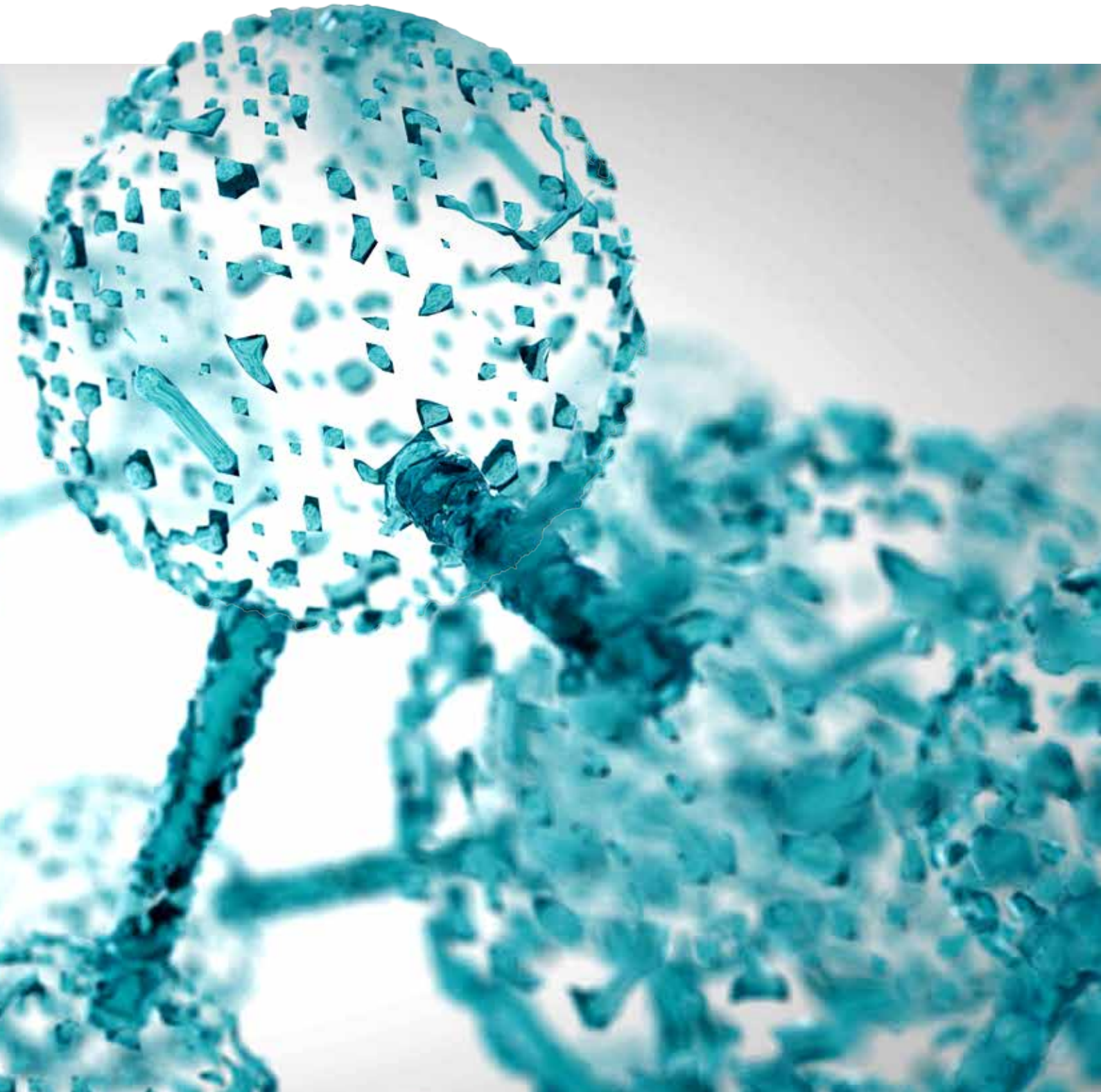
Technical University of Denmark

DTU

Annual Report 2016

Department of Chemistry



Content

The DTU Chemistry Management Group 2016 (left to right) Klaus B. Møller, Pernille Harris, Erling H. Stenby, Jens Ø. Duus and Inge Holkmann Olsen.

A Department on the move

Welcome to the DTU Chemistry Annual Report 2016 – a year marked by new initiatives and growth. In the past few years, DTU Chemistry has seen significant development, making considerable progress in areas such as recruitment, teaching, research, innovation, and international cooperation.

As a result of these positive developments, in 2016 we appointed four professors from within our own ranks. We have also appointed an Italian professor, Sonia Coriani, who took up her new appointment on 1 February 2017. She comes from the University of Trieste.

With the appointment of an impressive five new professors, DTU Chemistry is strengthening its research, particularly within physical chemistry and inorganic chemistry. In addition, Professor Sonia Coriani has a strong background in quantum chemistry – a field in which the Department wants to develop.

The new professors must, together with the rest of the faculty, work to consolidate the positive development, which will benefit both students and prospective employers alike.

Broad perspectives

I see considerable potential in our focus on academic excellence, and I am very happy that we are being seen as an attractive place to establish and develop strong research groups.

It is also reassuring to know that we are able to attract significant external funding. This is true, for example, within life science engineering and materials research, and the external funding is coming from a wide range of sources, for instance from the Danish Council for Independent Research, Innovation Fund Denmark, and from Villum Fonden.

We are proud of our new NMR Center, which was officially inaugurated in December 2016, and for which we received financial support from Villum Fonden, Carlsberg, and DTU. As you can read in one of the articles in the annual report, the strong magnetic field which the centre's NMR instruments uses attracts researchers and businesses from both Denmark and abroad.

Record number of applicants

Our recruitment strategies in recent years are not in vain. DTU Chemistry has seen a large increase in the number of students applying to study at the university, yet without lowering the admission requirements. For the fifth consecutive year, we now have a record number of applicants for the BSc in Chemistry and Technology programme.

We decided to create room for more than 20 new students, because the quality of the applicants was so impressive. However, the experimental courses in the laboratories pose a particular challenge when student numbers increase. The Department has consequently had an increase of the budget, and at the same time all our employees at DTU Chemistry have been incredibly flexible and made an extra effort.

In conclusion, we are in a very positive situation due to the strong engagement and tireless effort by everyone in the Department. We have created a framework where people can realize their potential. Thus, it will also be attractive to be here in the future, as a student and as an employee.

– Erling H. Stenby

***Organic and Inorganic Chemistry**: Jens Øllgaard Duus, David Tanner, Susanne L. Mossin, Robert Madsen, Hans Erik Mølager Christensen, Charlotte Held Gotfredsen, Søren Kegnæs, Rasmus Fehrmann, Jingdong Zhang, Mads Hartvig Clausen, Anders Riisager, Qijin Chi, Peter Fristrup, Jens H. von Barner (Absent. Emeritus 2016.).*

***Physical and Biophysical Chemistry**: Günther H. Peters, Wei Yan, Rolf W. Berg, Irene Shim, Niels Engholm Henriksen, René Wugt Larsen, Klaus Braagaard Møller, Esben Thormann, Jonas Rosager Henriksen, Kasper Planeta Kepp, Sonia Coriani, Pernille Harris, Kenny Ståhl.*

The Department is growing stronger

DTU Chemistry's trademark is scientific expertise founded in fundamental research in applied chemistry.

Since 2015, the Department's research groups have been organized in two major sections: Organic and Inorganic Chemistry with Professor Jens Ø. Duus as Head of Section and Physical and Biophysical Chemistry with Professor Klaus B. Møller as Head of Section. There is a lot happening both at DTU Chemistry and at DTU in general at the moment. For example, DTU Chemistry has recently appointed five new professors, and DTU Chemistry as well as other departments are building new facilities. One of DTU Chemistry's new professors in physical chemistry was recruited from the university in Trieste, Italy.

"We're pleased that we've been able to strengthen our team with a professor from outside DTU. Her research actually reinforces a field which the international research evaluation report from 2015 recommended we could profitably reinforce. With Sonia Coriani on our team, we can create new academic synergies at the Department, while boosting our impact and visibility externally," says Klaus B. Møller. Jens Ø. Duus smiles while looking at some of the new buildings shooting up at DTU in Lyngby. The new NMR Center is located by Kemitorvet, where DTU Chemistry is housed. The NMR Center was inaugurated in December 2016 and also forms part of DTU Chemistry. On the other side of Kemitorvet, the large DTU Life Science building will soon be ready for occupation. "This will strengthen us in several ways and provide scope for exciting partnerships," says Jens Ø. Duus. "The new professors offer new opportunities for collaboration. But I'm also looking forward to DTU Life Science moving in. I see huge potential for collaboration with our future neighbours".

Organic and Inorganic Chemistry
The Section of Organic and Inorganic Chemistry comprises activities within: Catalysis and Sustainable Chemistry, Nanochemistry, Metalloprotein Chemistry, and Organic Chemistry. Common themes are the synthesis and characterization of small to very large inorganic and organic molecules. The research areas are homogenous and heterogenous catalysis; gas separation and absorption; development of new materials; conversion of biomass, electrochemistry; bioelectrochemistry; graphene nanoparticles; coordination chemistry and biochemistry of metalloproteins; chemical biology; NMR spectroscopy.

Physical and Biophysical Chemistry
The Section of Physical and Biophysical Chemistry comprises activities within pure and applied physical chemistry. It covers both microscopic atomic-level descriptions and the macroscopic thermodynamic approach. Common themes are determination of structure and behaviour of small to medium-sized molecules as well as proteins, and many projects involve spectroscopy, scattering, and computer modelling. The research areas are Biophysical and Biomedicinal Chemistry; IR, THz, and Raman Spectroscopy; High Pressure Phase Behaviour for Oil and Gas Production; Protein and X-ray Crystallography; Polymers and Functional Interfaces; Theoretical, Computational, and Femtochemistry.

5 new Professors

Professor **ANDERS RIISAGER**, Inorganic Chemistry, works experimentally with catalysis and ionic liquids with special emphasis on the development of green chemistry utilizing renewable materials for the synthesis of valuable compounds. He has a strong track record in innovation and commercialization, which will also be a focus in the future.

Professor **JINGDONG ZHANG**, Inorganic Chemistry, works in nanochemistry and electrochemistry of especially graphene-based materials to obtain both basic knowledge and important applications within energy conversion, fuel cells, and bioelectrochemistry. She both synthesizes new materials and performs detailed characterization of these by means of electrochemical techniques and atomic scale microscopy.

Professor (MSO) **KASPER PLANETA KEPP**, Physical Chemistry, works with computational physical inorganic and biophysical chemistry with particular emphasis on fundamental aspects of chemical bonding in inorganic chemistry and the structure and function of metal sites in proteins. His research spans from the development of accurate theoretical benchmarks to elucidation of the chemistry behind neurological diseases such as Alzheimer's disease.

Professor **KLAUS BRAAGAARD MØLLER**, Physical Chemistry, utilizes theoretical and computational chemistry to explore molecular mechanisms for conversion of light into chemical energy, often in close interplay with experiments done at large-scale free-electron X-ray laser facilities around the world. His research is important to the development of new, improved materials for, e.g., photocatalysis and solar cells. Klaus Braagaard Møller is Head of Section for Physical and Biophysical Chemistry at DTU Chemistry as well as Head of Bachelor Studies in Chemistry and Technology.

Professor **SONIA CORIANI**, Physical Chemistry.
Read more on the right.

The Italian professor

In 2016, DTU Chemistry appointed four new professors from within own ranks, who were joined by a professor from the university in Trieste, Italy, on 1 February 2017. DTU Chemistry's last appointed professor is Sonia Coriani. She is a professor of physical chemistry and has a strong background in quantum chemistry, i.e. the use of quantum mechanics to solve problems of chemical interest.

"We need to have a better understanding of the properties of molecules, and that's exactly the purpose of my research", says Sonia Coriani.

