

**Annual Report 2011**

Department of Chemistry



## DTU Chemistry Annual Report 2011

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# A Prosperous and Dynamic Year of Chemistry

**Over the coming years we will continue to spearhead new science at the international cutting edge, while also educating outstanding candidates within applied chemistry.**

*Erling H. Stenby, Head of Department, DTU Chemistry, professor.*

In 2011 we celebrated the UNESCO International Year of Chemistry together with thousands of colleagues around the world. At DTU Chemistry it gave us the opportunity to showcase a comprehensive series of our contributions to research and education a key issue being dissemination. Events ranging from Nobel laureate Prof. Negishi to the Danish Olympic Team in Chemistry for high school students brought the role of chemistry in modern society to the attention of the general public too. In this report you will find more details on DTU Chemistry's Ph.D. Symposium, the Ph.D. videos, our contributions to national television programs on science, and many other activities.

## Recruitment of the Best

In many ways recruitment has been a key topic during 2011. We have employed four new members in the Faculty, 22 new Ph.D. students, several Post Docs, two Special Advisors within communication and funding support. Furthermore, we have been able to attract a record high number of applicants for our B.Sc. program as well as welcoming several new industrial collaborators. Thus the Year of Chemistry has been prosperous and dynamic.

## Four new Faculty members

DTU Chemistry has strengthened its efforts in several scientific areas with our new Faculty members:

- Assistant Professor Soren Kegnæs' field of research is design of functional nanomaterials
- Assistant Professor René Wugt Larsen studies spectroscopy of weakly bound systems
- Associate Professor Kasper Planeta Kepp investigates the function and evolution of metalloproteins
- Assistant Professor Jonas Rosager Henriksen is engaged with characterization of nanoparticles used for drug delivery and diagnostic purposes

## Gearing up on Bio-refining

As industry and academia are joining forces in a new Danish Bio-refining Alliance around the utilization of biomass, several groups at DTU Chemistry are also rising to the challenge.

The potential for biomass to replace an important part of oil and other fossil carbon resources is enormous and we will look at the challenges from many different scientific angles.

## New synergies

As for society as a whole, the landscape of DTU and of chemistry research is dynamic. As of 1 January 2012 our colleagues in the research group within Energy and Material Science became part of the newly created department DTU Energy Conversion. We wish the group all the best and look forward to a continuing close collaboration within catalysis and other fields of mutual interest.

Over the coming years we will continue to spearhead new science at the international cutting edge, while also educating outstanding candidates within applied chemistry. I am happy to note that 2011 showed positive trends in all important areas of our work.

This development has been supported by a strong and efficient organization, where Deputy Head of Department, Charlotte Mondrup, is securing the daily operation and administration of the Department. Furthermore, she is engaged in the Department's innovation strategy which brings our research into use both nationally and internationally.

Finally, I am happy to report that the planned improvement in our physical facilities is in progress. These efforts will result in both a new building with state-of-the-art laboratories scheduled to open in 2014, and a renovation of two existing buildings. This will create suitable surroundings for more excellent science, education and innovation.

ERLING H. STENBY |  
Head of Department,  
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# 1. Inorganic Chemistry

Biomass is a vast, renewable source of carbon, which currently covers just a fraction of the world's chemical production. The potential for biomass to replace an important part of oil and other fossil carbon resources is enormous. Based on this fact, the Inorganic Chemistry Section is expanding in practically all areas related to "green" transition including new catalytic pathways to be applied in bio-refineries.

The section consists of the Centre for Catalysis and Sustainable Chemistry (CSC) and the research groups on Metalloprotein Chemistry and NanoChemistry and until January 2012 the Energy and Material Science Group. The different research groups interact strongly, thus securing an efficient use of the sections' advanced research equipment.

The section is responsible for the education of students in all areas of inorganic chemistry and related applied fields such as catalysis and flue gas cleaning.

**Section Coordinator:** Professor Rasmus Fehrmann

# Denmark Gears up on Bio-refining

Industry and academia are joining forces in a new Danish alliance around the utilization of biomass. Several groups at DTU Chemistry are rising to the challenge.

The most critical feedstock in the chemical industry and refineries is oil. Biomass is a vast, renewable source of carbon, which currently covers just a fraction of the world's chemical production.

"The potential for biomass to replace oil and other fossil carbon resources is enormous. However, if we compare with the level of optimization obtained in the petrochemical industry, bio-refining is at an early stage where knowledge is scarce. We will need to look at the challenges from many different scientific angles," says Associate Professor Anders Riisager of DTU Chemistry's Inorganic Chemistry section.

While the tasks are vast, the department is far from working alone.

"We have strong collaboration with groups at DTU Chemical and Biochemical Engineering, DTU Systems Biology and other DTU departments, and also ongoing projects in collaboration with Novozymes A/S, Haldor Topsøe A/S, DONG Energy A/S and other companies," Anders Riisager says, adding:

"In this regard we note with enthusiasm that Novozymes A/S, Haldor Topsøe A/S, and DONG Energy A/S with Agriculture & Food have formed the BioRefining Alliance. We strongly support the alliance's call for accelerated investments in the field and its attempt to build a Danish large-scale industry around bio-refining."

