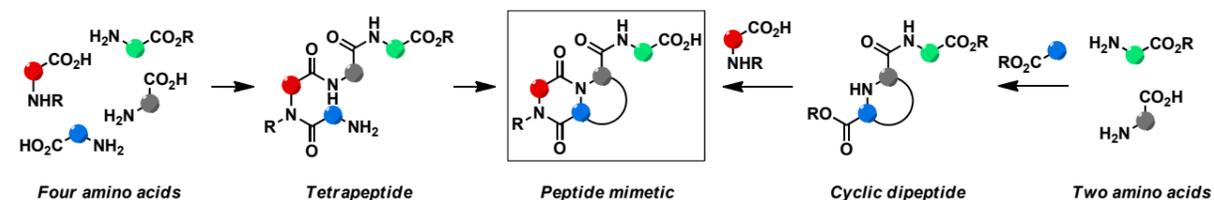
The second approach aimed for use of a cis-stereo-selective intermolecular Pictet-Spengler cyclization to construct the first part of the ring system and a subsequent diketopiperazine formation to close the second ring. Two distinct routes were applied. An ethyl glyoxylate route was found to be non-stereo-selective but well suited for the synthesis of diastereomeric mixtures of 2,5-diketopiperazino[6,1-a] tetrahydroisoquinolines in high purities (74 to 90 %), allowing for separation

In the project a methodology for solid-phase synthesis of peptide-derived fused 2,5-diketopiperazines with an emphasis on structural and stereo-chemical control was developed.

of the diastereoisomers. A route based on glyoxylic acid was found to be cis-stereo-selective (1:2) generating the 2,5-diketopiperazino[6,1-a] tetrahydroisoquinoline product in high purity.

Further, the project has evaluated a diastereomeric matrix of aminomethylthiophene hydroxamic acid biased HDAC inhibitors for biological activity. The compounds showed inhibitory activity against a nuclear extract of HeLa cells, on average 200-fold lower than the activity of the known anti-cancer drug SAHA. When screened towards HDAC 1 the compounds showed a lower inhibitory activity, except for one compound.

Finally, and most importantly, when screening the compounds towards HDAC 8 an activity which was on average 5-fold higher than the activity of SAHA was found. The profound difference in HDAC 1 and HDAC 8 inhibitor activity identifies the compounds as potential sub-type inhibitors.



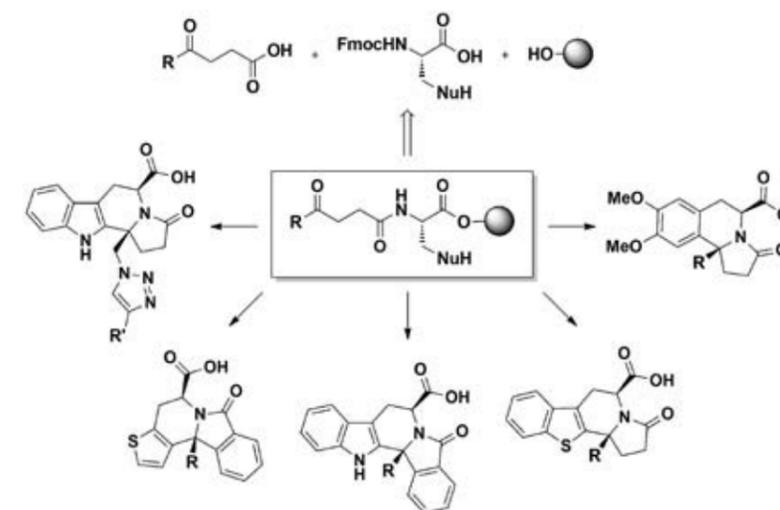
Medical devices with anti-microbial effects



Name: Vitaly Komnatnyy, PhD

Full title: "Solid-supported Synthesis: From Pharmacologically Relevant Heterocycles to Biologically Active Surfaces"
Supervisor: Thomas E. Nielsen

The project was financed by the DSF Center for Antimicrobial Research (CAR) and by DTU Chemistry



In recent decades, solid-phase organic synthesis (SPOS) has emerged as a useful tool for drug discovery. SPOS, introduced by Nobel Prize laureate Bruce Merrifield, has replaced traditional liquid-phase synthesis in most laboratories. Merrifield pioneered the technique for synthesis of peptides, which is a key process in drug discovery and organic chemistry in general. Peptides are organic compounds in which multiple amino acids are linked via amide bonds (peptide bonds).

In SPOS small polymeric beads - insoluble yet porous - are treated with functional units on which peptide chains can be built. The peptide will remain covalently attached to the bead until cleaved from it by a reagent. The peptide is thus immobilized on the solid support and can be retained during a filtration process, while liquid-phase reagents and by-products are removed. Further, the solid-phase split-and-pool approach gives access to large combinatorial libraries of relevant peptides.

In the project, a methodology for the synthesis of structurally diverse heterocyclic scaffolds via N-acyliminium intermediates on solid support was developed.

Firstly, an intermolecular Mannich-type reaction of solid-supported N-acyliminium ion was seen. The method is useful for the solid-supported synthesis of substituted γ -lactams, which constitute a class of pharmacologically relevant small molecule scaffolds. Secondly, readily available ketones were utilized as precursors for solid-supported N-acyliminium ions. Under acidic reaction conditions, peptidic levulinamides undergo intramolecular ketone-amide condensation reactions to form cyclic N-acyliminium intermediates, which in the presence of tethered nucleophiles bring about a second cyclization and the formation of a fused, bicyclic ring system.