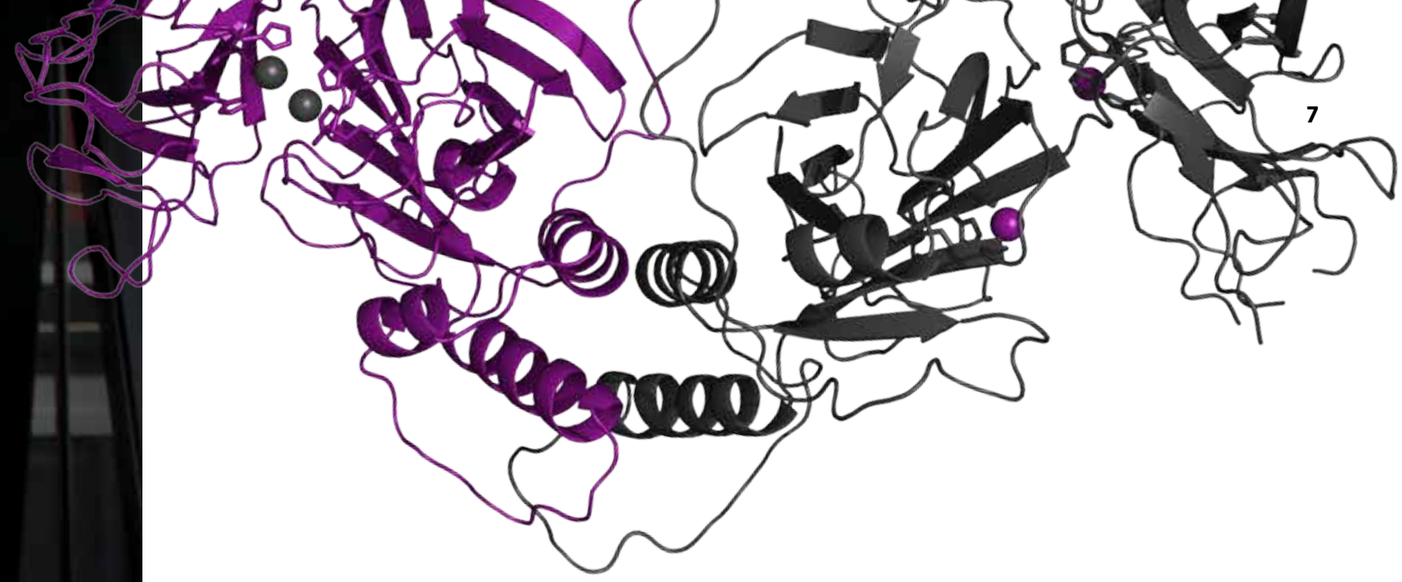
"In my research I investigate how molecules behave when probed with different types of light. Spectroscopy, or in broader terms the study of the interaction of matter with light, is indeed one of the most powerful means of gaining information about the molecular world".

The molecular response to light bears specific signatures of the structure and properties of the molecular systems and can be exploited in a variety of technological applications. The desired information, however, is not provided directly, but is encoded in the measured spectra, often in a complicated way.

Breaking the code
Computational simulations of the measured spectra are essential to help 'break the code' and obtain a deeper understanding of what is going on. They require reliable mathematical models of the underlying interactions and their implementation in efficient computational protocols. "The general objective of my research is thus the development of quantum-chemical methodologies and computer code to describe static and dynamic molecular properties and spectra", says Sonia Coriani. The developed methods are then applied on a broad range of contexts related to modern experiments, including those performed at last generation synchrotron and free-electron laser installations. "My research is thus at the borderline between chemistry and physics and involves interdisciplinary collaborations between theoretical/computational and experimental chemists and physicists".

Solving an intricate Life Science Riddle

When Associate Professor Hans E.M. Christensen, Associate Professor Pernille Harris and PhD student Trine Vendelboe from DTU Chemistry with colleagues from the University of Oxford identified the first structure of the enzyme dopamine β-hydroxylase that controls conversion between two of our body's most important neurotransmitters, dopamine and noradrenaline, they knew it was big news.



After all, a string of competent international research teams had tried to solve the riddle and hack this specific enzyme for more than 20 years to no avail. However, even the seasoned Danish researchers had not quite anticipated the enthusiastic media stir caused by the publication of the enzyme structure in Science Advances.

Within 24 hours of the press release, news media, broadcasting companies and science magazines were queuing up for a comment or an interview. That kind of media attention is quite unusual in the world of metalloproteins and the hectic days in the spotlight following breaking the news of the discovery showed very clearly, that this was no small achievement. But then, it was no chance discovery either. It took ten years of hard work and a lot of stamina to unlock the dopamine β-hydroxylase structure.

Dopamine and noradrenaline play a key role in regulating behavioral and physiological processes like memory, mood, arousal, and attention. The enzyme dopamine β-hydroxylase, that Associate Professor Hans E.M. Christensen and his team unveiled, controls the levels of dopamine and noradrenaline in our body. Malfunction in the control of the two transmitters has been linked to a number of disorders seriously affecting human life such as hypertension, depression, anxiety, Parkinson's disease, schizophrenia, Alzheimer's and drug dependence. Understanding the crystal structure of the enzyme, therefore, could provide an ideal target for future drug development.

"It's never easy to map an enzyme", Hans E.M. Christensen explains. "It's always a laborious process and you have to be persistent, but in this case it was somewhat harder to unlock the secrets than in most cases. There were quite a few setbacks and turns along the way, but we never really doubted that it could be done, that we were on the right track. These are competent people, and we were determined to see the process through to the end as a team".

Enzymes like these are rare in the human body, and therefore the team needed to produce sufficient material in so-called cell factories that can be controlled in vitro. After failed attempts with bacteria and yeast cells, the common fruit fly Drosophila Melanogaster provided the cells needed for the factories, and after five years of work, the first breakthrough came when the enzyme was produced, although the team still was not able to crystalize it and thereby decode the structure through X-ray crystallography. That problem was eventually solved in cooperation with researchers from University of Oxford, and in the end, Associate professor Pernille Harris from DTU and her PhD student Trine Vendelboe painstakingly build the 1200 amino acid structure by hand, one functional group at a time.

Using X-ray crystallography, the team found that the unraveled enzyme contained two new potential binding sites. One was a pocket where another molecule can bind, common to this class of enzymes. However, also a binding site for copper ions was entirely unanticipated. "This is the big surprise", Hans E.M. Christensen says. "We have uncovered a structure of this enzyme that no-one was expecting. Now we can help the biotech industry exploit these binding sites to develop new drugs targeting the binding sites".

One such use could be the design of inhibitors modulation the dopamine β-hydroxylase involvement in PTSD and drug dependence.

Hans E.M. Christensen and his coworkers also found that dopamine β-hydroxylase seems to function by a flip-flop mechanism, where one half of the enzyme carries out the enzymatic reaction, while the other half of the enzyme unloads the noradrenaline and loads dopamine. Then, the enzyme flip-flops and the function of the two halves of the enzyme are interchanged. "The flip-flop mechanism is another unexpected phenomenon we need to explore further", Hans E.M. Christensen states. "It could very well shed new light on some of the numerous poorly understood disorders associated with malfunction in the noradrenaline pathway".

Since the publication of the structure of dopamine β-hydroxylase, Hans E.M. Christensen has been busy as speaker at high-impact conferences and meetings, but back home at DTU Chemistry the work with the enzymes continue. "We have solved the original riddle and the patent is pending, but as it often is with science, the answer has bred a lot of new questions we need to tackle. This is just the beginning of an exciting journey I'm looking very much forward to embark on with my team", Hans E.M. Christensen states.

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Young Investigators lead new Research Groups

Significant grants from the Villum Young Investigators Programme allow two highly talented researchers to build strong groups at DTU Chemistry.

Of 16 Danish scientists granted funding in 2017 from the prestigious Young Investigators Programme sponsored by Villum Fonden, two will now be able to set up ambitious groups at DTU Chemistry. Kasper Steen Pedersen returns to his native country after Postdoc stays at French and Canadian universities. He has been granted DKK 8.6 million from Villum Fonden. Sophie Beeren was already employed at DTU Chemistry as Researcher. The grant of DKK 10.0 million allows her to expand her group from two to six members.

Foto: Simon Knudsen

Non-natural Selection of Carbohydrates

Carbohydrates are vital to our wellbeing. However, the synthesis of carbohydrates using traditional organic synthesis routes is notoriously difficult. A research team led by Sophie Beeren sets out to develop a smarter, very different method.

Carbohydrates, or saccharides, play important roles in chemical biology. For example, saccharides present on the cell surfaces are instrumental in processes such as cell-cell recognition and communication, surface adhesion, and immune response. Thus, the potential for using saccharides in both prophylaxis and treatment of diseases is huge. A 10.0 million DKK donation from Villum Fonden allows the efforts at DTU Chemistry in saccharide syntheses to be stepped up considerably. Recipient of the grant is Researcher Sophie Beeren who will expand her group from two to six scientists.

“Carbohydrates constitute one of the three major biological polymer groups. Exploration of the two other groups, which are DNA and proteins, has progressed strongly as efficient synthesis routes were found. Time is due to achieve similar progress by improving carbohydrate synthesis,” says Sophie Beeren.

Like building an arch

Rather than constructing saccharides step by step as seen in traditional organic synthesis Sophie Beeren’s idea is to synthesize a large number of related substances, also known as a chemical library. Subsequently, the number of candidates will be narrowed down as the substances are screened for the desired properties. The process is supported by addition of molecules which serve as a template for the saccharides.

”The method resembles the way arches have been constructed for centuries. Initially a wooden template is built. Then stones and cement are put on top. When the arch is complete, the wooden template is removed,” Sophie Beeren explains.

Non-natural selection

Sophie Beeren calls the method non-natural selection. In natural selection the most fit – or well adapted – organisms survive, as Charles Darwin famously noted. In chemistry, this is reflected in the observation that the most stable molecules survive.

“The most stable molecules are not necessarily those best suited for the applications we seek. The addition of the template molecules steers the selection away from the one which would have taken place spontaneously. We obtain products with the desired properties rather than just stable products,” says Sophie Beeren.

SOPHIE BEEREN is Australian. She moved to Great Britain in 2006 to take on a position at the University of Cambridge. In 2011, she accepted a position as Postdoc at the Carlsberg Laboratory in Copenhagen and went on to become Researcher at DTU Chemistry in 2014. Sophie Beeren has published a long range of scientific articles in the Journal of the American Chemical Society (JACS), Angewandte Chemie, and other prestigious journals.

In 2014, **KASPER STEEN PEDERSEN** received a Sapere Aude grant. This national program is designed to boost the careers of especially talented young Danish scientists. He used the grant for Postdoc stays at various institutions under the CNRS (Centre National de la Recherche Scientifique), France, and at the University of Montreal, Canada. The new grant from Villum fonden allows him to set up a group in his native country.

Chemistry for The Quantum Society

Extremely powerful computers, better catalysts and airport security sensors able to detect hidden explosives – these are three examples of future technologies based on molecular level phenomena.

Based on the laws of quantum mechanics, which govern physics on an atomic scale, a wave of new technologies are about to help solve many of today’s global challenges. A new research group led by Kasper Steen Pedersen will work at the international forefront of chemistry for such applications.

The focus of the group will be 2D materials science – meaning layers of material so thin, that their thickness can be regarded as just one molecule.

“At this level the properties of the material can be very different from the same material in a thicker 3D version. For example, the magnetic and conductive properties are often entirely different,” explains Kasper Steen Pedersen.

Computers, catalysts, and sensors

The magnetic and conductive properties at the molecular level are crucial to a number of future applications, one of them being quantum computers. Computers based on quantum mechanical phenomena are predicted to become far more powerful than even today’s super computers.

Other potential applications are novel types of catalysts, and sensors able to trace extremely small amounts of chemical substances – in principle down to a single molecule. For instance, such highly sensitive sensors may be used in airport security to detect a range of explosive which give off trace amounts of matter to the surrounding air.

A new world opens up

Obviously, a number of groups around the world are engaged in quantum mechanics chemistry, but the Pedersen Group has a unique angle, Kasper Steen Pedersen notes:

“Over the latest years, graphene has attracted large interest within the field of 2D science. Graphene has, indeed, several exiting applications, but when the magnetic and conductive properties are in focus – as they are in our research – neither graphene nor any other existing 2D materials are quite satisfactory.

Our approach will be designing suitable building blocks at the molecular level and assemble them to form the structures we want. We are confident that this will open up a new world of advanced 2D materials with chemically tailor made properties.”

THE VILLUM YOUNG INVESTIGATORS PROGRAMME

Villum Fonden supports research in the technical and natural sciences, as well as environmental, social and cultural projects in Denmark and abroad. In 2012, the foundation established its Young Investigators Programme. ”Villum Fonden has doubled the program since the first grant of DKK 75 million for young researchers in 2012. The result is that many of the younger researchers have set up independent research groups, and several have been able to attract additional attractive research funding, for example from the EU. Furthermore we are pleased to know that many of the researchers due to their high professionalism subsequently have achieved a tenured position at a Danish university”, says Director of Science Thomas Sinkjær, Villum Fonden.

Novel Skin-friendly Polymers

Topical film formers for sunscreens and adhesives for attachment of ostomy bags are examples of polymers designed for contact with the human skin. Such products may be improved by application of state-of-the-art knowledge on polymer surface chemistry.

Gore-Tex, a fabric co-invented by Wilbert Gore and his son Robert Gore, allows sweat to exit from within a raincoat while not hampering the coat's ability to resist rain. A research group led by Associate Professor Esben Thormann is looking to achieve the same thing for sunscreens and polymer adhesives in direct contact with the human skin.

"The specific solutions will be very different since sunscreens and polymer adhesives are not really similar to a raincoat, but the image illustrates our fundamental challenge. It is well known that sweat and bathing dampens the effect of sunscreens considerably. Similarly, adhesives that attach ostomy bags and other medico-technical products to the body will gradually deteriorate because of moisture at the skin surface. Both types of products can be improved significantly, if we succeed in transporting moisture swiftly away from the skin surface," explains Esben Thormann, who is heading the group on Polymers and Functional Interfaces.