## Catalysis may replace fermentation

One type of bio-refinery targets energy resources. Spurred by both market developments and policy initiatives – for instance, current EU policy mandates a share of 5.75 % energy content derived from bio-fuels, rising to 10 % in 2020 – various bio-fuels are already in production.

Biomass is currently the only viable non-fossil resource for liquid hydrocarbons that can be used as an additive to conventional liquid transportation fuels. One example produced on the commercial scale is bio-ethanol through fermentation. The Catalysis and Sustainable Chemistry group at DTU Chemistry is strongly engaged in finding catalytic pathways that may yield bio-alcohol directly from cellulose and other biomass waste products, without fermentation.

Another type of bio-fuel is fatty acid alkyl esters – commonly referred to as bio-diesel. Production of bio-diesel is already growing and a number of catalytic methods have been established. Two methods have been used industrially for a number of years; namely transesterification (and esterification) of fats and oils with methanol to form fatty acid methyl esters

(FAME), and hydrodeoxygenation (HDO) of fats and oils to form straight-chain alkanes. Both methods rely on the utilization of catalysts, and the group is involved in various projects aiming at make such catalytic systems more efficient.

## Huge investments are due

Finally, the production of commodity chemicals rather than fuels could represent an economically attractive utilization of biomass. In principle, utilization of biomass in bio-refineries could be based on renewable platform chemicals identical to the current chemicals produced from crude oil. However, the group at DTU Chemistry is focused on an alternative chemical infrastructure based on platform chemicals that may only or at least more readily be derived from biomass. Examples are lactic acid from glucose, 5-(hydroxymethyl)furfural (HMF) from fructose (or glucose), furfural from xylose and 1,3-propanediol from glycerol. Some of the chemicals may be polymerized into materials that can replace a number of plastics produced from crude oil today.

While DTU Chemistry has a strong tradition in this type of sustainable chemistry, Anders Riisager also notes that the level of international competition has risen over the latest years:

"The fast expanding international focus on bio-refining may require modifications in our research strategies. Still, we see the rise in international competition in bio-refining as a good thing. There will be plenty of work to do. Huge investments are due, and in such situations you would desire many types of confirmation before you move ahead."

**"We note with enthusiasm that Novozymes A/S, Haldor Topsøe A/S, and DONG Energy A/S with Agriculture & Food have formed the BioRefining Alliance."**

*Associate Professor Anders Riisager, DTU Chemistry*

# Catalysis for a Necessary Transition

As an increasing part of our demand for energy and chemicals is met by utilization of biomass and other renewable resources, the role of catalysis is growing in importance.

Efficient, economical and environmentally sound chemical production already requires the help of catalysis to run at acceptable rates. However, as it is evident that humanity faces unprecedented challenges in terms of future resources for energy and chemicals, the role of catalysis will soon become even more important, according to Professor Rasmus Fehrmann, head of the Catalysis and Sustainable Chemistry group at DTU Chemistry:

"To us, as a research group with a long-standing high profile in catalysis, this development is generally good news. However, we also see that international competition in the field has become much fiercer. For instance, the U. S. has initiated tre-

mendous efforts over recent years, as have a number of other nations. This means that we will need to focus our efforts more selectively than we have done in the past"

Much as is the case for current oil refineries, the utilization of biomass will require a dedicated and flexible processing apparatus. A wide range of possible designs and concepts for bio-refineries can be imagined.

"Even though catalysis will probably play a role in most of these concepts, we may not be able to address all of them. Our role should be to specifically target the concepts, where catalysis is absolutely essential to their success," Rasmus Fehrmann states, adding:

"And even for those concepts, we may not be able to cover the entire catalytic process from A till Z, but rather selected niche processes where we will be able to contribute with unique capabilities."



# A "Radically" New Look at Chemical Processes

By applying tailor-made radicals it is possible to increase the signal in nuclear magnetic resonance (NMR) imaging by several orders of magnitude. This will enable chemists to follow complex chemical reactions like catalysis in-situ.

Nuclear magnetic resonance (NMR) is already widely used in the world of chemistry and medicine for following the behaviour of various substances. With the method of Dynamic Nuclear Polarisation (DNP) it will also be possible for chemists to use this useful tool to study complex chemical reactions. This is the aim of a new project at DTU Chemistry.

"The first applications are likely to be monitoring of palladium-catalyzed reactions in organic chemistry. These reactions are of interest in the production of sustainable chemicals and similar green chemistry products," says project leader, Assistant Professor Susanne Mossin, DTU Chemistry.

"For instance our technique can be used for locating the active site of a catalyst and also for establishing which intermediate products are formed. This will improve our understanding of these reactions and allow for the further improvement of catalysts. However, what we are developing is really a new tool with a wide range of possible applications in both organic and inorganic chemistry."

## Enhancing signals of interest

In DNP the spins of nuclei are aligned, thereby "ear-marking" them, which in turn makes it possible to follow their fate once

inserted into a reaction. Susanne Mossin and her colleagues use a technique called electron paramagnetic resonance (EPR), which is analogous to NMR but instead of nuclei it is the spin of electrons that is excited.

The interaction between a free electron in one molecule and atomic nuclei in other molecules is then exploited to align the nuclear spins and therefore enhance the signal intensity in NMR by many orders of magnitude.