Also, the problem of bacterial biofilm-related infections in manufacturing and the use of indwelling medical devices, such as catheters and implants, was dealt with. More specifically, new methods for the controlled organo-functionalization of titanium are suggested. Titanium is one of the most prominent materials in the medicinal device industry. Initial acidic and oxidative treatments of the metal surface generate hydroxyl moieties, which are subsequently modified with synthetically versatile amine-containing reagents. Subsequent applications in antimicrobial peptide synthesis, metal-catalysis, release

from the surface, and polymer grafting, were also investigated.

While SPOS is still most frequently used to produce polypeptides and other oligomeric compounds, with the recent advances in screening techniques and resin technologies, of which several are highlighted in the project, it is clear that the development of reliable synthetic protocols for the synthesis of small heterocyclic molecules may impact medical chemistry and chemical biology more profoundly in the future.

Solid-phase organic synthesis (SPOS) has emerged as a useful tool for drug discovery. With the recent advances (...) it is clear that the synthesis of small heterocyclic molecules may impact medical chemistry and chemical biology more profoundly in the future.

Closing in on bacterial biofilm formation



Name: Yifan Hu, PhD

Full title: "Bacterial biofilms investigated by atomic force microscopy and electrochemistry"

Supervisor: Jens Ulstrup, Jingdong Zhang

The project was supported by the Danish Strategic Research Council, the Danish Research Council for Technology and Production Sciences, and the Lundbeck Foundation

Bacterial biofilms are aggregates of microorganisms in which cells adhere both to each other and to a solid surface or an animal host cavity. They mainly consist of bacteria wrapped in secreted bacterial polysaccharide polymer membrane proteins and e-DNA; referred to as extracellular polymeric substances (EPS).

Bacterial biofilms live on surfaces in human tissues such as teeth, gums, skin, lung, urinary tract and other organs. They are able to cause periodontal disease, dental caries, chronic bronchitis, septicaemia, thrombophlebitis, intractable diseases such as lung infections, and endocarditis. Further, bacterial biofilms can attach to artificial medical devices such as contact lenses, and artificial joints and heart valves causing serious diseases. It is estimated that approximately 65 % of human bacterial infectious diseases are caused by bacterial biofilms.

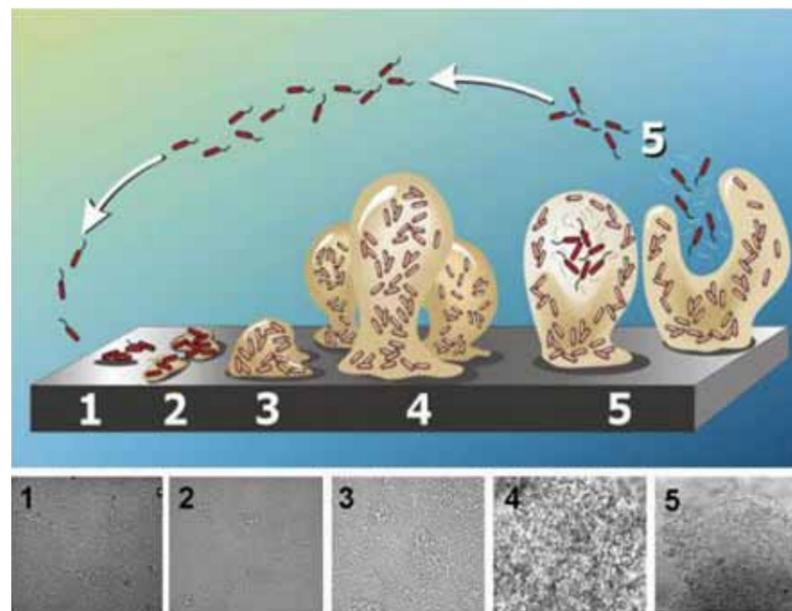
Bacterial biofilms have been shown to have strong resilience in the host immune system and resistance to antibiotics. There is, therefore a strong need for further in-

sight in bacterial biofilms formation. The focus of the present study is on the initial steps of biofilm formation.

As a novel combined approach, Atomic Force Microscopy (AFM) and electrochemistry have been applied to investigate *Pseudomonas aeruginosa* (cystic fibrosis pneumonia), *Staphylococcus epidermidis* (contamination of e.g. surgical catheters), and *Streptococcus mutans* (dental carries) including the effects of growth inhibitors.

One study focused on bacterial biofilm formation on well-defined Au(111)-sur-

It is estimated that 65 % of human bacterial infectious diseases are caused by bacterial biofilms. The combination of AFM and electrochemistry is a new approach to understand bacterial biofilm formation.



faces, to determine the surface charge and growth pattern of *Streptococcus mutans* biofilms. The inhibition and voltammetric patterns showed that *S. mutans* biofilms are negatively charged. Addition of DNAase suggests that the negative charge to a large extent originates from DNA excreted by the biofilm. Further, both AFM images and electrochemical data show that the biofilms are bound more strongly to hydrophobic surfaces than to hydrophilic surfaces.