The relevance of the idea is underscored by the strong industry involvement. While Innovation Fund Denmark is the main sponsor of the project – with DKK 12.2 million – two companies contribute significantly to the total budget of DKK 22.5 million. Coloplast is a world-leading supplier of ostomy bags and a range of other medico-technical products. Riemann is a dedicated supplier of high-end sunscreens with strong long-lasting protective effects.

Allowing the skin to breathe

"The two companies do not have any mutual commercial conflicts as they operate in completely separate markets. Yet, their fundamental problem in relation to this project is very similar. Their products can benefit considerably if we identify paths to remove water from the skin surface," Esben Thormann states. "We note that the two companies not only contribute to the funding, but are also highly active with significant internal resources allocated in relation to the project."

The potential benefits reach well beyond the competitive advantages for the involved companies. The annual societal cost of skin cancer is estimated to DKK 250 million in Denmark alone. Exposure to direct sunlight without sufficient protection is known to be a contributing factor. Sunscreen with better ability to withstand sweat can thus hopefully help to reduce the large number of skin cancer cases.

Similarly, adhesion failure represents a large discomfort for ostomy bag users. Should the bag suddenly detach, this may lead to highly unpleasant and difficult situations. The notion alone, that this could happen will impose insecurity and psychological stress.

"A supplier like Coloplast needs to balance the need to prevent adhesion failure with the discomfort associated with excessively adhesive products. If the product binds too strongly to the skin or hamper the skins' ability to breathe it may lead to dermatological problems. Our idea is to manufacture an adhesive which on the one hand binds strongly, but at the other hand allows the skin to breathe," says Esben Thormann.

Water transporting polymers

As the two companies may seek commercialization, the specific ideas for improvement of their products cannot yet be revealed. However, Esben Thormann is able to outline the broader scope.

"Textbook graphic illustrations of polymers usually give them as prolonged molecules with a strong tendency to curl up. However their physical functionalities can be moderated by various either chemical or physical changes and different chemical and physical structures can lead to different water transporting and water storing capacities."

An obvious example is a diaper. Here, polymers are able to hold surprisingly large amounts of liquid, while keeping baby's skin fairly dry. However, while a high water storing capacity is the main functionality of a diaper, a new water transporting property of sunscreens and polymer adhesive is a secondary property which cannot significantly affect the products primary functionalities. Thus, for these products the solutions are much more complex.

Further improvements ahead

Actually, Esben Thormann hopes to be able to improve these types of polymers even further:

"This is not a part of the before mentioned project, but we are also conducting studies on so called responsive adhesives. The idea is to synthesize adhesives which can be altered by either physical or chemical changes. For instance, certain polymers can be strongly adhesive at room temperature, but if heated above a given threshold temperature, the adhesion suddenly decreases."

Again, a possible application could be for an ostomy bag:

"You want the bag to be strongly attached, but when it is time to remove the bag, it would be nice if you could remove it easily without causing any harm to the skin. If the adhesive is sensitive to temperature this could be achieved by use of a heat source like for instance a hair dryer. Alternatively we might be able to use light or a chemical change to achieve the desired effect."

Also, the applications might be for adhesion of other medico-technical products, or in entirely different fields.

"I never liked the idea that a scientist should be either engaged in fundamental or in applied research. It is highly satisfying when one is able to inspire development of new products in cooperation with industry, but at the same time we also need to do research which is primarily driven by curiosity. Just now, the efforts on responsive adhesives are curiosity-driven, but I have a feeling, industry applications will open up. It is a typical feature of polymer surface chemistry that the road from fundamental research to application is often very short."

SEVERAL PROJECTS ON POLYMER SURFACES

Besides the joint industry project highlighted in the article, the group on Polymers and Functional Surfaces is currently engaged in several other major projects. One is on "Biomimetic and responsive adhesives for a challenging biological environment". This project with a budget of 2.6 million DKK is sponsored by the Danish Council for Independent Research (DFF) / Technology and Production. Another project regards "Studies of tuneable inter-chain forces in highly charged poly(ionic liquid) brush layers". It is sponsored by the Danish Council for Independent Research (DFF) / Natural Sciences, also with a budget of DKK 2.6 million.

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The magnetic Field at NMR Center • DTU attracts Researchers

Magnetic fields are attractive. That is old news. But only a special magnetic field can attract international researchers and companies. Such a magnetic field has been installed at DTU Chemistry.

The inauguration of the NMR Center • DTU on December 13th 2016 attracted a broad audience of both academic and industrial researchers and collaborators. In connection with the inauguration, a scientific symposium was held. Here, international speakers illustrated the diversity and opportunities that high field NMR spectroscopy has to offer in many research projects. NMR spectrometers present in the NMR Center • DTU hosted by DTU Chemistry are state of the art and enable DTU to be at the forefront of research in this area.

NMR spectroscopy is a versatile analytical technique that is employed in countless applications across several scientific fields such as chemistry, biology, physics, food science, materials science and medicine. Within chemistry and biology, NMR spectroscopy is primarily utilized in structural and functional studies of molecules, of synthetic or natural origin.

Solving the structure of a molecule is much like solving a 3D puzzle, except that one does not know the final solution.

Research targets include identifying biological active molecules, their functions and biosynthesis, structural studies of large carbohydrate molecules and their interactions with receptors or degradation and the molecular pathways in biomass degradation by chemical or biological catalysis.

Strengthening NMR spectroscopy was identified as a strategic initiative by DTU's Board of Governors in 2010 with the aim of supporting all of DTU. In 2014, DTU Chemistry received a DKK 16 million grant by Villum Fonden for establishing an infrastructure with state of the art NMR spectrometers. This grant resulted in the acquisition of two new NMR systems and an upgrade of a third spectrometer, generously donated by Carlsberg. These three instruments now reside in their own building at DTU Chemistry, the newly constructed building 212.

The official speakers and contributors on the official opening of DTU's new centre for Nuclear Magnetic Resonance (NMR) on December 13th 2016: Head of Department Erling Stenby, DTU Chemistry – Professor, Head of Section Jens Ø. Duus, DTU Chemistry – Research Director Birgitte Skadhauge, Carlsberg Group – Dean of Research Katrine Krogh Andersen, DTU – Head of NMR Center DTU, Associate Professor Charlotte Held Gotfredsen, DTU Chemistry – Director Lars Hansen, Villum Fonden.

Almost one million fold stronger than the Earth's magnetic field

The superconducting magnet is the heart of the NMR spectrometer, which provides a stable magnetic field almost one million fold stronger than the Earth's magnetic field. When placed in this field, molecules act as small antennae and emit radiowaves with frequencies depending on the physical and chemical properties of the individual atoms in the molecule. Analysis and interpretation of the radiowave signal can then help to elucidate the exact structure of the molecule.

Increasing the magnetic field both increases the signal strength and facilitates the distinction of different frequencies. These improvements with increasing magnetic field are essential when dealing with large molecules and complex mixtures.

THE NMR CENTER • DTU is now entering into its next phase where the large potential of NMR spectroscopy will be explored and exploited in collaboration with researchers across DTU and beyond. Many new projects are being initiated with academic partners as well as partners from industry. There are already many new users at the center exploring how their projects can benefit from the use of NMR as a key analytical tool that allows the detection and tracking of molecules. Many of these projects require close interaction with collaborators and call for method developments and implementation of new NMR techniques to solve the challenges. The NMR Center • DTU is not only a Center with large and expensive equipment but also functions as a "Hub of Knowledge" which will be explored and used in the diverse range of projects that the Center engages in.

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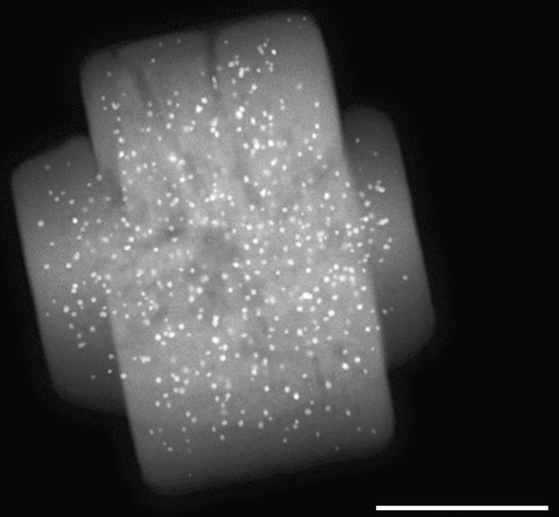

"By adding different elements to the structure, we can enhance the catalytic capacity and target specific, new reactions relevant for clean tech and more sustainable chemical production forms."


Foto: Dirte Valente

Designing Catalysts for the Future

Pioneering the field of highly selective heterogeneous nanoparticle catalysts Associate Professor Søren Kegnæs from Centre for Catalysis and Sustainable Chemistry at DTU Chemistry was granted a total of DKK 13,5 million supporting two distinctive research projects in 2016.

The Danish Council for Independent Research granted DKK 6,5 million in a DFF Starting Grant supporting the effort to design bifunctional heterogeneous catalysts for the chemical industry.

Catalysts are vital in accelerating and facilitating chemical processes making them essential in close to 90% of all commercially produced chemical products worth an estimated 1000 billion dollars worldwide. Therefore, designing better catalysts for a variety of chemical processes has an enormous economic potential.

Being the world's largest industry with an immense impact on global energy consumption and CO_2 dispersion, focus on sustainable processes in the chemical industry is notable and at the same time, the ability of well-designed catalysts to reduce the amount poisonous byproducts and environmentally hazardous waste associated with many chemical production processes generates considerable interest.

This is one of the reasons Søren Kegnæs work with catalysts is attracting so much attention. "Our catalysts are 'tweaked' synthetic minerals with a unique structure", he explains.

"By adding different elements to the structure, we can enhance the catalytic capacity and target specific, new reactions relevant for clean tech and more sustainable chemical production forms. Today we have a fair understanding of what it takes to design an efficient catalyst. To create next generation of even more efficient catalysts and thereby facilitate a more sustainable chemical production, we need to control the synthesis of new materials on an atomic scale".

"This grant allows my team to explore new and exciting ideas on a longer scale, hopefully raising the bar for what's possible in my area of research", Søren Kegnæs explains. Since the release of the grant, he worked hard to establish the team of young researchers and has begun setting up the reactor rigs needed for the research.

The Villum Young Investigators Programme granted DKK 7 million to support Søren Kegnæs' effort to engineer highly selective heterogeneous nanoparticle catalysis vital for many processes in the chemical industry.

Nano metal catalysis is well-known in the automotive industry, coating industry and other large production industries, but the metal nanoparticles are often prone to sintering, which decreases the catalytic activity over time. In spite of the aforementioned technological, environmental, and economic interests, general methods for the stabilization of metal nanoparticles against sintering are missing.

Søren Kegnæs and his team have developed several different catalytic systems where metal nanoparticles are confined in different materials. As an example, gold nanoparticles were encapsulated inside silicates.

The aim with encapsulation of metal nanoparticles in a porous matrix is to prevent the metal nanoparticle from sintering during a high temperature catalytic reaction. Furthermore, the porous matrix can also contribute actively to the catalytic reaction.

"We have already produced the first exciting results in this project, and I'm proud to say the resulting paper have been accepted for publishing by ChemCatChem", Søren Kegnæs explains.

"It's a very good start, and now we are looking forward to the day where our catalysts can be tested and ultimately put to good use by our international academic and industrial partners".

Top: Gold nanoparticles encapsulated in a porous matrix of silicalite-1. Left: Søren Kegnæs' grant from the Danish Council for Independent Research was celebrated on February 23rd 2017 in Glyptoteket, where Minister for Higher Education and Science, Søren Pind participated. Right: Associate Professor Søren Kegnæs.

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PhD from DTU Chemistry

DTU Chemistry takes pride in educating PhDs at the highest international level. We present a diverse research education in modern chemistry, which contributes to the development of cutting edge science at the Department. The goal for all PhD-students is to publish in leading journals and participate in leading international conferences during their three year long research education.

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The PhD-students at DTU Chemistry is strengthening their professional and social network at the Department. They do this through the PhD ChemClub. The PhD ChemClub is run by PhD-students and they arrange several annual events: PhD Symposium, post-graduate career events with experts from industry and academia, inspiring talks by invited speakers, social gatherings. We invite interested candidates to have a look at our website kemi.dtu.dk/English where you can read more about our PhD programme as well as the DTU Chemistry research areas.

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Contact us!
In the following you can witness the diverse DTU Chemistry PhD Defences 2016. All supervisors invite you to get in touch, if you are interested in the full thesis, in further information or in possible collaboration.

You are also welcome to contact the Head of the PhD School, Professor Erling H. Stenby, Head of Department, ehst@kemi.dtu.dk.

The Water Molecule – still Secrets to reveal

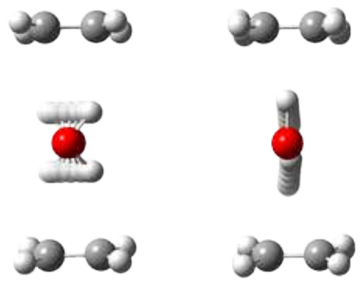
Understanding of the ability of the water molecule to form complex networks is relevant to a range of fields including materials science, oil and gas exploration, and medicine.