In order to obtain optimal results, radicals containing free electrons need to be designed so they are tailor-made for the specific purpose. In some cases this strategy may enhance the signals of interest by as much as 10,000 times. They will thus be detectable among the background signals and allow otherwise intractable reactions to be investigated.

**"Our goal is to create an experimental protocol for studying chemical reactions in situations where nuclear magnetic resonance cannot be applied today."**

*Assistant Professor Susanne Mossin, DTU Chemistry*



## Unpaired electrons - limitation and advantage

A key element in the new project, which has been made possible by a donation of close to EUR 250,000 from the Lundbeck Foundation, is the design of radicals with a specific EPR signal.

The radicals created are organic molecules with an unpaired electron and the ability to transfer spin polarisation to the nuclei in a molecule of interest to the specific study. Molecules with unpaired electrons are called paramagnetic – hence the technique's name. Spin labelling was first developed as a tool for probing proteins or biological membrane-local dynamics, but to Susanne Mossin the possible applications are wider:

"Our goal is to create an experimental protocol for studying chemical reactions in situations where nuclear magnetic resonance cannot be applied today."

On the one hand, the fact that EPR uses unpaired electrons is a limitation as most stable molecules have all their electrons paired. On the other hand, this limitation also means that the EPR technique is of great specificity, since ordinary chemical solvents and matrices do not produce EPR spectra.

## No time for sitting idle

An underlying breakthrough behind the new project is a technique developed by another member of the project team, Professor Jan Ardenkjær-Larsen of DTU Electrical Engineering. The technique allows for the spin-labelled samples to be produced in one instrument and then transported to another after DNP and a rapid dissolution process – still with the spin-labelling in place and the nuclear spins aligned.

This achievement does not allow the team to sit idle once the sample has been dissolved, Susanne Mossin emphasises:



*Magnet at work: The DNP magnet at DTU Electrical Engineering polarise the electron spin of the radical.*

"As the polarization is rapidly lost, you have no more than a few minutes to do your experiment. But then again, in many chemical reactions a few minutes is a very long time."

Over the short time span the polarization is gradually lost, which makes it necessary to apply algorithms to correct the results.

"This is not rocket science but still something you need to do. All in all, EPR does involve a bit more effort and know-how on interpreting results compared to other methods. The equipment is also relatively expensive. These factors may explain why EPR instruments are rare," Susanne Mossin comments.

To her knowledge, in Denmark only DTU and the University of Copenhagen have active EPR instruments.

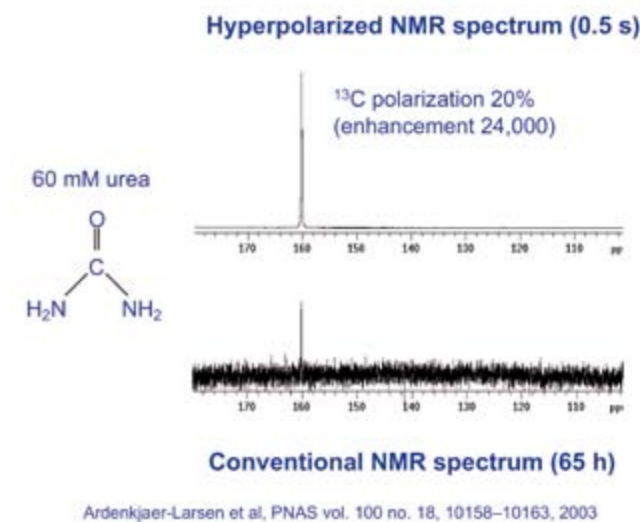
## Between chemistry and physics

Even internationally, EPR is not a widely used technique – at least not in chemistry.

"Centres with EPR are normally highly specialized, and most of them are dedicated to physics. To my mind, we are in a border area between physics and chemistry here," says Susanne Mossin, adding:

"As a chemist my angle is a bit different to that of a physicist as my interest is not so much the basic physics involved but rather to use EPR as a tool for understanding chemical reactions. For my use it would be best to have fairly standard procedures for doing EPR measurements. This is quite a novel approach."

The new project – titled "Radicals for Dynamic Nuclear Polarisation" – will run for three years.



*The NMR spectrum can be enhanced by up to four orders of magnitude when the magnetised radicals induce polarisation of the NMR active nuclei in solution.*

# Potatoes Cooked into Advanced Nanotechnology

The NanoChemistry group at DTU Chemistry not only excels in producing metallic nanostructures that are tailor-made in size and shape for specific purposes; the group even does so in a highly environmentally friendly fashion.

Do potatoes, carrots and onions – vegetables known from everyday cooking – and metallic nanoparticles sound like an unexpected match? To the NanoChemistry group at DTU Chemistry the merger has not only proven to be possible; it actually promises great advantages.

“Presently we are using metallic nanoparticles for a number of scientific purposes. By coating these particles with ultra thin layers of starch from vegetables, the particles are given necessary protection. Also, when looking further ahead at possible future applications of nanotechnology in medicine, it is highly desirable to use natural compounds which are likely to be well tolerated by the human body,” says Ph.D. student Christian Engelbrekt, DTU Chemistry.