AFM was also used to study the relationships of *Pseudomonas aeruginosa* and *Pseudomonas putida* to EPS. The study suggests that polysaccharides and e-DNA

contribute to *P. aeruginosa* biofilm development. Protein clusters were observed during *P. putida* biofilm formation, but further investigation is needed to identify or distinguish surface proteins.

Summing up, the combination of AFM and electrochemistry is a new approach to understand the bacterial biofilm/medium/ bare or modified Au(111) interface. Future efforts aim at observing live bacterial biofilms with high resolution and controlling biofilm formation.

Building blocks for "green plastic"



Name: Yury Y. Gorbanev, PhD

Full title: "Catalytic Aerobic Oxidation of Bio-renewable Chemicals"

Supervisor: Anders Riisager, John Woodley

The project was funded by The Danish National Advanced Technology Foundation and by Novozymes

Contemporary chemistry is highly focused on minimizing its environmental footprint. Also, the continuous exploitation of petroleum resources, together with an ever-increasing demand, clearly indicates that the price will greatly rise in the near future. These factors have led the chemical industry to shift towards renewable feedstock.

This project investigated processes where useful chemicals are derived from agricultural biomass by carbohydrate transformations. More specifically, the focus was on furan derivatives. These compounds have been named by the US Department of Energy as being among the top of chemicals from biomass.

Supported gold and ruthenium hydroxide catalyst systems were explored for the aerobic oxidation of 5-hydroxymethylfurfural (HMF) to 2,5-furandicarboxylic acid (FDA). FDA is considered to be a substitute building block for the plastic industry, instead of the currently used terephthalic acid, which is normally obtained from fossil resources. FDA's dimethyl ester (FDMC) was also investigated. High product selectivity and high yields

were obtained for both substances.

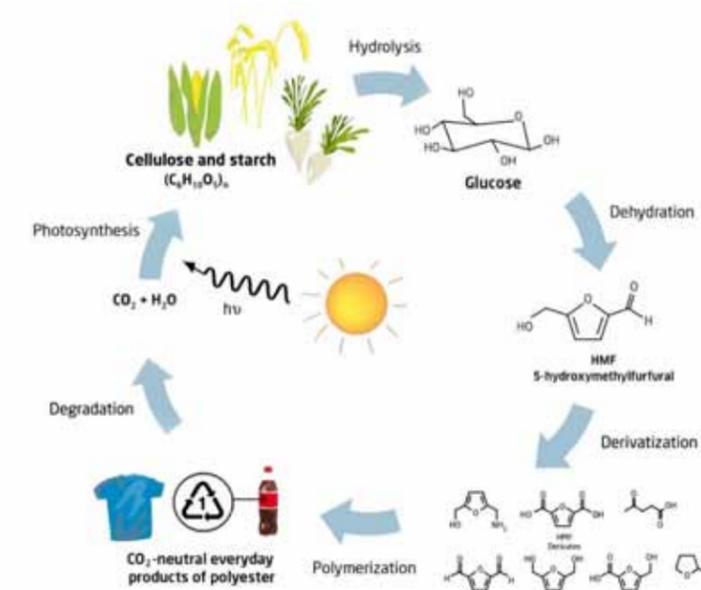
Heterogeneous catalysts consisting of gold nanoparticles on different supports were shown to efficiently oxidize HMF to FDA or FDMC in water or methanol, respectively. Additionally, the reaction conditions were shown to be adjustable for the exclusive production of intermediate products of the oxidation. Catalysts consisting of Ru(OH)_x deposited on metal oxide supports, such as CeO₂ and MgAl₂O₄, were employed in aerobic oxidation of HMF in different "green" reaction media, e.g. water and various ionic liquids, under base-free conditions.

Aerobic oxidation of HMF to form another added-value chemical, 2,5-diformylfuran (DFF), was also investigated. DFF is a potential starting material for various medicinal and cosmetic chemical products. The process was carried out with supported Ru(OH)_x catalysts in organic solvents. The catalyst systems and reaction conditions examined were also shown to be applicable for efficient oxidation of other substituted furans.

Oxidation of alcohols to produce acetic acid was also investigated. Acetic acid is an important product with many appli-

cations in the food and polymer industry, as well as other industries. In the project, ethanol and higher alcohols were shown to be readily and selectively oxidized over supported Ru(OH)_x and RuO_x catalysts producing acetic acid from ethanol, or corresponding acids from higher alcohols, in high yields. Furthermore, catalytic aerobic oxidative degradation of higher alcohols over supported ruthenium hydroxide catalysts was also carried out. A very efficient oxidative cleavage of vicinal diols to form respective acids was also shown.

Furan derivatives have been named by the US Department of Energy as being among the top of the most promising chemicals from biomass.



Reaction network and lifecycle of HMF as a renewable platform molecule.

Master Theses 2012

Solmas Kocak

Studies by Analytical Chemistry of Metal Ions coordination to Liposomes in order to clarify possible relationships with Alzheimer's disease.

Maria Northved Elf

Influence of Small Molecule binding to Microsomes on the in vitro Intrinsic Clearance Calculation.

Guan Zhang

EPR Characterisation of Cu species in Zeolite based Catalysts.

Lasse Bohn Olsen

Solid-Phase Synthesis of HDAC Inhibitors.

Saba Gebremedhin Siyum

Solid-phase Synthesis and Biological Evaluation of Histone Deacetylase Inhibitors.

Ater Baker Al-Ward

Development of Inorganic Proton Conducting Electrolytes by Tape Casting.