All forms of life on Earth depend on water. The ability of water to function as an almost universal solvent is largely defined by the ability of the water molecule to form complex hydrogen bonding networks involving water itself and organic molecules. Understanding of this unique ability is relevant to a range of scientific and industrials fields. Examples are materials science, gas hydrate inhibition in oil and gas exploration, and medicine. In the project, advanced low-temperature spectroscopy was utilized to study the ability of water to participate in various classes of weak intermolecular hydrogen bonds.

The macroscopic thermodynamic properties of condensed phases, the mechanical properties of functional materials, and the molecular organization of biological organisms result from the subtle interplay between different classes of non-covalent interactions on the molecular level. A range of intermolecular interactions were investigated by use of far-infrared and terahertz cluster spectroscopy at the nanoscopic scale for a series of weakly bound molecular hydrated cluster molecules embedded in solid cryogenic neon matrices below 4 K and/or isolated in supersonic jet expansions. It has been demonstrated how the interaction strength, directionality and anharmonicity of intermolecular hydrogen bonds can be effectively probed directly via the class of large-amplitude hydrogen bond vibrational modes introduced upon complexation. These direct spectroscopic observables detected in the challenging far-infrared spectral region are shown to enable an accurate characterization of the conformational potential energy landscape spanned by the hydrogen-bonded subunits.

The main focus has been on the unexplored class of weak CH··O, CH··F and OH··π hydrogen bonds besides the stronger classical OH··O hydrogen bond, respectively. The ability of water to participate in various classes of weak intermolecular CH··O and OH··π hydrogen bonds was investigated for mixed cluster molecules of water and prototypical unsaturated hydrocarbons as ethylene and acetylene. The interaction strengths and potential energy minima were shown to be determined largely by the degree of sp-hybridization of the involved carbon atoms. The ability of water to participate in stronger, classical intermolecular OH··O hydrogen bonds was investigated for mixed cluster molecules of water and primary, secondary, tertiary, and fluorinated alcohols. It was shown that water always is the donor for intermolecular OH··O hydrogen bonds with aliphatic alcohols. The ability of alcohols to be acceptors for intermolecular hydrogen bonds is significantly increased for tertiary alcohols compared with primary. Further, the interaction between water and flexible alcohols with degrees of freedom for internal rotation was shown to be determined by cooperative interactions between strong OH··O and weak CH··O hydrogen bonds. Finally, fluorination of alcohols was shown to hamper the ability of the alcohol to function as an acceptor for OH··O hydrogen bonds. Fluorinated alcohols will function as donors of OH··O hydrogen bonds to water supported by cooperative secondary CH··F hydrogen bonds.

The performed low-temperature spectroscopic investigations were all complemented by high-level quantum chemical modelling, and the coupling of "first principles" theory and experimental observables provides insight into the nature of non-covalent interactions of relevance to more complex supra-molecular chemistry. Examples might be the formation of gas hydrates, molecular recognition and enzyme-substrate complex formation as well as the 3-dimensional folding mechanisms for biological macromolecules in aqueous solutions.



Animations of the two IR-active liberational modes to the ternary $H_2O(C_2H_4)_2$ complex.
Left) *The hindered rotation of the water molecule out of the mirror plane spanned by the two intermolecular OH··π hydrogen bonds.*
Right) *The hindered rotation of the water molecule in the mirror plane spanned by the two intermolecular OH··π hydrogen bonds.*

Jonas Andersen
PhD

"Far-infrared Spectroscopy of Weakly Bound Hydrated Cluster Molecules"

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Funded by:
The project was funded by DTU.

Better Utilization of Plant Cell Walls

The project presents synthesis of analogues to inhibitors of enzyme activity involved in degradation of hemicelluloses, a major group of plant wall components.

Beatrice Bonora
PhD

"Synthesis of S-linked oligoxylans"

Utilization of biomass has attracted much interest, not only for bio-fuel production but also for a range of other products such as paper, food ingredients, dietary and industrial fibres, pharmaceuticals and nutraceuticals. The largest source of biomass is plant cell walls. However, processing of this type of biomass is challenging. The project presents synthesis of analogues to certain inhibitors of enzyme activity involved in degradation of hemicelluloses, which constitute the second largest group of plant wall components (next to celluloses). These enzyme inhibitor analogues may serve as tools to analyze and characterize key enzymes, and thus contribute to the understanding of hemicelluloses.

The plant cell wall is a composite of many different polysaccharides, proteins and aromatic substances. The polysaccharides are constructed of complex carbohydrates. The main group is celluloses which – among other functions – can form microfibrils, which serve as the core of the plant wall contributing strongly to the overall structural stability of the plant.

Hemicelluloses are low-molecular-weight polysaccharides that strengthen the cell walls through their interaction with celluloses. Xylan-type polysaccharides are a major group of hemicelluloses components, constituting about 20-30 % of the biomass of hardwoods and up to 50 % in grasses. Examples of xylan-type hemicelluloses components are xyloglucans, arabinoxylans, and glucoarabinoxylans.

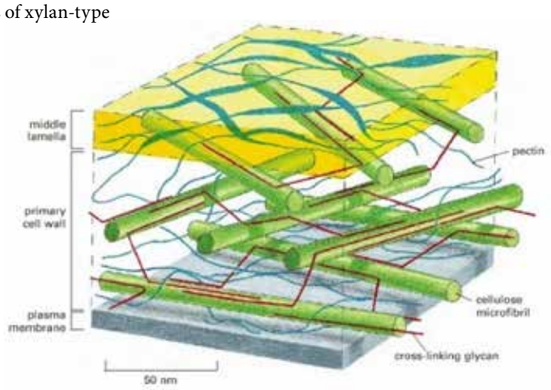
The synthesis of hemicelluloses is catalyzed by a group of enzymes, the glycosyltransferases. It is generally accepted that understanding of the enzymatic processes which regulate both synthesis and degradation of hemicelluloses will be important in order to optimize bio-refining. A promising path forward for such studies is to construct analogues of key components involved in the enzymatic processes.

In the project, methods for incorporation of thiolinkages in the synthesis of oligoxylans were developed.

One method involved 1-thioglycoside donors. Here, the protecting groups present on the acceptor were shown to influence the stability of the C4-triflate acceptor strongly and therefore also the yield of the coupling reaction.

In a second strategy involving thioacceptors, the type of glycosyl donor employed proved to be critical for the success of the coupling.

Both routes were thoroughly investigated through by-product determination, and both were shown employable for the synthesis of thiolinkages in oligoxylans assembly.



Segment of the primary cell wall. Hemicellulose is represented here as cross-linking glycans[10].

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Funded by:
The project was a part of the Sustainable Enzyme Technologies for Future Bioenergy (SET4FUTURE) project involving industry and academic partners from Denmark, USA and UK.

Synthesis of key Biomass Fragments

The stepwise glycosylation method based on preactivation is a viable path towards arabinoxylans as well as glucuronoxylans – two important groups of biomass fragments.

Maximilian Felix Böhm
PhD

"Chemical Synthesis of Hemicellulose Fragments"

Hemicellulose is one of the three main classes of compounds in the plant cell wall, and therefore an important resource for biomass utilization. Some utilization of hemicellulose is seen, primarily in the food industry. However, the abundance of hemicelluloses makes it attractive to look for wider utilization, but so far this has been difficult. Lack of access to this class of molecules prevents the use of enzymatic studies which could increase our understanding of the biochemical processes relevant to the synthesis and degradation of hemicellulose. In the project, two important groups of hemicellulose fragments have been synthesized.

Hemicellulose contributes to the strength of the plant cell walls. Some hemicelluloses have been shown to be critical in the growth of plants by functioning as the vessel walls necessary to transport water. The vessel walls need to be strong to withstand the high negative pressure generated by transpirational pull. In seeds, hemicelluloses can function as storage for carbohydrates, analogous to starch.

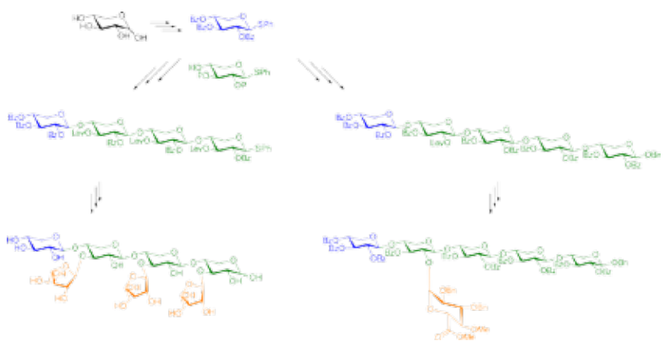
In the food industry, hemicelluloses are currently used for improvement of the quality of cereal flours and dough or as a starting material for xylitol, a popular substitute for sugar. However, several other industrial applications can be imagined, e.g. in the production of bioethanol.

Hemicelluloses are a group of polysaccharides having β-(1→4)-linked backbones of glucose, mannose or xylose. The latter are the most common, constituting the second most abundant group of polymers in plants.

In the project, the synthesis of arabinoxylans as well as glucuronoxylans is demonstrated.

Two alternative strategies to synthesize a variety of xylan backbones were investigated. The first strategy attempted to use an unprotected xylose acceptor in a tin-mediated glycosylation, but did not produce satisfactory results. The second strategy was based on the preactivation of thioglycosides to be glycosylated with thioglycoside acceptors which in turn can be preactivated again in a second step. Optimization of this latter strategy led to a viable pathway towards a variety of protected xylan backbones. The use of protecting groups allows for the specific introduction of branching units to the backbone. Subsequently arabinose as well as glucuronic acid were attached to the xylan backbone.

In conclusion, it has been shown that the stepwise glycosylation method based on preactivation is a viable path towards arabinoxylans as well as glucuronoxylans. The building blocks are easily accessible and the method allows for a rapid assembly of at least pentaxylans. Furthermore, it has been shown that the chosen protecting group strategy allows for an easy deprotection of the xylan backbone. It also gives both options on where to install the branching sugars. The 0-2 as well as the 0-3 position are easily accessible and conceivably both positions could be accessed at the same time.



Synthetic strategy for assembling arabino- and glucuronoxylans.

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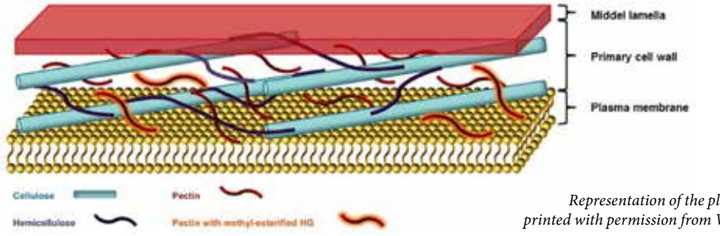
Funded by:
The project was funded by the Danish Council for Strategic Research.

Pectin – more than a Gelling Agent

Pectin is known as a jellifying agent in the food industry, but may find numerous other applications. The project presents synthesis of well-defined pectic oligosaccharides.

Mathilde Daugaard
PhD

"Synthesis of Oligo (1→5)-α-L-arabinofuranosides related to the Plant Polysaccharide Pectin"



Representation of the plant cell wall printed with permission from Willats et al.

Pectins are an important group of polysaccharides found in the plant cell wall. The plant cell wall represents almost 50 % of plant biomass. Pectins are already used as food ingredients and in pharmacy, but with the increasing focus on biomass utilization also other applications become of interest. The project presents chemical synthesis of well-defined pectic oligosaccharides.

Pectin is known as a jellifying agent in the food industry, and is also used for manufacture of encapsulated drugs and skin-care products. In plants, pectin polysaccharides have a similar but wider role contributing heavily to the mechanical strength and physical properties of the cell wall.As is the case for several other natural polysaccharides it is challenging to isolate pectins from degraded plant material. Chemical synthesis, on the other hand, is able to produce structurally diverse oligosaccharides of excellent purity, and in larger quantities.

The pectic oligosaccharides oligo-(1→5)-α-L-arabinofuranosides were chosen as the main subject of the project. These oligosaccharides have been reported to possess a wide range of biological activity profiles including immunological activity and being a promising dietary supplement for improvement of human intestinal health. Recently the monosaccharide L-arabinose has been found to pose selective intestinal sucrase inhibition effect as well as protective effects in high-carbohydrate, high-fat diet-induced metabolic syndrome in rats, and usage in cancer treatment as inducer of bacterial gene expression.

Chemical synthesis of two branched structures of oligo (1→5)-α-L-arabinofuranosides was developed. Due to the high reactivity of arabinofuranosides, the most efficient route to a disaccharide donor employed a perbenzoylated monosaccharide serving as glycosyl donor. Three monosaccharides donors with a chloroacetyl group as alternative protecting group were also prepared. The following coupling of these donors in different combinations resulted in three different hexasaccharide backbone structures. The chloroacetyl group employed in different positions of the fourth monosaccharide of the hexasaccharides was removed selectively, converting the hexasaccharides into the corresponding glycosyl acceptors. Two of the hexasaccharides were further branched through reaction with a diarabinofuranoside donor to furnish two branched octasaccharides.