“Further, our new processes allow for the synthesis of both nanoparticles and more sophisticated metallic nanostructures such as wires, polyhedra, bimetallic flowers etc. with controlled size and shape and under mild and environmentally friendly conditions.”

## When gold salt and potatoes merge

Metallic nanoparticles and molecular scale structures have attracted much attention in evolving nanoscience and nanotechnology due to their unique physical and chemical properties and as potential building blocks for nanodevices. Among many metallic structures, the high stability, broad applications ranging from medicine to catalysis, and unique chemical properties have prompted particular interest in the synthesis of gold nanoparticles.

An example of the applications for gold nanoparticles at DTU Chemistry is as tools for investigations of metalloproteins – a large group of proteins involved in a wide range of key biological processes. As the exact type of gold nanoparticle desired for a given type of investigation varies, being able to synthesize nanoparticles of controlled size and shape in high yield and high purity is essential.

“Starch and glucose are biological molecules available in large quantities in nature. Our synthesis extends directly to using extracts from natural starch-rich food sources such as potato, carrot and onion for gold nanoparticle preparation,” Christian Engelbrekt and Ph.D. Palle S. Jensen explain.

The group has dubbed this new “green” saccharide-based approach to metallic nanostructure synthesis by the acronym SAMENS. Boiling the fresh vegetables provides large amounts of starch and glucose by hydrolysis.

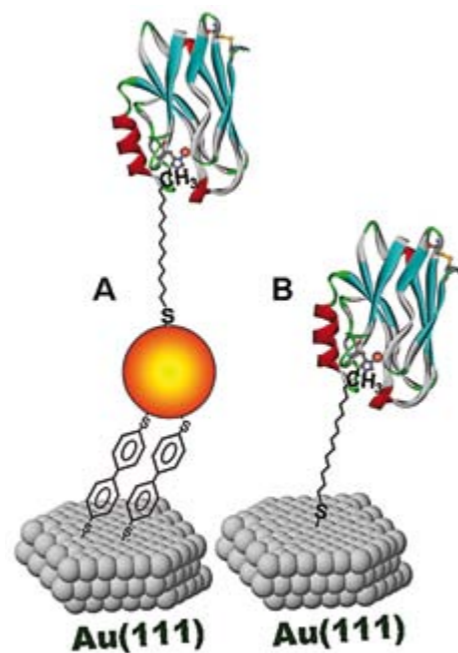
“Synthesis of metallic nanostructures using glucose or starch based recipes is a new activity in the group. Producing new materials with novel structures is one of the main roles of chemistry. Novel properties and functions are expected,” Associate Professor Jingdong Zhang and Christian Engelbrekt add.

## Novel bioelectro-catalytic functions

The method has implications for both larger-scale production of stable and variable-size gold nanoparticles, and for biological applications of these particles.

“The starch coating layers may evoke new properties of the gold nanoparticles, and strategies for new nanostructures, investigations which have now been initiated,” Jingdong Zhang states.

One successful application is that gold nanoparticles enhance the rate of interfacial electrochemical electron transfer redox proteins, for example the blue copper protein azurin, which is entirely absent on bulk gold electrode surfaces. This protein is encountered in the bacterial respiration and a robust probe molecule for biological electrochemistry. Studies of the reaction of gold nanoparticles with azurin demonstrate the highly efficient, electronically rooted electrocatalytic properties of the gold nanoparticles and pronounced size-dependent bioelectro-catalytic function of the nanoparticles.



A molecule of the copper protein azurin bound to a gold surface either via a 3 nm gold nanoparticle or directly. The small orange sphere in the protein is the copper atom, the large orange sphere the gold nanoparticle.

“Our work in these areas focuses on two aspects. One is electrocatalysis functions for redox reactions such as  $O_2$  reduction,  $H_2$  oxidation and enhancement of the electron transfer rate constant of biological metalloproteins. The other aspect is to study these chemical reactions in situ by advanced nanoscale spectroscopy methods,” explains Jingdong Zhang.

For these studies, STM (Scanning Tunneling Microscopy) is often the group’s method of choice. In an STM microscope an atomically sharp metal needle is scanned extremely close to a surface without actually touching it. The atom at the end of the tip will then interact with the closest atom at the surface through a phenomenon known as the quantum mechanical tunnelling effect. An STM microscope is able to map a surface with an accuracy of 0.1-0.2 nanometres. The actual accuracy in a given situation is determined by the properties of the given target molecule in question. Also, AFM (Atomic Force Microscopy) based on measuring the force between a sample and a tip is frequently applied.

“Both STM and AFM offer a unique platform for us to study chemical reactions in situ at the nanoscale, including those based on the new metallic nanostructures,” Jingdong Zhang explains.

“The NanoChemistry group has developed these methods for use directly in aqueous biological and chemical media and under electrochemical potential control, instead of the vacuum or air environment otherwise mostly encountered. Along with

our new single-molecule experimental science we also aim to develop the necessary theoretical frames.”