Pifu Zhang

Graphene Nanosheets for Chemical and Biological Sensing.

Jonas Andersen

In situ Spectroscopic Studies of Chromium Catalysts in Ionic Liquids.

Cristina Fernandez Gomez

Catalytic Decarbonylation in Ionic Liquids.

Janie Regitse Waël Clausen

Metal-Catalyzed Cross-Coupling/Isomerization/Cyclization.

Bastian Brink

Ordering Phenomena of Carbon and Nitrogen in Iron based Systems investigated by X-ray Synchrotron Methods.

Mette Ishøy

Synthesis of Heterocyclic Compounds via Ru-Catalyzed Ring-Closing Metathesis/Isomerization/Cyclization Sequences.

Casper Mørck

Synthesis of Permeability Glycoprotein Inhibitors: Application as in vivo Pharmacology Tools.

Dionysios Giannatos

Synthesis of Modified Tyrosine for Selective Radiolabeling of Peptides.

Agata Gallas

Synthesis and Electronic Properties of Prussian Blue Analogue Nanoparticles.

Betül Kitir

Synthesis and Structural Studies of Solonamides.

Caralee Rose Nelson

Theoretical Calculation of Rate Constants using the "Polyrate" Program.

Andreas Hougaard Laustsen

Development of Benzimidazole-pyrimidine-carboxamide-based JAK Inhibitors for Psoriasis Treatment.

Gyrithe Lanz

Towards a Synthesis Strategy for Selectively Acetylated Homogalacturonans.

Sara Kildgaard

Discovery of Fungal Anticancer Compounds.

Mads Bøjden Erichsen

Flue Gas Cleaning- Catalytic Decomposition of Nitrous Oxide.

Thomas Flagstad

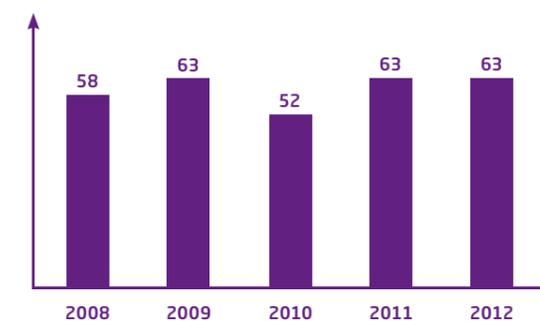
A Build-Couple-Pair Strategy for the Synthesis of Structurally diverse Small Molecules using Multicomponent and Cyclisation Reactions.

Funding 2012

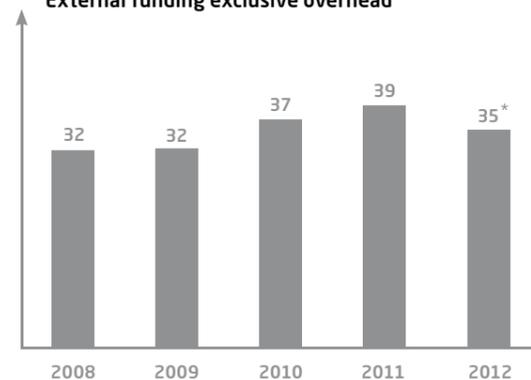
DTU Chemistry's position as a leading research institute was solidly maintained in 2012. Once again the Department had a high success rate in applications for external funding, and we are pleased to note that the chosen set-up has a positive effect. Furthermore, we have met our quota of PhD admission, the co-financing from the industry contributing partly to this.

Additionally, we have maintained the full uptake for the B.Sc. in Chemistry and Technology having even more subscribers that we could accommodate.

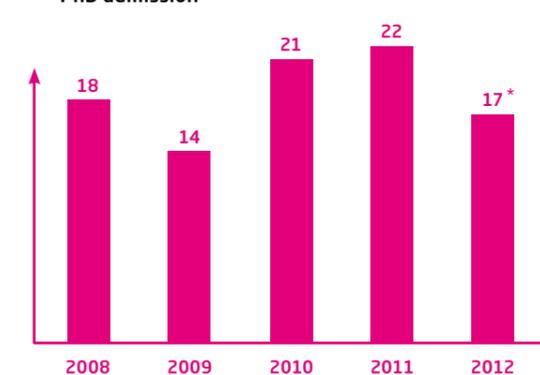
Chemistry and Technology Admission



DTU Chemistry External funding exclusive overhead



DTU Chemistry PhD admission



* The decline is solely due to that the Energy and Material Science Group is no longer part of DTU Chemistry but part of DTU Energy Conversion.



DTU Chemistry staff and external participants at the Department's annual Ph.D Symposium, November 2012 at Comwell in Holte.

Acknowledgement

DTU Chemistry highly appreciates the active involvement of our Advisory Board:

- Kim Andersen, Lundbeck A/S
- Thomas Högberg, Leo-Pharma A/S
- Tue Johannessen, Amminex A/S
- Ole Kirk, Novozymes A/S
- Jesper Nerlov, Haldor Topsøe A/S

DTU Chemistry has wide cooperation with industry. 2012 saw a number of new projects with Danish and international industry initiated. Among the Department's industry partners are:

Amminex A/S	Danish Power System ApS	Maersk Oil
Arla	Dong Energy A/S	NovoNordisk A/S
Arrayjet	Ferring	Novozymes A/S
Bayer	Grundfos A/S	OK a.m.b.a.
Bollerup-Jensen A/S	Haldor Topsøe A/S	PlantProbes
Clauson-Kaas	Johnson Matthey	QuantiBact A/S
CP Kelco A/S	LAB S.A.	Teknologisk Institut
Daka a.m.b.a.	Leo Pharma A/S	Vattenfall A/S
Danisco	Lundbeck A/S	Veloxis
	MAN Diesel	Wacker Chemie



Highlights at DTU Chemistry

Prestigious Thorkild Holm-Award (1)

Associate Professor Thomas E. Nielsen, DTU Chemistry, was awarded the 2012 Torkil Holm Science Prize. Candidates for the prize are younger Danish scientists who have already established themselves in chemistry research and show a high potential for further discoveries.