The results constitute the first reported synthesis of (1→5)-α-L-arabinofuranosides branched at the 2- or the 3-position within the chain. In order to harness the full potential of the target molecules and apply them in the study of for example protein-carbohydrate interaction, deprotection remains. This should be achievable using Zemplén conditions, but will require future work.

Furthermore, a linker system using small molecules to link oligosaccharides to an array surface was investigated. The small linkers were found to be superior to the use of neoglycoconjugates of bovine serum albumin, when studying enzyme activity.

Finally, an assay to screen for novel glycosyl transferase/hydrolase activities was developed. The studies showed that it was possible to detect transglycosylation activity on a microarray.

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Funded by:
The project was a part of the GlycAct project in collaboration with University of Copenhagen. The project was sponsored by the Danish Research Council for Strategic Research.

Enzyme Substrates for Biomass Refining

Synthesis of model substrates for development of enzymes for processing of lignocellulose into bioethanol, paper, fine chemicals or other higher value products is presented.

The most abundant biomass source is lignocellulose, which is the non-edible part of plants. It can be an environmental problem when accumulated as waste from forestry, agriculture and agroindustry. In other words, lignocellulose is a cheap, renewable resource with the further advantage that it is not in demand by the food industry unlike most other biomass resources. The project presents synthesis of model substrates for development of enzymes that can enable the processing of lignocellulose into bioethanol, paper, fine chemicals or other higher value products.

Lignocellulose largely consists of a mixture of different, complex polymers. While the potential for lignocellulose as a sustainable resource is obvious, the practical applications are hampered by the intrinsic recalcitrance of these polymers to degradation. This is especially true for the so called lignin-carbohydrate complexes (LCCs), involving both hemicellulose residues and lignin.

Several physical, chemical, physicochemical and biological processes have been developed in the past decades to overcome this problem. Generally, the aim is to improve the enzyme digestibility. A key technology is the design of enzyme mixtures. An essential tool for biotechnology companies designing enzymes for biomass delignification is the access to well-defined model substrates. Understanding of the enzymes substrate specificity can be used to optimize enzyme mixtures towards natural, complex substrates. The chemically synthesized substrates often perform better in an industrial context than those isolated from natural sources.

In the project, synthesis of two glucuronoxylan fragments was designed. Both fragments may serve as model substrates for the enzyme group xylanases. The synthesis involved the use of thioxyloside building blocks in an iterative, linear glycosylation strategy. A protecting-group manipulation strategy was delveloped for the regioselective protection of the 2-position of the xylose residue on the fourth residue of (1→4)-β-pentasaccharide with a Lev group. The glycosylating procedure involved the use of the shelf-stable promoter p-NO2PhSCl and AgOTf. The length of the glycosyl donor, varying from a monosaccharide to a tetrasaccharide, did not affect the outcome. The method was effective and consistent for the type of substrates chosen and led to the desired pentasaccharide with a good 27 % overall yield.

In a second part of the project, three alkylaromatic and aromatic esters were prepared as mimics of lignin-carbohydrate complexes found in lignocellulosic biomass. These may serve as model substrates for the enzyme group glucuronoyl esterases. These esters have been used to characterize a novel glucuronoyl esterase from Cerrena unicolor (CuGE), produced by Novozymes, to obtain insight into the substrate specificity of the enzymes. HPLC analysis of the enzymatic reactions led to the determination of kinetic parameters that gave information about bonding affinity and catalytic efficiency.

In conclusion, the results suggest that glucuronoyl esterases could be effective on natural LCCs. This encourages further experiments aiming at future utilization in biomass delignification for forestry, feed and biofuel industries.

Clotilde D'Errico
PhD

"Glucuronic Acid Derivatives in Enzymatic Biomass Degradation: Synthesis and Evaluation of Enzymatic Activity"

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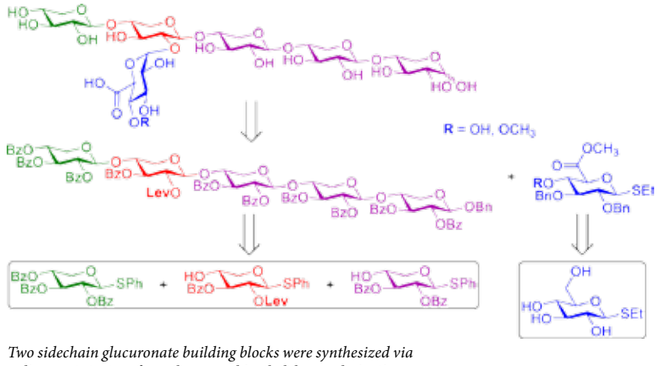
Funded by:
The project involved an external stay at Novozymes. The project was funded by the Danish Council for Strategic Research.



Two sidechain glucuronate building blocks were synthesized via a divergent strategy from the same thioethylglucose derivative.

Structures of Natural Anti-cancer Agents

The project investigates how nuclear magnetic resonance (NMR) can be an efficient tool for solving 3D structures of novel compounds from fungal and synthetic sources.

Casper Hoeck
PhD

"Solving a 3D Structural Puzzle"

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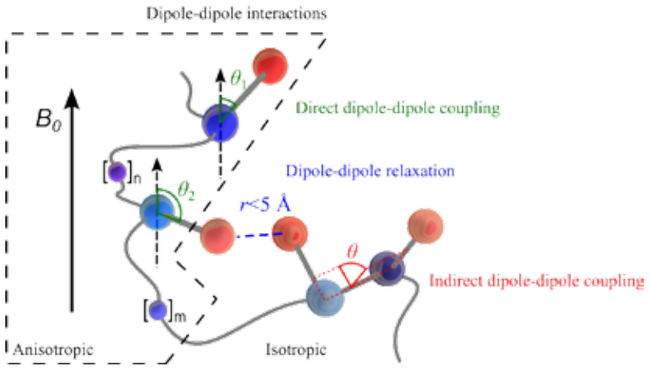
Funded by:
The project is funded by DTU Chemistry.

The effect of pharmaceuticals is not only connected to the utilized chemical elements, nor their numbers or sequence, but also to the physical shape of the molecule. Substances which appear to be chemically nearly identical may be very different if the molecules inhabit different 3D structural spaces. The best example is enantiomers; two mirror-image forms of an otherwise identical structure, where only one may have the desired effect. The need for this structural information is increasing with e.g. the demand for enantiomeric information regarding drug candidates of, or inspired by, naturally occurring substances.

The project investigates how nuclear magnetic resonance (NMR) can be an efficient tool for solving 3D structures of novel compounds from fungal and synthetic sources, which in case of the latter have been suggested as potential anti-cancer agents. NMR has been used in analytical chemistry for more than half a century, with constant developments always increasing the applicability of the technique.

The stereochemistry and 3D structural space of several compounds from fungal sources was determined, using NOEs, yielding distance information between nuclei, coupled to another method, $^{3}J_{HH}$-coupling constants, yielding dihedral information. 3D structural information of e.g. a bicyclic non-ribosomal peptide (with a novel structural motif), a steroid and several polyketides was thus gained. Furthermore, structural insights were gained for potential anti-cancer agents, the azumamides, including synthetic analogues. Differences in the conformational space of solution state compounds were identified experimentally between structural analogues, and compared to the *in vitro* potency of the compounds. The structures of two peptides that exhibited a high degree of molecular recognition were also investigated, resulting in the elucidation of a possible mode of interaction.

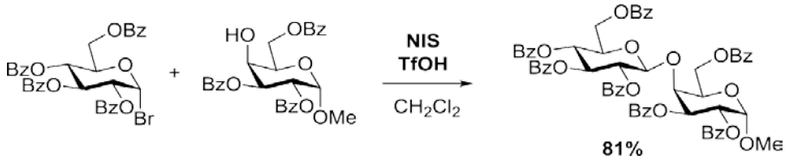


In parallel, new NMR experiments were developed based on spin-state selective (S^3) methods. Thus, the S^3 HMBC (Heteronuclear Multiple-Bond Correlation) experiment resulted in spectra with $^{n}J_{CH}$ correlated cross-peaks, from which $^{n+1}J_{HH}$-coupling constants were sign-selectively determined with high accuracy. Very small coupling constants, including previously unreported coupling constants from strychnine, were extracted, with all experimental values correlating very well to theoretical coupling constants. The technique was extended to yield $^{n}J_{CH}$-coupling constants accurately by changing the polarization in methine pairs. The experiments have great potential for extensive usage in for example carbohydrate chemistry where methines are abundant.

In a final project, residual dipolar coupling (RDCs), a relatively new technique in small molecular NMR is investigated. Homonuclear RDCs were extracted from the homonuclear S^3 HMBC that correlated well to alignment tensors from $^{1}D_{CH}$-coupling constants, thus increasing the number of inter-nuclear vectors. Also, novel alignment media, chiral polymers, were synthesized and their ability to differentiate enantiomers investigated. Finally, a new method of back-calculation of RDCs from 3D structures was developed. The approach coped better with multiple conformers than commonly used methodologies, and resulted in good conformer populations for several small molecules, including multiple cinchona alkaloids.

Smarter Synthesis of Key Biological Components

The project presents smarter ways to create glycosylation, which is highly important in drug discovery and organic chemistry in general.



Gyrithe Lanz
PhD

"Glycosyl Bromides in Glycoside Synthesis: Development of New Promoter System and Metal-mediated Regioselective Glycosylations"

Oligosaccharides are a type of carbohydrates crucial to numerous biological processes. Included in the functions pertaining to oligosaccharides are the conformation, half-life and stability of proteins, antibodies, toxins, and cell signaling. Oligosaccharides consist of monosaccharides connected via glycosidic linkages. The reaction creating these linkages – glycosylation - is highly important in drug discovery and organic chemistry in general. The project presents smarter ways to create glycosylation.

Alterations in glycosylation patterns in many different proteins have been shown to result in change or loss of function for the protein. This has spurred great interest in improving the understanding of this biologically important process. A key tool in these investigations is synthesis of well-defined and pure carbohydrates and glyco-conjugates.

An important element of glycosylation synthesis is activation of glycosyl halides. The Koenigs-Knorr reaction has been the paramount coupling reaction for more than a century. However, in this and related procedures glycosyl halides are generally activated by metal salts, which most commonly contain silver or mercury. As these salts often are both toxic and expensive, it is attractive to create smarter pathways.

In the project, iodonium ions have been applied for activation of disarmed glycosyl bromides in the glycosylation of glycosyl acceptors. A method employing iodonium ions generated from N-iodosuccinimide and a protic acid was developed. The best results were obtained with the benzoyl protected glycosyl donors and acceptors. This method allows for the use of highly disarmed glycosyl bromides in a metal free glycosylation.

Further, a straightforward procedure for regioselective glycosylation of unprotected glycosyl acceptors using metal complexes was investigated. Here, disarmed glycosyl bromides and unprotected glycopyranoside acceptors were used.

Phenyl 1-thio-D-glycopyranosides and benzyl D-glycopyranosides derived from D-glucose, D-galactose, and D-mannose were treated with various metal complexes. Treatment with copper complexes followed by glycosylation did not yield any desired disaccharide products, however for tin, molybdenum and zirconium selective glycosylation of either the 3 or the 6 position was achieved. Acceptors derived from D-galactose underwent regioselective glycosylation of the 3 position in 51 % yield employing dibutyltin dichloride.

Molybdenum dioxide complexes facilitated a regioselective glycosylation of the 6 position for acceptors derived from D-glucose and D-mannose in 52 % and 35 % yield, respectively. Zirconium complexes achieved the best results with benzyl D-mannopyranoside acceptors resulting in 40 % yield of the 1,6-linked product.

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Funded by:
The project was funded by the Danish Council for Independent Research - Natural Sciences.

Synthesis of Drug Discovery Molecules

Solid-phase synthesis of a range of biologically interesting molecules, including several relevant to drug discovery was performed.

Remi Mikkelsen
PhD.

"Solid-phase Synthesis for the Construction of Biologically Interesting Molecules and the Total Synthesis of Trioxacarcin DC-45-A2"

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Funded by:
The project is funded by DTU Chemistry.

Solid-phase organic synthesis offers several advantages over conventional solution phase chemistry, primarily easier purification and experimental simplicity. In the project, solid-phase synthesis of a range of biologically interesting molecules was performed. Several of these are relevant to drug discovery, one example being Trioxacarin DC-45-A2, a naturally occurring anti-tumor antibiotic.

Half a century ago chemist Robert Bruce Merrifield revolutionized peptide synthesis by introducing solid-phase organic synthesis. He was later awarded the Nobel Prize. Merrifield's method relies upon a linker, which anchors the substrate to the solid support. Through iterative circles of amino acid coupling and de-protection the desired peptide is built and ultimately released from the solid support by cleavage of the linker. The method has greatly expanded the number of chemical transformations which can be applied for the routine synthesis of organic molecules on solid support. This has triggered the generation of combinatorial libraries both in academia and industry, ultimately leading to the identification of new drugs and catalysts.