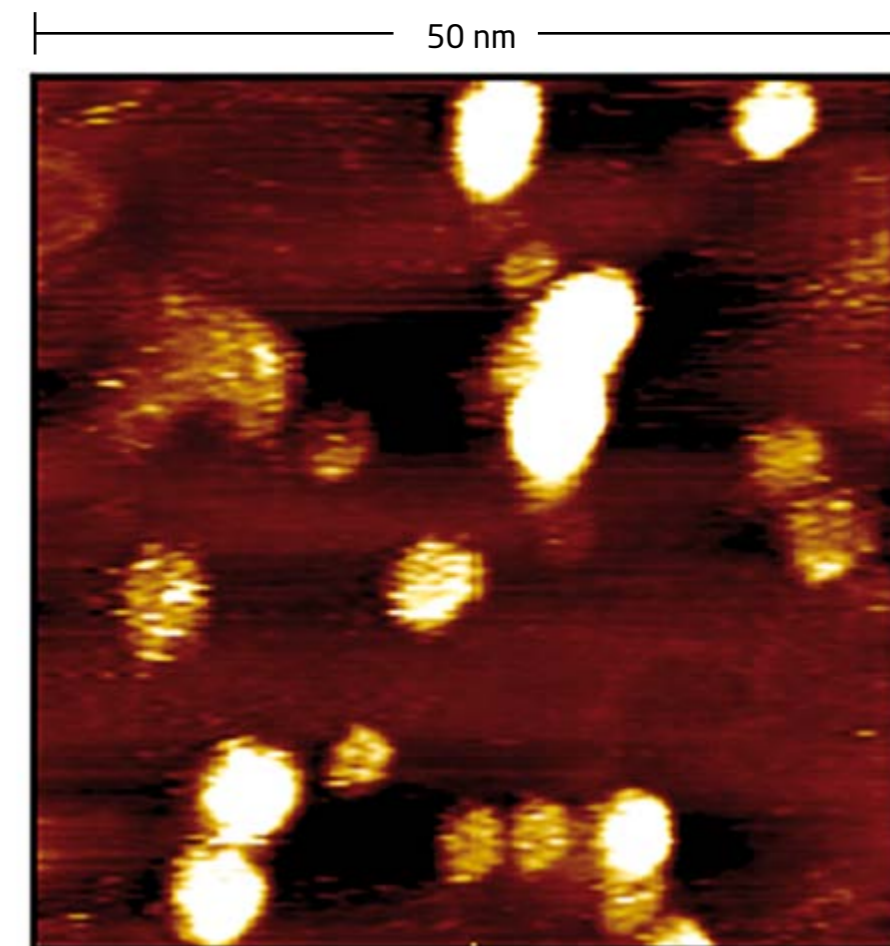
## Findings may inspire nanosensors

While the group remains focused primarily on applications in basic research, these findings will find commercial applications at some point.