Thomas E. Nielsen, 37, heads a group in the Organic Chemistry section at DTU Chemistry, which is devoted to design and synthesis of small molecules. He is also co-leader of the Centre for Antimicrobial Research (CAR), which is a joint effort with University of Copenhagen.

Also receiving the prize was Dr. Morten Jørgensen of H. Lundbeck A/S. Morten Jørgensen specializes in the use of metal catalysts for organic synthesis. His PhD was written at DTU

Chemistry under the supervision of Professor Robert Madsen.

Both prizes were given at an international chemistry symposium held by the Danish Academy of Technical Sciences (ATV). More than 300 participants from both industry and academia attended the event, which, just like the prizes, was sponsored by the Torkil Holm Foundation. The foundation has its name from Dr. emeritus Torkil Holm, DTU Chemistry.

DTU Chemistry Flourishes (2)

To have an article accepted by the journal ACS Combinatorial Science, published by the American Chemical Society, is an achievement in itself. A team from DTU Chemistry topped this success by also being selected as the cover story.

In the article, the group led by Associate Professor Thomas



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1. The Torkil Holm Prize Winners: Dr. Morten Jørgensen, member of the prize committee Professor Klaus Bock, Dr. emeritus and founder of the prize Torkil Holm, and prize winner Associate Professor Thomas E. Nielsen. Photo: ATV / Tom Jersø.

2. ACS Combinatorial Science front page - designed by PhD student Mette Ishøj of DTU Chemistry.

3. DTU Chemistry researchers found a key enzyme behind the tomato's polymer skin.



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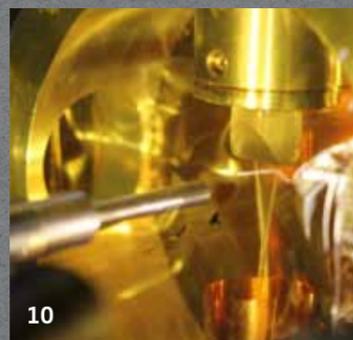
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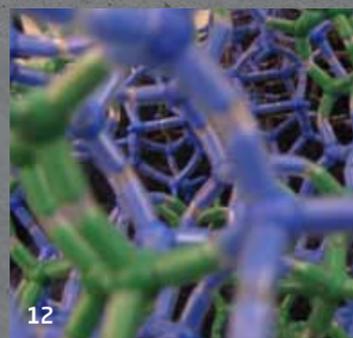
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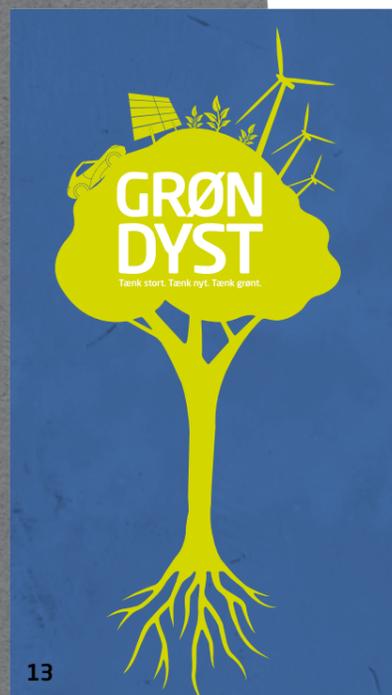
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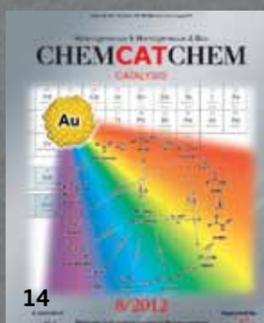
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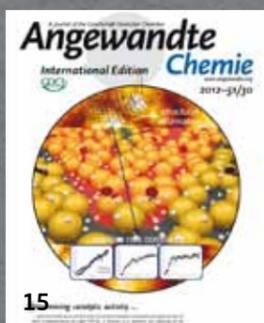
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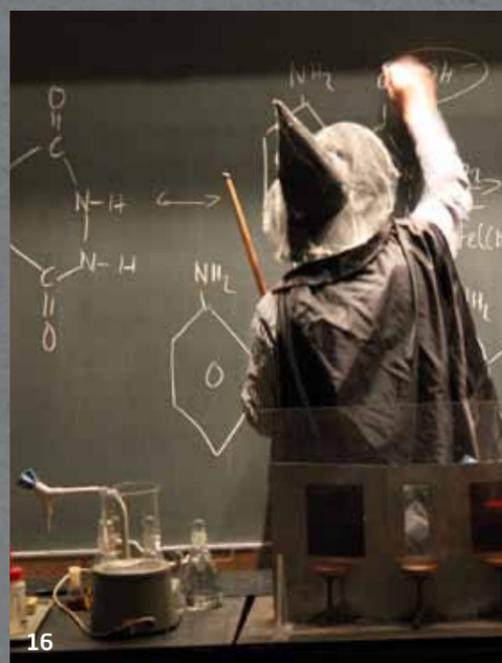
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- 4-5. In 2012 DTU Chemistry was highly involved in the recruitment efforts of DTU.
6. As of January 1st 2013 Jens Ø. Duus joins DTU Chemistry, filling a newly created position as Professor in NMR.
- 7-9. René Wugt Larsen, Martin Nielsen, Andreas Stahl Madsen.
10. Filming chemical reactions at XFEL-facilities SACLA, Japan.
11. The inauguration of Center for Nanomedicine and Theranostics.
12. Chemistry attracting research grants.
13. Green Challenge at DTU.
- 14-15. DTU Chemistry communicates.
16. Explosive Lectures.