Firstly, derivatives of the well-known drug doxorubicin, used in treatment of a wide range of cancers including leukemia, were synthesized. The doxorubicin derivatives were synthesized on photo-labile solid support, compatible with bead-based screening. Two different strategies were developed leading to the synthesis of doxorubicin derivatives with both amino acids and peptide fragments attached in good to excellent crude purities.

Secondly, total synthesis of Trioxacarcin DC-45-A2 was performed during an external stay with the Nicolaou group at the Rice University, USA. Trioxacarcin DC-45-A2 is a naturally occurring anti-tumor antibiotic and a biosynthetic precursor to a variety of other biologically active molecules. A new synthetic route was developed. The new route featured distinct and high yielding steps and thus provided superior access to one of the key building blocks in terms of overall yield, step count and scalability. Furthermore, a route to another major building block was developed featuring a Stille cross-coupling as the key step.

Thirdly, synthesis of poly-fused heterocycles was investigated. Poly-fused heterocycles are a class of compounds relevant to drug discovery – specifically the search for new biologically active compounds. The efforts led to the development and optimization of a key aldol condensation/conjugate addition sequence for the synthesis of poly-fused heterocycles.

Finally, the project involved a literature survey on solid-phase organic synthesis and photo-labile linkers.

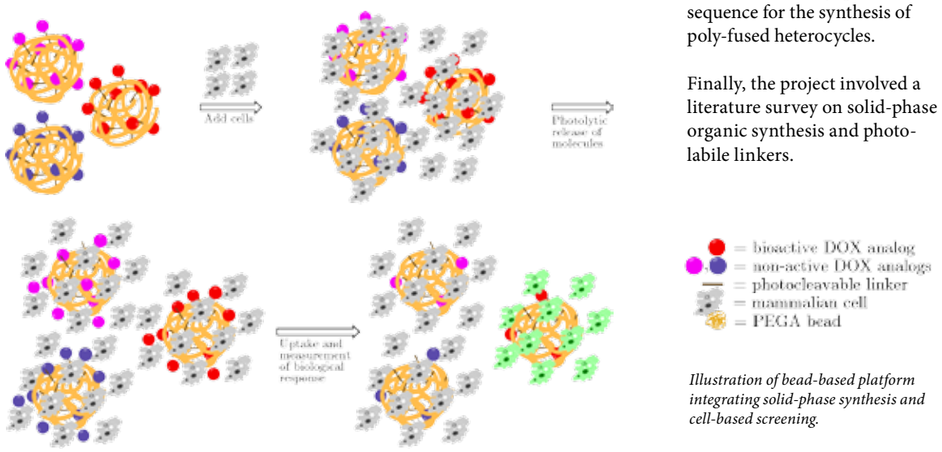


Illustration of bead-based platform integrating solid-phase synthesis and cell-based screening.

Plant Cell Walls as Bioenergy Feedstock

Synthetic, well-defined substances are able to function as tools for investigations of key functions of the plant cells walls.

Biomass has great potential for sustainable production of chemicals and fuels and already contributes about 9-13 % to global energy supply. Unlike animal cells, the plant cells are surrounded by a wall, which provides a tough protective and supportive casting of the cell. The plant cell walls constitute almost half the biomass in plants. Thus, plant cell walls are a major target for biotech research. The project has developed synthetic, well-defined substances which are able to function as tools for investigations of key functions of the plant cells walls.

The plant cell wall is a highly organized composite of many different polysaccharides, proteins, and aromatic compounds. The diversity of polysaccharides makes structural studies challenging, as it is difficult to isolate well-defined fragments of specific polysaccharides simply from degradation of plant material. Chemical synthesis, on the other hand, is able to provide structurally diverse and well-defined oligosaccharides with excellent purity in large quantities.

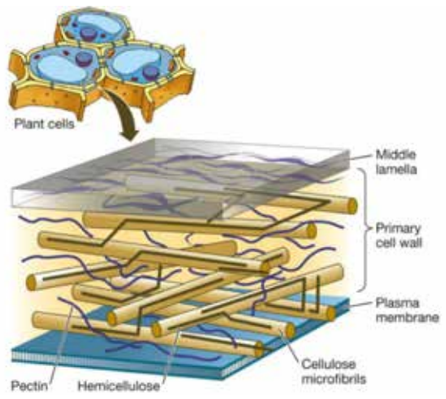
Cellulose, the component present in plant cell wall in the largest quantity, was chosen as the focus of the project. To study the process of degradation of this polysaccharide, two non-natural substrates of cellohexaose were chosen as synthetic targets.

During natural degradation of plant cell walls, various enzymes play key roles. Structurally well-defined oligosaccharides made by chemical synthesis can be used as models for the more complex polysaccharides in investigation of properties such as polysaccharides biosynthesis, degradation and protein-carbohydrate interactions.

In the project two approaches for assembly of target molecules were applied. Initially, a 4-thio-acceptor was coupled with a PTFAI-donor. This afforded the product in a modest yield, in maximum 15 %.

A nucleophilic displacement of a leaving group with a 1-thiol improved the yield of the thio-linkage. The use of a thio-acetate, which was deacylated in situ, as a precursor to the thiolate, prevented the formation of the disulfide. This strategy relied on a convergent synthesis of both targets through two common building blocks: a S-trisaccharide and an O-trisaccharide. Both trisaccharides can be converted into a donor or an acceptor depending on the desired target. In this approach, a new acceptor was formed by a regioselective opening of a benzylidene acetal.

Finally, the activity of the glycosyltransferase GalAT was studied and partially characterized. The addition of a galacturonic acid residue onto a chemically synthesized fragment of RG-1 was investigated using crude microsomes containing Golgi membrane fragments from mung beans. An easy one-step assay was employed relying on the determination of the activity measured by luminescence. The optimal conditions were determined by varying pH, temperature and salt concentration.



Schematic model of a segment of the primary plant cell wall.

Faranak Nami
PhD

"Synthesis of S-linked cello-oligosaccharides"

CONTACT

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Funded by:
The project was a part of the Sustainable Enzyme Technologies for Future Bioenergy (SET4FUTURE) project involving industry and academic partners from Denmark, USA and UK.

Short-cut Methodology for Drug Discovery

Methods for the isolation and synthesis of complex carbohydrates with pharmaceutical relevance have been improved.

Dominika Alina Niedbal
PhD

"Method Development in the Regioselective Glycosylation of Unprotected Carbohydrates.""

Carbohydrates are highly important biomolecules involved in numerous diseases, but on the other hand also with great potential as medicine. For instance, synthetic versions of glyco-molecules have been developed as carbohydrate-based therapeutic agents. The field is known as glyco-science. The project contributes to the field by providing improved methods for the isolation and synthesis of complex carbohydrates.

In nature, the majority of carbohydrates are polysaccharides (cellulose, starch, chitin) or glyco-conjugates (glyco-peptides, glyco-lipids) in which monosaccharides are connected via glycosidic linkages. The reaction creating these linkages is known as glycosylation.

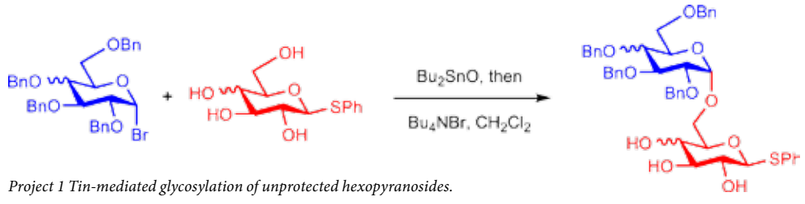
Creating synthetic version of carbohydrates – either as drug candidates or for scientific purposes – requires glycosylation, but this is not always straightforward. Especially now, when the glyco-biology field is expanding, there is a need for glycosylation methods that are both reliable and stereo-controlled (meaning that not just the chemical composition but also the physical structure of the molecule is controlled).

A major trend in the field is extensive use of protecting groups in order to achieve the desired control. These groups suppress glycosylation at undesired positions. The drawback is that additional steps are required to install and remove the protecting groups. Therefore clever manipulations which limit the need for protecting groups are in high demand.

In the project, the role of tin was investigated in regioselective glycosylation of 2,3,4,6-unprotected hexopyranosides with perbenzylated glycosyl bromide donors. Reactions with phenyl 1-thio-β-glucopyranoside and phenyl 1-thio-β-galactopyranoside with glucosyl and galactosyl bromide donors afforded exclusively the corresponding α(1→6)-linked disaccharides in decent yields. The coupling was highly dependent on the solubility of the acceptors with dibutyltin oxide in dichloromethane. Further, it was successful for glucose and galactose, while no coupling occurred with mannose. The same behavior was observed for donors, where no conversion took place with mannosyl bromide.

In a second stage of the project, diphenylborinic acid catalyzed glycosylation was conducted with the NIS/CSA promoter system. Yet again, poor solubility of the acceptors prevented the desired reactions. The only positive result was achieved when methyl 3-O-benzoyl-α-D-manno-pyranoside was used as an acceptor. The glycosylation with borinic catalyst and this acceptor led to the (1→6)-linked disaccharide in a 45 % yield. However, glycosylation under the same conditions but without the catalyst afford the (1→6)-linked product in a 15 % yield.

Overall, the project has shown that tin- and boron-mediated glycosylation with unprotected carbohydrates is successful, when the components of the reaction mixture are soluble in a given solvent. Insolubility of the unprotected acceptors puts a considerable limitation on the developed method. Therefore further research on the matter would be valuable for the field.



Project 1 Tin-mediated glycosylation of unprotected hexopyranosides.

CONTACT

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Funded by:
The project was funded by the Novo Nordisk Foundation.

Graphene Nanomaterials for Chemical Sensors

The project presents novel nanotechnology based materials for extremely sensitive chemical sensors.

Medical diagnostics, environmental protection, and detection of explosives in security controls at airports are examples of fields with a demand for detection of chemicals in very low concentrations. It has been suggested that nano-sensors will be well suited for the task, as they will be able to detect extremely small quantities, in principle down to a single molecule. The project presents new active sensing nanotechnology materials for the purpose.

With crucial properties such as high surface area, high conductivity, and low production cost with easy up-scaling, graphene-like materials are promising for many applications. By functionalization with molecular receptors already known from other types of chemical sensing, graphene-like materials can be endowed with increasing selectivity to form better and cheaper sensing composite materials.

In the project, reduced graphene oxide (RGO) was covalently functionalized with supramolecular moieties to create active sensing materials. Two different strategies were applied.

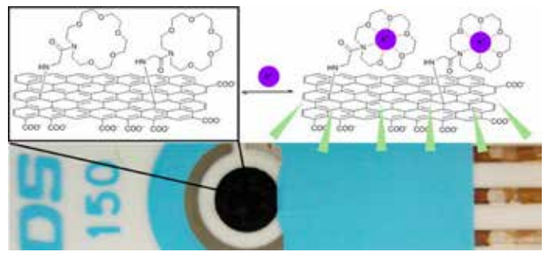
The first approach consisted of covalently attaching crown-ethers – a type of chemically resistant supramolecular moieties – to graphene oxide (GO). The functionalized GO was then reduced chemically. This resulted in monolayer RGO nano-sheets functionalized with crown-ether to an extent of up to 30 % of the theoretically available surface area. These materials were shown to selectively bind alkali metal ions. Potentiometric sensing based on the materials was achieved with a detection limit of 10^{-5} M.

The described first approach is, however, only applicable to supramolecular moieties that are not subjected to chemical reduction. In order to widen the possibilities of functionalization to include less chemically stable moieties an alternative strategy was developed.

In the second approach, Azido-RGO was prepared as a general platform for post reduction modification. GO was here functionalized with a short linker terminated in an alcohol. The intermediate material was then reduced effectively with $NaBH_4$, followed by chemical transformation of the alcohol into azide, thus providing a chemical handle for click chemistry in the form of CuAAC.

This platform material was then functionalized with ferrocene as a redox probe to accurately determine surface coverage in which one azido functionalized group was attached per 16 carbon atoms in the RGO sheet.

This Azido-RGO platform was then used in successful functionalization with a large supramolecular receptor molecule, TTF-calix[4]pyrrole. The resulting composite material can sense Cl^- and potentially TNB. The coverage achieved was one molecule per 50-60 carbon atoms in the RGO sheet. In view of the size of this molecular moiety, the coverage is actually very high. The material was used for Cl^- sensing showing sensitivity at very low concentration with linear response in the concentration range 10^{-8} to 10^{-5} M.



Crown-ether functionalized graphene nanosheets and sensor for selective sensing of potassium ions.

Gunnar Olsen
PhD

"Supramolecular Derivation of Graphene Nanomaterials for Chemical Sensors"

CONTACT

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Funded by:
The project was funded by DFF - the Danish Research Council for Technology and Production Sciences.

A Promising Platform for Bio-refining

The project focusses on removal of oxygen from biomass, in the form of carbon monoxide, which is used in further "bio-refinery" processes.