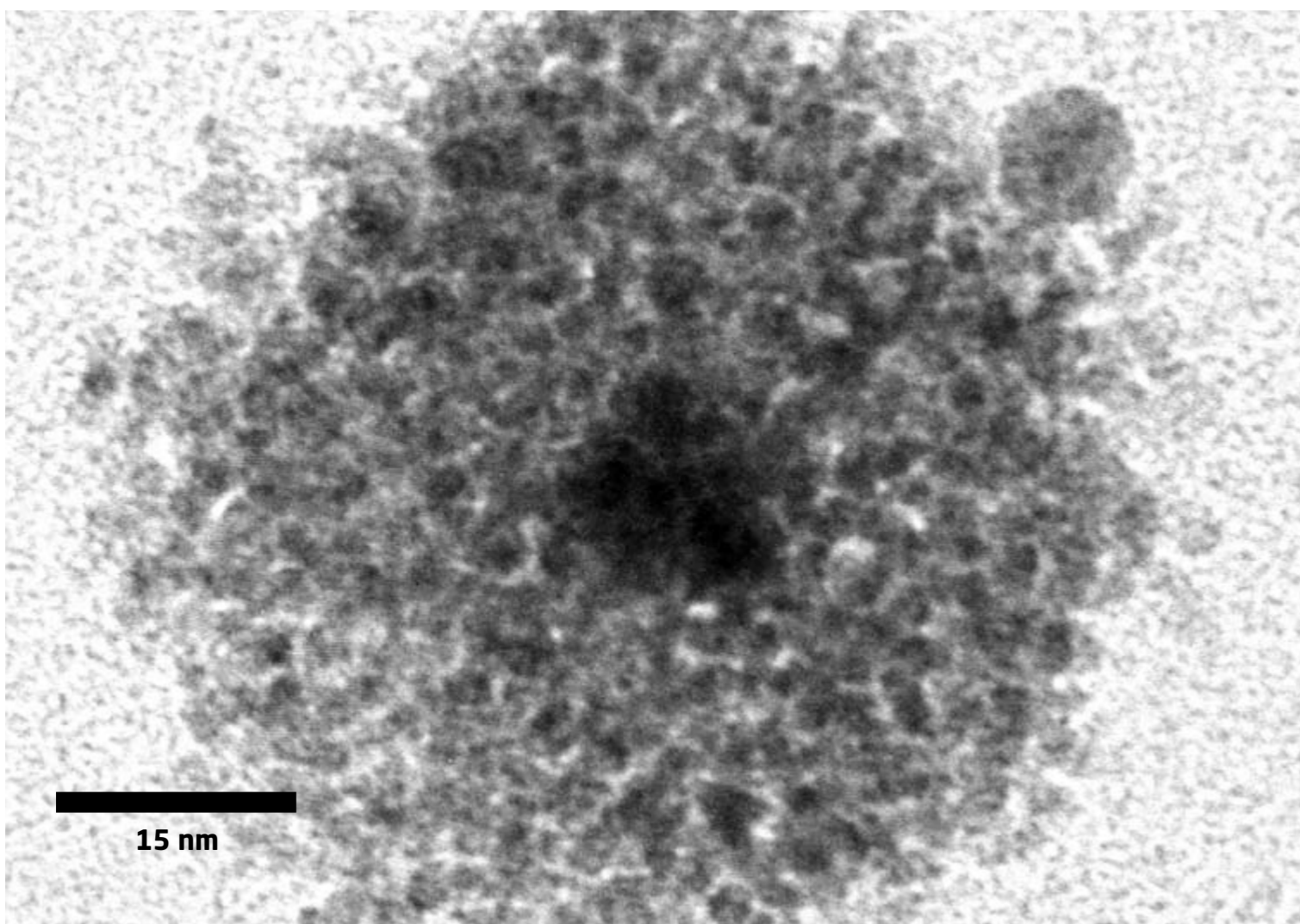
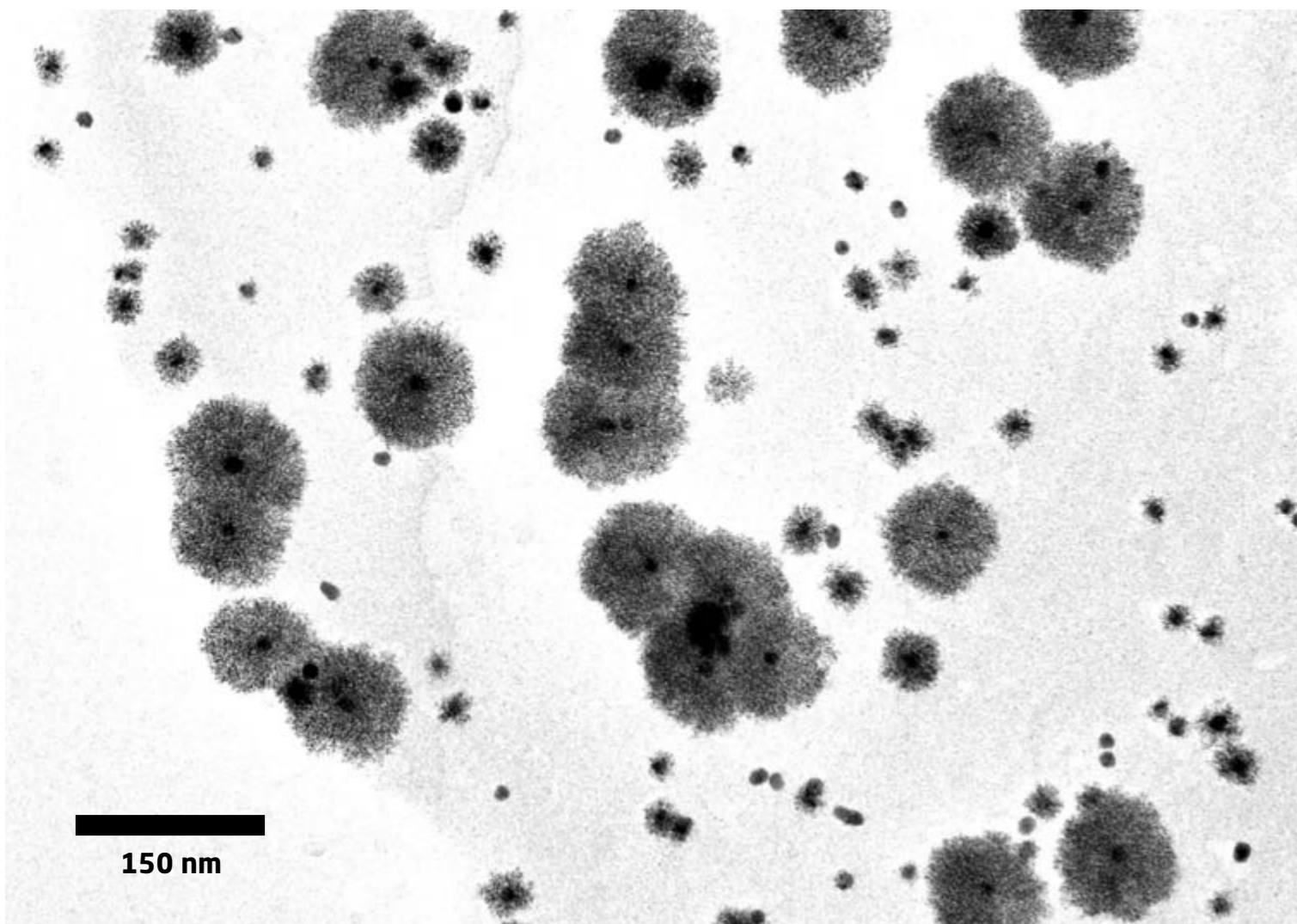
“For instance, the distinct enhancement of electron transfer could be a mechanism in a biological sensor, where the presence of a given substance would trigger an electrical signal. We have presently identified real systems where this is important,” Professor Jens Ulstrup notes.