E. Nielsen presented promising results on how to create libraries of small molecules in organic synthesis. Small molecules are of interest to all areas of the life sciences, e.g. as drug candidates or as tools for obtaining fundamental insight into key biological processes. Usually a library consisting of many molecules are synthesized and then screened in biological assays for the given purpose. But what is the best strategy for constructing these libraries? The article suggests a “build/couple/pair” strategy for the synthesis of structurally distinct skeletons.

After being accepted for publication, the article was also chosen as a cover story candidate. PhD student Mette Ishøy took on the task of designing a front page illustration. Her aesthetic use of a flowering branch to illustrate nature's efficiency in creating structural diversity from a given starting point decided the matter.

The full article “Build/Couple/Pair Strategy Combining the Petasis 3-Component Reaction with Ru-Catalyzed Ring-Closing Metathesis and Isomerization” can be found through www.kemi.dtu.dk

Enzyme behind the Strong Tomato Skin (3)

A fresh tomato can be so red and shiny you'd think it was made of plastic. And actually it almost is! Just as plastic consists of long chains of monomers – polymers – so does the skin of tomatoes and several other vegetables.

Two researchers at DTU Chemistry, Associate Professor Mads H. Clausen and PhD Hélène Viart, have identified and characterized the enzyme behind the strong tomato skin. The effort was done in collaboration with a group led by Professor Jocelyn Rose, Cornell University, USA.

Initially Hélène Viart was able to identify and synthesize the relevant monomer. This paved the way for testing the enzyme which spurs the construction of the biopolymers.

“It was the first time that an enzyme involved in the production of a plant's skin was identified and characterized,” says Mads H. Clausen, who adds:

“This is a fundamental discovery in botanic biology. In the future plants will play an ever larger role as a source of energy production and renewable chemicals. The better we understand them, the better we will be able to utilize them.”

The discovery was published in Nature Chemical Biology. An online version of the article is accessible through www.kemi.dtu.dk

High School Trainees come on Board (4-5)

Spend three days at DTU Chemistry. This offer was issued to Danish high school students for the first time at DTU.

The arrangement is a natural extension of the many recruitment and outreach activities of the Department. As usual, students and staff from DTU Chemistry have also been active during the 2012 versions of the general recruitment events held by DTU in March and November respectively, the so-called Open Doors, which attracts hundreds of interested students.

Another tradition is the participation of the department in the national branch of the International Chemistry Olympics. The department was the venue for the 3rd national round, where 16 selected high school students competed to be among the four Danes travelling to the international final, which was held in Washington DC.

Leading NMR Specialist joins the Department (6)

As of January 1st 2013 Jens Ø. Duus joins DTU Chemistry, filling a newly created position as Professor in NMR (nuclear magnetic resonance) spectroscopy. He comes from a position as Professor and Director at the Carlsberg Research Centre, home of the Danish Instrument Center for NMR Spectroscopy of Biological Macromolecules. The centre has worked closely with the NMR group at DTU Chemistry for a number of years. Jens Ø. Duus has a background at DTU, where he obtained both his Master and PhD degrees in organic chemistry.

Sapere Aude-grants - Daring to know (7-9)

A DKK 7 million grant from the Danish Council for Independent Research will allow Associate Professor René Wugt Larsen to establish his own group and advanced experimental facilities at DTU Chemistry. In his research René Wugt Larsen studies interactions between matter and light, involving a blend of spectroscopic techniques known from other chemical fields as well as from physics. The grant is a part of the research council's “Sapere Aude” programme – Latin for “Dare to know” – which is designed to boost the careers of especially talented younger Danish scientists.

The programme also includes a Post Doc section, in which two DTU Chemistry researchers were selected, namely Martin Nielsen and Andreas Stahl Madsen. Both receive DKK 1 million.

Martin Nielsen has recently completed a project on the conversion of biomass into substances of use in sustainable chemistry, in which poly-nuclear iron clusters were utilized as catalysts. The new grant will enable him to extend his research and strengthen his collaboration with the group of one of the field's leading scientists, Professor James Dumesic of University of Wisconsin-Madison, USA.

Anders Stahl Madsen studies lysine deacylases, a group of enzymes which are potential drug targets. As lysine deacylases are involved in fundamental genetic processes, knowledge of their function and how they respond to drug candidates may lead to novel treatments for a range of diseases. Besides continuing his research, the Sapere Aude grant will allow Anders Stahl Madsen to host an international symposium with top-level participation.