Dario Paolicchi
PhD

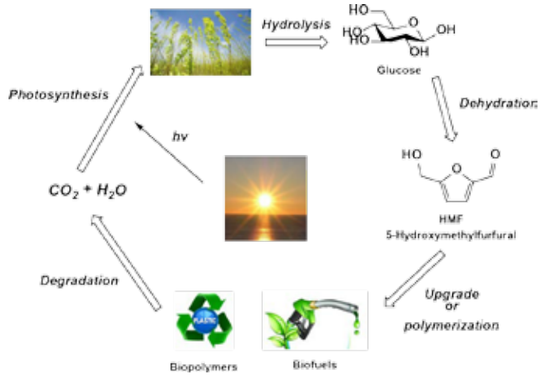
"Methoxycarbonylation of Alkenes with Biomass-derived CO"

Biomass is the only widely available carbon source apart from oil and coal. Unlike these fossil feedstocks, biomass is CO_2 neutral, since the CO_2 release during use equals the amount taken up by the plants during their growth. Thus biomass is a highly attractive alternative feedstock for production of chemicals and energy. Unlike fossil feedstocks, biomass contains a relatively large quantity of oxygen. The project focusses on removal of oxygen from biomass, in the form of carbon monoxide, which is used in further "bio-refinery" processes.

It is generally accepted that the most effective use of biomass is in so called bio-refineries, which – just like refineries based on crude oil as feedstock – are able to produce a range of both fuels and chemicals. Further, it seems clear that bio-refineries will need a technology platform based on intermediate substances suited for further processing into the desired end products. One such promising platform is the furanic platform based on HMF (5-hydroxymethyl furfural).

In the first part of the project a Pd-catalyzed methoxycarbonylation reaction with HMF was investigated. The reaction yielded methyl heptanoate (MH), methyl levulinate (ML), and γ–valerolactone (GVL). The latter is a promising green fuel, while MH and ML are well-known intermediate products in chemical industry. The reactions were optimized, both in terms of utilized catalysts, reaction time, the nature and the amount of the palladium precursor and ligand, reaction temperature, and different alkene and alcohol substrates.

The optimized catalytic system gave good yields in a one-pot reaction from HMF. The use of a catalytic Pd complex with the ligand 1,2-bis(di-tert-butylphosphinomethane)-benzene (DTBPMB) in the transfer hydrogenation for the production of GVL was reported successfully for the first time. The presence of a dissolved Brønsted acid proved of crucial importance. An inverse proportionality between ML and GVL was discovered and explained in a mutual conversion of ML to GVL, via hydrogenation.



Further, a small screening of various cheap alkenes and alcohols was carried out, proving the viability of the reaction on different reagents. Products such as ethyl heptanoate and dimethylsuccinate were yielded.

In a second part of the project, the same methodology was tested with sugars as substrates. Fructose and glucose proved to be susceptible to the reaction conditions and gave considerably high yields of both MH and GVL. Glucose, in particular, yielded notable amounts of MH, despite its lower reactivity towards the catalytic complex.

A screening of different carbohydrates – aldoses, ketoses, pentoses, disaccharides, and polysaccharides – proved the catalytic system to be active on all these compounds. Structural differences were shown to be crucial for the variation in the yields of the final products. In conclusion, further experiments on polymers can be recommended to expand this catalytic system to a broader range of compounds in order to improve the utilization of biomass and minimizing waste.

CONTACT

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Funded by:
The project was funded by a Sapere Aude Starting Grant from the Danish Council for Independent Research (FTP).

Utilization of Lignin in Biomass

Heterogeneous catalysis provides great advantages in relation to utilization of biomass in terms of separation and recyclability, and also providing the ability to use molecular oxygen as oxidant.

Lignocellulosic biomass – the non-edible part of plants – consists mainly of three components: cellulose , hemi-cellulose (both carbohydrate polymers), and lignin (aromatic polymers). While several commercial processes have been developed for cellulose and hemi-cellulose, the lignin fraction has received less attention.

Lignin is the second most abundant natural polymer, representing 30 % of the weight and 40 % of the energy content of lignocellulosic biomass. It is essential for the economic feasibility of future bio-refineries that all fractions, including lignin, are utilized.

Lignin is an amorphous polymer with many chemical functionalities and a structure that varies from plant to plant. While this complexity makes utilization challenging, the phenyl propane units contained in lignin are a potentially rich source for chemical production. Among the most abundant structural unit of lignin, is the β–O-4 which represents approximately 60 % of the bonds in hardwood and 45-50 % of those in softwood. Birch and beech sawdust were subjected to the organosolv treatment for extraction of lignin, which was further processed.

Lignin depolymerisation with selective bond cleavage can be achieved by several alternative processes. One of these is heterogeneously catalysed oxidation, which results in the production of a platform of aromatic compounds.

In the project, the lignin model products veratryl alcohol and guaiacyl glycerol-β-guaiacyl ether (GGGE) were tested in oxidation reactions. An 89 % yield of veratraldehyde was obtained from the aerobic oxidation of veratryl alcohol in water at elevated temperature and pressure with Ru/Al_2O_3 catalyst. When the same catalyst was used in the oxidative transformation of GGGE, 34 % yield of guaiacol, 13 % of vanillin, and 11 % of vanillic acid were obtained. The catalyst was easy to regenerate and recycle. Importantly, it was found to be stable over five consecutive runs.

Further, a novel one-pot, two-step conversion route from lignin to aromatics was developed. The first step consisted of the oxidative depolymerisation of lignin at elevated pressure with pressurized oxygen. A second step followed, wherein the oxidation products were subjected to catalytic hydrogenolysis at elevated temperature with a pressure of hydrogen. Different catalysts were tested. The tandem Ru/SiO_2 – Ni/H-mordenite catalyst system gave the highest degree of degradation of the organosolv lignin binding motifs, with 57 % of the β-O-4 binding motifs, and 46 % of the phenylcoumaran interunits cleaved. Prolonged reaction times for the oxidation step resulted in increased degradation of the organosolv lignin linkages, resulting in the cleavage of 76 % of the β-O-4 binding motifs, and 64 % of the phenylcoumaran interunits.

In conclusion, heterogeneous catalysis provides great advantages, not only in terms of separation and recyclability, but also providing the ability to use molecular oxygen as oxidant. While oxidation is not the only option for the depolymerisation of lignin, it is a relevant route as an eco-efficient process.

Mayra Melián Rodriguez
PhD

"Lignin Biomass Conversion into Chemicals and Fuels"

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Saravanamurugan Shunmugavel,
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Funded by:
The project was funded by the Danish Agency for Science, Technology and Innovation, Haldor Topsøe A/S, and DTU.

Protein-protein interactions

Understanding of protein-protein interactions provides a means for utilizing nature's own resources in the development of new and better drugs.

Pernille Sønderby
PhD

"Solution Behavior of Human Serum Albumin and GLP-1 Variants."

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Günther Peters
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Funded by:
The project was funded by DTU and was carried out in cooperation with Novozymes Biopharma (now Albumedix).

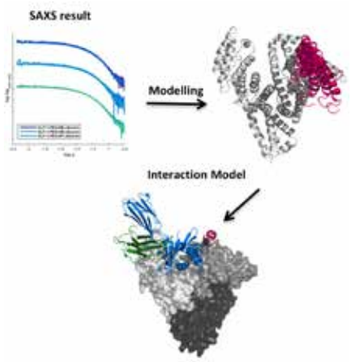
Proteins are the body's building blocks and are involved in the communication cascades in and between cells. Specific protein-to-protein interactions are involved in the processes, and understanding these interactions provides a means for utilizing nature's own resources in the development of new and better drugs. Pharmaceutical products derived from proteins are increasingly used as medicine. Examples are insulin and insulin derivatives and recombinant therapeutic proteins such as monoclonal antibodies used for chemo therapy.

Small angle X-ray scattering (SAXS) is a technique which can provide us with information about the shape and behavior of a macromolecule in solution. Where X-ray diffraction gives us detailed atomic resolution from crystals, SAXS is limited in resolution due to tumbling of the molecules. Instead we gain information about the protein in a more native-like environment and the technique is applicable to a wide range of proteins and protein complexes where we are not dependent on the molecule(s) ability to crystallize. At low concentrations SAXS reveals the overall envelope of molecules in solution, while at higher concentrations analysis of the SAXS curve provides information of inter-molecular interactions. This means that by using SAXS, it is possible to study both the protein structure and the protein-protein interactions. In this project, SAXS was used to investigate protein structure and protein-protein interactions.

The latter either as specific binding between two proteins to form a protein complex or as non-specific interactions, which refers to the inter-molecular forces that govern a solution and relate to the stability of a protein solution. This has been supplemented by static light scattering and in-silico modelling. The focus has been on the interaction of Human serum albumin (HSA) and target proteins, in particular derivatives of the naturally occurring glucagon-like peptide 1 (GLP-1). HSA is utilized in many ways in the pharmaceutical industry, e.g. in formulations of other proteins and in particular for half-life extension of peptides. GLP-1 is an incretin hormone and derivatives hereof are used in the treatment of diabetes type 2. The very short half-life of this peptide makes the peptide itself unsuitable as a drug but increasing the half-life can be done by methods such as conjugation to other molecules such as HSA.

In order to give a better understanding of the interaction of HSA with other proteins, the behavior of HSA was examined in three different solution systems. The non-specific inter-molecular interactions were highly dependent on the other chemicals present in the solution. This is important when investigating binary systems as the self-interaction of HSA could affect the interaction with other proteins. Conjugation of peptides such as GLP-1 to HSA can increase the half-life of the peptide by taking advantage of the large size of HSA and its interaction with the neonatal Fc receptor (FcRn), both of which are responsible for the extraordinary half-life of ~21 days of HSA. It is important that the interactions of the conjugate with the FcRn and the GLP-1 receptor are conserved for optimal retention time and potency. SAXS was used to derive a molecular structure of the conjugate and hereby it was possible to shed light on the molecular mechanism behind the binding studies and the pharmacokinetic studies.

Docking tools can be used to analyze the molecular envelopes derived from SAXS studies on protein complexes, when the structures of the individual proteins are known. This has its limitations though and the last chapter of the thesis presents a theoretical study on the use of the protein docking tool RosettaDock in combination with SAXS. Here it is shown that SAXS decreases the conformational space explored by RosettaDock and ultimately increases the chance of identifying a near native protein complexes.



Crystal structure of HSA in complex with Myristic acids (PDB 1E7G). Domain names are highlighted in bold with FA binding sites in italic. Fatty acids (FA) are presented as grey spheres with oxygens in red. Domain colouring and naming of domains and FA binding sites, have been done in accordance with the nomenclature adopted by Bhattacharya et al.(14). References in the text to the FA binding sites are shorthanded to FA1-7.

Master Theses 2016

Agathe Emma Pomme Peyrottes
Investigation of the stereochemical outcome of a Reformatsky reaction between an Ellman imine of an acetophenone and an ethyl α-halo-acetate.

Ahmad Adyarso Wibowo
PVT study of model reservoir fluids at HPHT conditions

Christos Panagiotis Chatziagapiou
Joule-Thomson coefficients of hydrocarbon mixtures at high pressures

David Benjamin Christensen
Dual element doped 3D graphene electrocatalysts

Eleonora Cavani
Monitoring of atopic dermatitis flare-ups and identification of its triggers in chronic patients

Eva Stensgaard
Biochemical and computational characterization of tryptophan hydroxylase

Finlay Gordon Mackenzie Bertram
Simulation of Low Salinity Water Flooding

Gianluca Lubelli
Phase Equilibrium Calculation in the Presence of Capillary Pressure

Gianni Ferrero
Development of 3D Graphene Structures for Oil-Water Separation

Kathrin Rentzius Troelsen
Synthesis of the coagulation factor VIII a3 acidic peptide

Kathrine Kirk Øgendahl
Purification and crystallisation of brain-specific human tryptophan hydroxylase

Kristoffer Hauberg Rasmussen
Application of catalytic active platinum nanoparticles encapsulated in zeolites

Line Abildgaard Ryberg
Protein complexes studied by small-angle X-ray scattering and in-silico modeling

Mads Winther
Enantioselective Synthesis of (+)- Sieboldine A

Márton László Szanyi
Near-wellbore flow modeling with Computational Fluid Dynamics

Mathilde Sophie Piel
Synthesis and characterization of fluorogenic substrates for phospholipase assays

Mehrshad Ashrafi
PVT study of hydrocarbon mixtures at high pressure and high temperature conditions

Michael Bæk
Synthesis of acetylated homogalacturonan oligosaccharides

Mikael Sandgren Bock
Nitrogen and sulfur doped graphene 3D hydrogels for catalysis and energy storage

Nicklas Møller
Chemistry of various copper species in zeolites studied by EPR

Nikolaj Sten Andersen
Selective Prodrugs for the Treatment of Rheumatoid Arthritis

Saioa Oscoz Cob
Development of antitoxins against black mamba venom

Sara Britta Riehm Pedersen
Synthesis of Lipid Components of the Plant Polyester Cutin

Tobias Løvgren Madsen
Complexes between cyclodextrins and drugs investigated by isothermal titration calorimetry and phase solubility diagrams – Similarities and discrepancies

Vinca Bonde Andersen
Theoretical and experimental investigations of mutarotation of selected sugar molecules

Yiqun Liu
PVT study of model reservoir fluids at HPHT conditions

Zahra Nasrudin Abdulqadir Ali
Synthesis of Mesoporous Zeolites for the Conversion of Methanol to Aromatics

Find DTU Chemistry Students at:
facebook.com/DTUChemistryStudents
For more information: Teaching Administrator Signe Møller Jørgensen, smjo@kemi.dtu.dk

Acknowledgement

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

Kim Andersen
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Leo Pharma A/S

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Ole Kirk
Novozymes A/S

Jesper Nerlov
Haldor Topsoe A/S

DTU Chemistry has a wide cooperation with industry.