Biological sensors at the nanoscale are interesting for several reasons. Firstly, as nanosensors could be tiny, a range of sensors could be deployed on a single chip. From a drop of blood or another biological sample an individual could be screened for a wide range of health factors using a “laboratory” less than the size of a finger nail. Secondly, these sensors could be extremely sensitive. Thirdly, they could be much faster than traditional chemical methods.

“When you apply measurements based on fluorescence or other traditional methods you typically have to wait days or at least hours and do complicated chemistry before you have a result. The great attraction of nanochemical sensors, in our view, is that if designed correctly, they will provide you with



Scanning tunneling microscopy image with both single protein/nanoparticle complexes (weak contrast) and single free protein molecules (strong contrast). The scale bar illustrates the size of the molecules. The molecules on the surface as shown in the figure to the left are “seen” from the top. The free molecules show a stronger contrast because the electric current runs over a shorter distance.



an electrical signal directly. Thus, you would have your result within seconds, and as data are electronic they would be easy to process," Ph.D. Pelle S. Jensen and Professor Jens Ulstrup explain.

#### At the nanoscale everything conducts

But just how can nanochemical sensors produce electronic signals directly? The answer is that once you zoom down to around the scale of single atoms or molecules most of our normal physical laws take quite different forms. For instance the renowned Ohm's law describing the simple relation between voltage, current and resistance in an electrical system has a quite different form at the nano-scale, where the laws of quantum mechanics apply.

While large molecules like proteins and DNA that form the basics of biology are insulators on a large scale, they actually become conductors at the nano-scale. Just like energy is moved around in our everyday world, the same is the case in a biological cell. A key vehicle is transfer of electric charge (current) from one place to another. In the biological cell and at the molecular scale this is done by moving single electrons from one molecule to another. This can take place in a controlled manner, in the right order and without short-circuits because nature's important building blocks are large complex molecules optimally developed over billions of years of evolution.

"So, one might say "everything is conductive at the nano-scale". The implication is that we can transmit an electronic signal through a biological molecule without destroying it. This opens up a range of interesting practical perspectives," Jens Ulstrup states.

#### Science comes first

The scope of the group differs from those of other groups working on projects closer to applications.

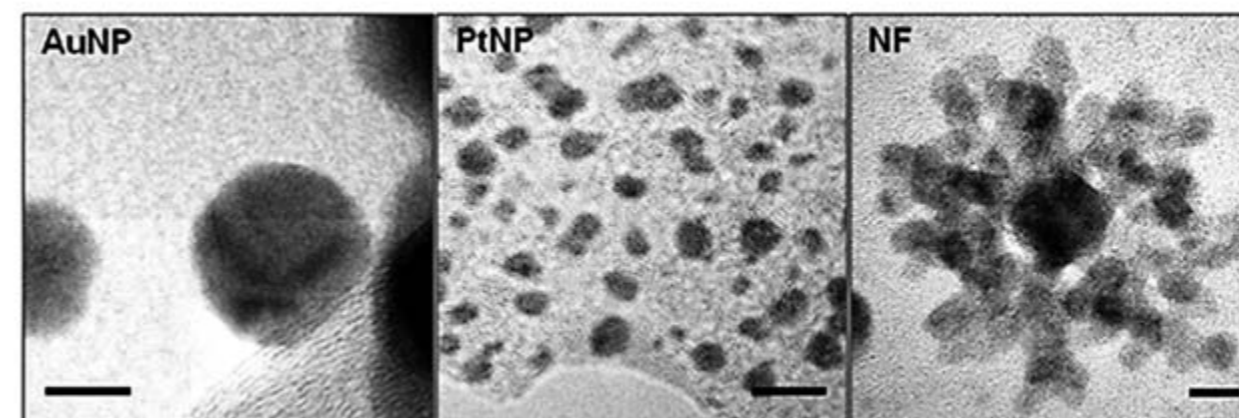
"The chemical property values that you find in a textbook are only accurate when you look at a normal scale sample of the substance in question – which would be billions of molecules. If you look at, say, ten molecules, each of them is expected to behave differently. Of course, if you study enough molecules eventually you will end up with an average equalling that of the text book. But to us these so called stochastic fluctuations between the individual molecules are of very great interest. These and other novel chemistry and physics observations are core activities in our group and will provide us with fundamental new insight," says Jens Ulstrup.

When considering whether to engage in a specific new project, the group is guided by a key question:

"Does this involve new natural science? If the answer is "yes, we are likely to see some new physics or some new chemistry" then there's a good chance it can be applied at a later stage – even if we are not able to say right now what the precise application might be."