Industrial Post Doc with Novozymes

For several decades Industrial PhD's have bridged the gap between industry and academia, and The Danish National Advanced Technology Foundation has decided to expand the principle by also granting Industrial Post Doc projects. Christian G. Frankær of DTU Chemistry was one of the 10 younger Danish scientists to be chosen. In his PhD project on the characterization of metalloproteins and biomaterials by x-ray absorption spectroscopy and x-ray diffraction, Christian G. Frankær cooperated with Novozymes on protein characterization. The cooperation is continued into his Post Doc project.

Molecular Movie Shot in Japan (10)

No Hollywood stars were in the cast, but that didn't stop a small team from DTU Chemistry from feeling like celebrities as they carried out a three-day film shoot in the vicinity of Osaka. Japan operates one of the world's only two X-ray Free Electron

Lasers (XFEL). Here scientists are able to follow chemical reactions at the femtosecond time scale. The extremely high resolution makes it possible to construct molecular “movies” showing what goes on during a chemical reaction. PhD student Asmus Ougaard Dohn in particular had a lot at stake, as the experiments will form the basis of his PhD thesis. Nevertheless he found time during his stay to describe his adventure in Japan in a diary you can read in DTU Avisen, no.9/2012, allowing friends, colleagues and fans of molecular movies to get a glimpse of the unique event.

The full article '72 timer der kan oplyse verden' can be found through www.kemi.dtu.dk

Center for Nanomedicine and Theranostics (11)

Center for Nanomedicine and Theranostics is the name of a new entity at DTU involving groups in several departments. The scope will be development of advanced biotechnological tools supporting personalized medicine. Unlike today when large groups of patients are treated with the same drugs in similar doses, the future is likely to bring more individual treatment. This will allow for higher efficiency and fewer side-effects. Nanomedicine can play a role both in treatment and in assessing the effect in each patient. An approach where treatment and diagnosis are integrated is known as “theranostics”. The new center is a result of cooperation between DTU Nanotech and DTU Chemistry, and also involves DTU Veterinary and DTU Nutech.

A Steady Influx of Research Grants (12)

2012 was a highly successful year in terms of obtained funding for the research at DTU Chemistry. The Novo Nordisk Foundation was behind two major grants for organic chemistry research. One was a DKK 1.3 million donation for the group of Associate Professor Mads H. Clausen, while the other contribution, made jointly with The Danish Council for Independent Research/Natural Sciences (FNU), amounted to DKK 4.0 million for research led by Professor Robert Madsen.

The nanochemistry group led by Professor Jens Ulstrup attracted a DKK 1.5 million grant from The Danish Council for Independent Research/Natural Sciences.

Last, but certainly not least, a series of donations from The Danish Council for Independent Research/Technology and Production Sciences (FTP) deserves mention. The groups of Associate Professor Thomas E. Nielsen, Associate Professor Qijin Chi, and Assistant Professor Søren Kegnæs were all granted DKK 5.0 million, while the groups of Associate Professor Kenny Ståhl and Post Doc Uffe Vie Mentzel attracted DKK 0.7 million and DKK 2.0 million respectively.

Green Challenge Winners (13)

Each year, all students at DTU are invited to compete for the best sustainable projects in the Green Challenge competition (Grøn Dyst). Peter Thomassen of DTU Chemistry won 1st prize, while a team of DTU chemistry students won 3rd prize.

In his winning project, Peter Thomassen applied a novel catalyst to remove NOx from the exhaust gas of a diesel engine. The catalyst was designed as a SILP (Supported Ionic Liquid

Phase) catalyst and had [BMIM]NO₃ as the ionic liquid. The study showed that NOx from the exhaust gas could be converted into nitric acid, which could then be captured and stored. Nitric acid is used in the chemical industry.

Conversion of biomass was the topic of the 3rd prize winning project. In their study Simon Suhr Borkenfelt, Jesper Brandt Rasmussen, Nanette Zahrtmann, Trine Marie Hartman Arndal, and Anne Margrethe Loft Andersen used a solid catalyst to convert biomass directly into esters at room temperature and atmospheric pressure.

More than 400 students took part in the Green Challenge 2012 submitting a total of 150 projects.

Reaching out to Colleagues and the Public (14-15)

Among the year's many articles written by DTU Chemistry scientists were: “Gold Nanoparticle-Catalyzed Formation of Nitrogen-containing Compounds – from Mechanistic Understanding to Synthetic Exploitation” by PhD student Jerrick Mielby, Assistant Professor Søren Kegnæs, and Associate Professor Peter Fristrup in ChemCatChem; “Characterizing the Kinetics of Nanoparticle-catalyzed Reactions by Surface-enhanced Raman Scattering” by PhD student Christian Engelbrekt, Associate Professor Jingdong Zhang, and Professor Jens Ulstrup in Angewandte Chemie; and a column on “The Need for Novel Molecular Ideas in the Quest for New Pharmaceutical Drugs” by Associate Professor Thomas E. Nielsen and PhD Rico Petersen in The Engineers Weekly (Ingeniøren). Also an interview given by Associate Professor Peter Fristrup on conversion of biomass into fluid fuels reached a wider audience. The interview appeared in the European Union magazine Projects, targeting readers in industry across Europe. Associate Professor Kasper Planeta Kepp combined an academic article with public outreach as his article on “Bioinorganic Chemistry of Alzheimers Disease” in Chemical Reviews spurred an interview on the subject in national daily Politiken.