Among the Department's industry partners are:

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Amminex
Arla
Arrayjet
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Bioenergy 2020+
Biolin Scientific
Carlsberg
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Pharmacosmos
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Riemann
Scandinavian Micro Biodevices
Total
Vattenfall
Veloxis
Wacker Chemie
Welltec
Wyatt Technology Europe GmbH

Publications 2016

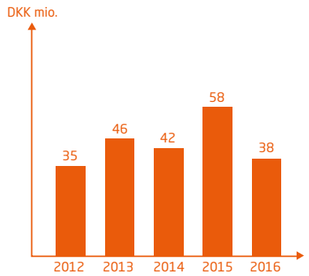
DTU Chemistry has a high performance in the world of chemical science. This is reflected in all the publications produced and published in high impact journals every year. In this Annual Report you can find examples of some of the Departments exciting results and projects during 2016. The Department has a strong track record in scientific publications and we keep on increasing the ISI publications. For a complete list of DTU Chemistry's publications in 2016, please scan the code or see: kemi.dtu.dk/Omos/Publikationer.

A Leading Research Department

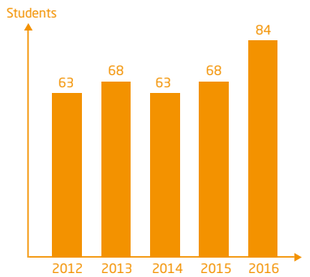
DTU Chemistry focuses on scientific excellence through people, projects, and results in order to stay a leading research department. DTU Chemistry is still very successful in attracting scientific talent. We keep on having a very high number of applicants for the BSc in Chemistry and Technology exceeding the number of applicants, we can actually accommodate.

Once again the Department had a high success rate in applications for external funding in 2016. We are pleased to find that sources outside DTU as public funds, private companies, and private foundations take increasing interest in our Department.

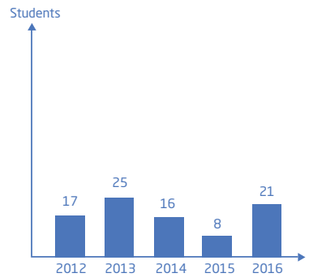
External funding



BSc admission



PhD admission



Left: Associate Professor Günther H.J. Peters. Centre: Nobel Prize Winner Ben L. Feringa at DTU Chemistry in 2013. Right: DTU's Annual Open House Event.

Highlights 2016

DTU Chemistry has selected various highlights from 2016 to supplement the articles on pp 6-15. You can read more at our website kemi.dtu.dk/English/Nyheder, or follow our activities on Facebook/Kemi på DTU.

GRANTS & HONOURS

Innovation Fund Denmark

Danish researchers will transform sugar into plastic. Researchers from DTU Chemistry and the private company Haldor Topsøe A/S are now joining forces with the Swedish company Perstorp to develop eco-friendly plastic from sugar (carbohydrates)—and at a price that can compete with oil-based plastic. Innovation Fund Denmark is supporting DTU Chemistry's stake in the project with DKK 9.3 million. The project manager is Professor Robert Madsen from DTU Chemistry, and Professor Anders Riisager and Senior Researcher Sebastian Meier are also participating.

Villum Fonden

Professor Robert Madsen from DTU Chemistry received DKK 3.6 million from the Villum Fonden for the project 'Metal-catalyzed Dehydrogenation and Decarbonylation of Primary Alcohols'. The purpose of the project is to develop new metal catalysts to split off hydrogen and carbon monoxide from primary alcohols.

Grant from the Danish Council for Independent Research (DFF)

The Danish Council for Independent Research | Natural Sciences granted funding of more than DKK 2.5 million for a project which will study the enzyme TPH2 (Tryptophan Hydroxylase isoform 2), which is found in the brains of humans. Associate Professor Günther H. J. Peters has, together with Associate Professors Hans E.M. Christensen and Pernille Harris, all from DTU Chemistry, received funding for the project, in which researchers from the University of Copenhagen and the University of Manchester in the UK are also participating.

Fellowship from Carlsberg

Senior Research Scientist Katrine Qvortrup from DTU Chemistry was awarded the Carlsberg Foundation Internationalization Fellowship. An article about her research into chemical biology has been published on the Carlsberg Foundation website. Chemical biology is evolving at an unprecedented pace, and holds unique potential for fundamental discoveries within natural sciences in general.

Other grants and honours

The project '3D Nanocarbon chips for microsupercapacitors and ultrasensitive detection' by PhD students Arnab Halder from DTU Chemistry and Suhith Hemanth from DTU Nanotech has received a grant of DKK 250,000 by the Poul V. Andersen Foundation. In 2016, PhD student Mats Simmermacher from DTU Chemistry participated in Roche Continents in Salzburg, Austria. Roche Continents brings together a number of highly talented students from Europe to inspire them in the interface between science and art, as well as the creative processes that drive innovation.

The first ever DTU Award for Development of Teaching and Learning went to Associate Professor Günther H. J. Peters from DTU Chemistry for his continuous and diligent development of the notoriously challenging basic course 'Physical Chemistry for the Biological Sciences'. The award comes with a DKK 25,000 travel grant, as well as one year's custody of a three-metre-tall sculpture.

Nobel Prize in Chemistry 2016

In 2016, the Nobel Prize in Chemistry was awarded to the Dutch professor Ben L. Feringa, whom DTU Chemistry had the pleasure of presenting in 2013 for the Department's lecture series DTU Chemistry Lecture. Ben L. Feringa was awarded the Nobel Prize in Chemistry together with Frenchman Jean-Pierre Sauvage and the English chemist Sir J. Fraser Stoddart for the design and manufacture of molecular machines. The title of Ben L. Feringa's lecture on DTU Chemistry was "Dynamic Molecular Systems, from Switches to Motors.

REACHING OUT TO HIGH SCHOOL STUDENTS

Open House event

The Department is always very active during DTU's annual Open House event. We distributed 800 leaflets and did guided tours with more than 175 interested high school students. These efforts appear to be having an effect. This year, a record 84 students were enrolled on the BSc in Chemistry and Technology programme.

DTU ScienceShow

DTU ScienceShow is a group of students, who use their energy, enthusiasm and academic surplus to deliver a professional scienceshow with show elements from chemistry and physics. DTU ScienceShow is an important part of DTU's branding and recruiting strategies. From july 2016 DTU ScienceShow is hosted by DTU Chemistry. Professor Anders Riisager from DTU Chemistry is heading the DTU ScienceShow advisory group.

Online game - "Oliejagten"

Oil production is under pressure at the moment, and a lot of new knowledge is needed to find the oil. This is also the case in the online game 'Oliejagten' (The Oil Hunt), where high school students have to combine their knowledge from different subjects to win the contest to be the best oil producer. The game, and the follow-up oil and education day at DTU, is coordinated and sponsored by the Danish Hydrocarbon Research and Technology Centre at DTU and Maersk Oil.

HIGH-IMPACT PUBLICATIONS

Associate Professor Qijin Chi, postdocs Chengyi Hou and Christian Engelbrekt and PhD Minwei Zhang from the NanoChemistry Group at DTU Chemistry, have recently demonstrated that photoresponsive microfibres with a plasmonic core-shell structure can respond to visible light to achieve self-protection against oxidation in an open environment. The microfibres are synthesized via a newly developed reagent-free electrolytic method, and have unique interfacial structures and high surface activity. The new findings have been published in the high-impact journal of materials science, Advanced Materials. The work is a collaboration with DTU Cen and Donghua University in Shanghai, China.

DTU researchers have shown that it is possible experimentally to record 'molecular movies' of the interactions between light-activated molecules and their surroundings. This exciting achievement brings us one step closer to exploiting the sun's energy for photo-catalysis. Professor Klaus B. Møller from DTU Chemistry headed the computational studies that proved invaluable in interpreting and modelling the experimental data. Former PhD student Asmus O. Dohn and Associate Professor Niels E. Henriksen from DTU Chemistry also worked on the project. The work is a result of a collaboration with researchers from DTU Physics and from Stanford University, supported by partners at European XFEL in Hamburg, Lund University, and KAIST in South Korea. The new findings have been published in the high-profile journal Nature Communications.

Professor Emeritus Jens Ulstrup and Associate Professor Qijin Chi from DTU Chemistry, former postdoc Xian Hao and former PhD student Nan Zhu, have demonstrated the synthesis of highly stable and water-soluble mixed-valence nanoparticles under mild conditions, and mapped their enzyme-mimicking catalytic properties and controlled electron transfer to single-nanoparticle resolution. This has been achieved by using a combination of surface-assembly chemistry, electrochemistry and liquid atomic force microscopy. The latest results have been published in ACS Catalysis, one of the top journals in catalysis science.

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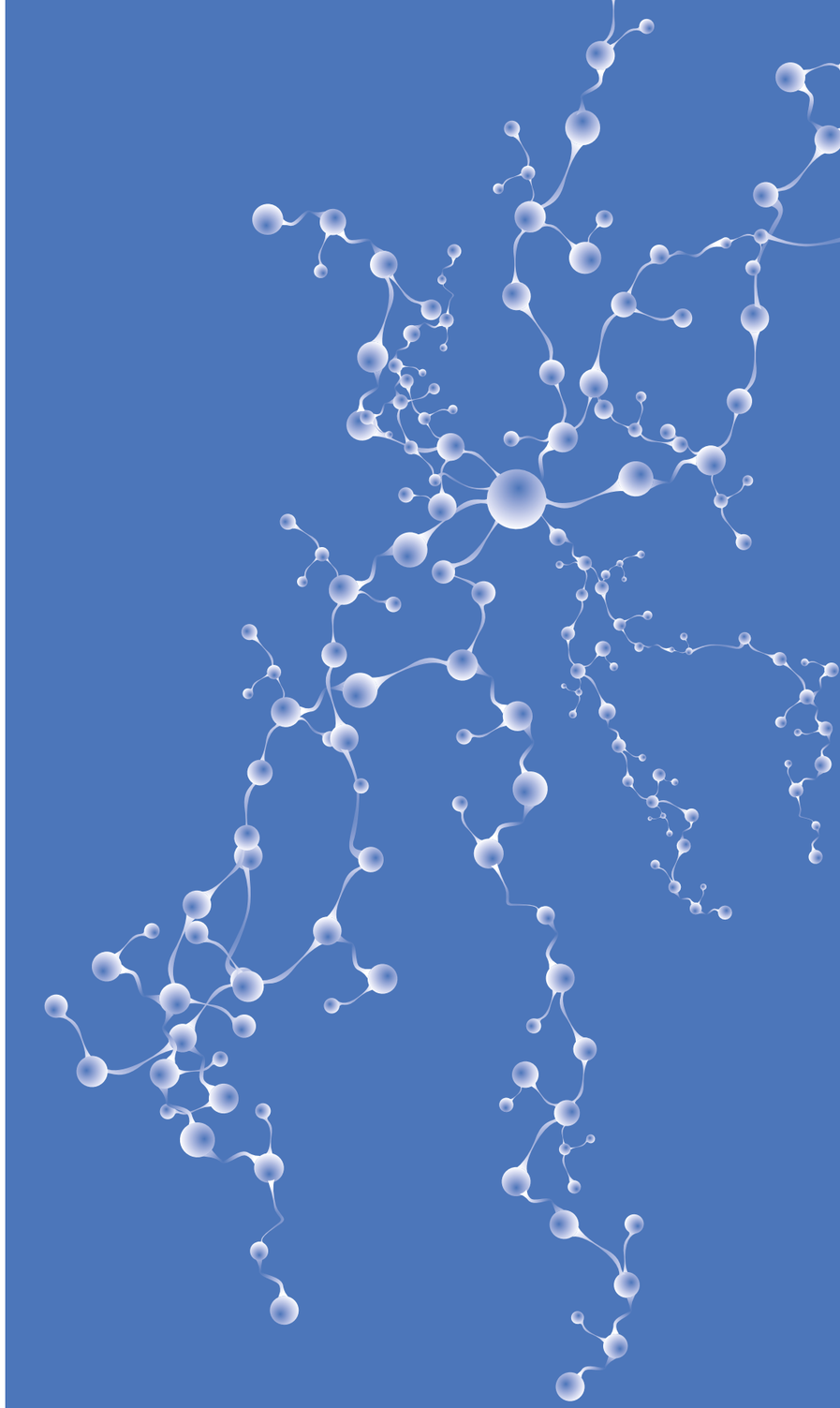

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