Explosive Lectures (16)

More than 1,000 high school students visited DTU Chemistry during November and December. They were drawn by a lecture on explosions, gun powder and cannons. Would that include practical demonstrations? Oh yes. The lecture was co-organized by the Association of Chemistry Teachers and is an annual event.

Spacy X-rays at the National Science Day

As Denmark celebrated its annual National Science Day on April 19th 2012, a public event was displayed at DTU. Associate Professor Pernille Harris showed how she and her DTU Chemistry colleagues apply X-ray spectroscopy to the study of molecular structures, while Senior Scientist Finn Erland Christensen from DTU Space demonstrated how X-rays provide invaluable information on distant cosmic phenomena such as black holes and white dwarfs.

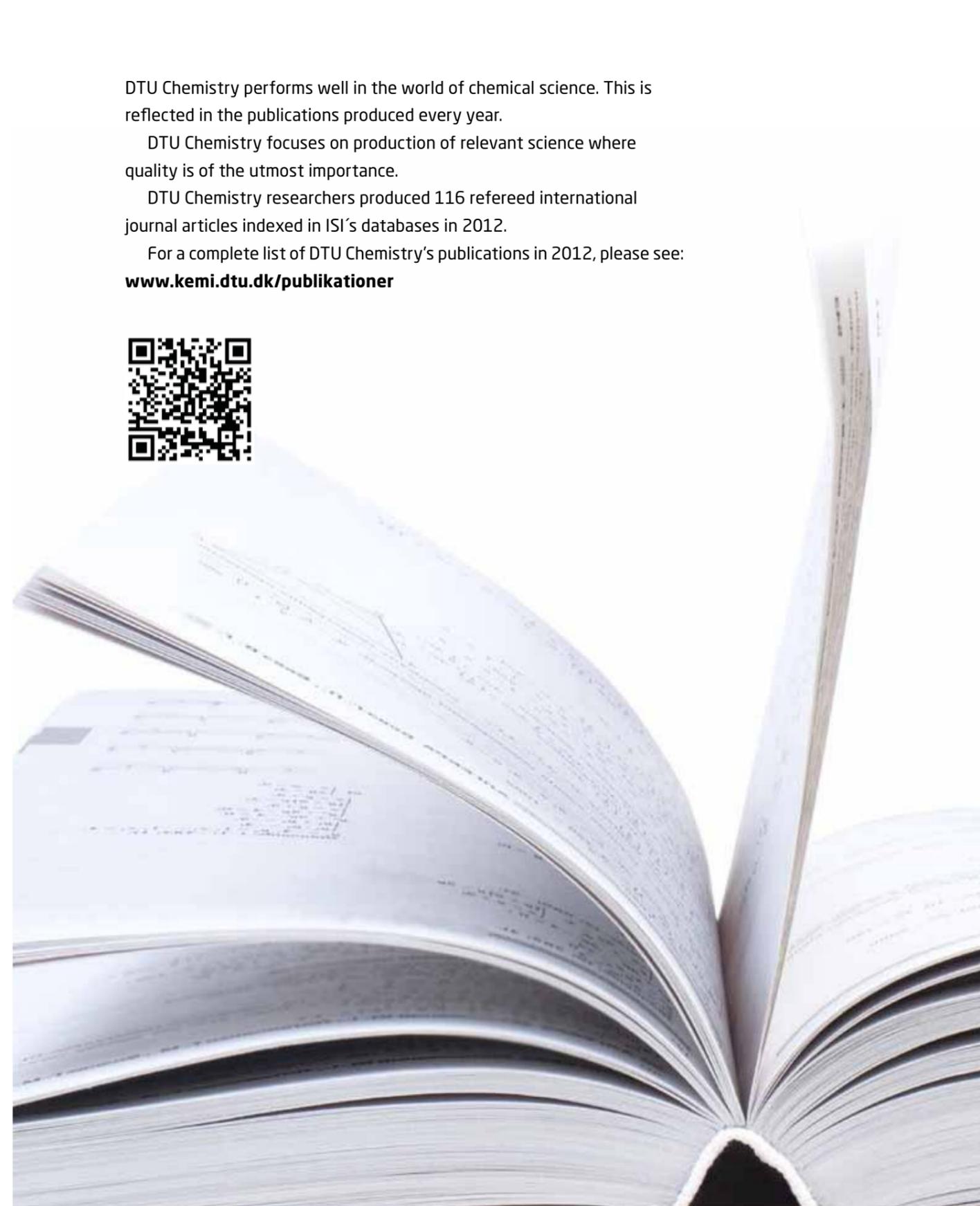
Publications in 2012

DTU Chemistry performs well in the world of chemical science. This is reflected in the publications produced every year.

DTU Chemistry focuses on production of relevant science where quality is of the utmost importance.

DTU Chemistry researchers produced 116 refereed international journal articles indexed in ISI's databases in 2012.

For a complete list of DTU Chemistry's publications in 2012, please see: www.kemi.dtu.dk/publikationer



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$pH = -\log\{H^+\}$ $\int_a^b \epsilon \Theta + \Omega \int \delta e^{i\pi} =$
 $\sqrt{17}$ ∞ χ^2 Σ \gg $\{2.7182818284$