**"Synthesis of metallic nanostructures using starch based recipes is a new activity in the group. Novel properties and functions are expected."**

*Associate Professor Jingdong Zhang, DTU Chemistry*



*All scale bars correspond to 5 nm.*

*Transmission electron microscopy images of three metallic nanostructures prepared by the "green" method. Left: A single gold nanoparticle crystal. Middle: A group of small platinum nanoparticle crystals. Right: A "nanoflower" with a core of gold and leaves of tiny ( $\approx 2$  nm) platinum nanoparticles. A collection of nanoflowers (top) and a magnified nanoflower are shown on the opposite page. (1 cm = 10 million nm).*





## 2. Organic Chemistry

Using organic chemistry as a tool to learn more about fundamental biology is a new trend known as Chemical Biology. Having the ultimate goal of suggesting new drug candidates the field has been a strategic focus area at DTU Chemistry over the recent years. A new activity rising in importance at the Organic Chemistry Section is bio-refinery applications of organic chemistry. Research under the section will typically have a dual approach of looking both at fundamental science, while also contemplating biological and pharmaceutical applications including bio screening, drug discovery and drug delivery systems.

The section's educational activity consists of introductory courses in all disciplines of organic chemistry followed by high-level courses in e.g. NMR spectroscopy and modern synthetic strategy and methodology, including synthesis of compounds of interest to the pharmaceutical industry.

**Section Coordinator:** Professor Robert Madsen until 31 December 2011  
Professor David Tanner from 1 January 2012

# Making Bio-plastics Affordable

With crude oil gradually becoming scarcer, interest in creating polymers from biomass is increasing. A new project at DTU Chemistry will investigate catalysis based on transition metals as a way of producing the relevant organic building blocks in an economically feasible way.

**“It is extremely important to develop new processes for converting biomass into useful compounds for the chemical industry.”**

*Esben Taarning, researcher at Haldor Topsoe A/S.*

The ultimate exhaustion of fossil resources requires that alternative pathways to fuels and materials are developed. Utilization of biomass is one of the more prominent solutions, and it has been suggested that the use of catalysis will improve present pathways for producing the organic building blocks needed for polymer production from biomass. This is the focus of a new project at DTU Chemistry.

“The chemical components of biomass are typically richer in oxygen than the desired products, thus requiring chemical reactions capable of reducing the oxygen content. Although

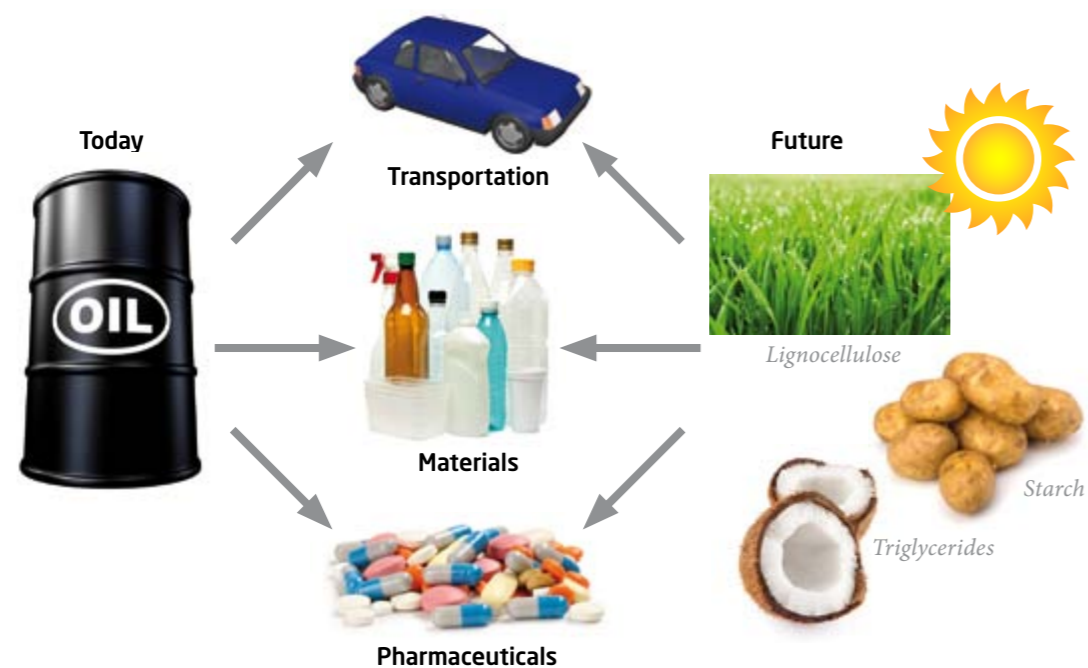
traditional chemical routes involving dehydration, oxidation and hydrogenation have shown some promise, more efficient solutions are needed,” explains the project leader, Associate Professor Peter Fristrup, DTU Chemistry.

A commercial market for bio-polymers already exists. A number of companies and public organisations prefer bio-polymers to polymers produced from crude oil, due to either environmental, health safety, climate or green image considerations. However, bio-polymers are currently produced from food resources like corn. Both for cost and food supply reasons, it would be highly desirable to produce bio-polymers from materials like straw and other agricultural waste products instead. “It is extremely important to develop new processes for converting biomass into useful compounds for the chemical industry,” comments Esben Taarning, researcher at Haldor Topsoe A/S.

## A newly emerging field

Raw materials for bio-polymers are currently produced via fermentation, which unavoidably results in a high level of by-product formation. Researchers with a background in biology are striving to invent better biological processes, while chemists are looking at novel catalytic tools.

A possible advantage of catalysis over fermentation is likely to be a better ability to sustain high temperatures and pressures. This should allow for more stable production, which in turn means higher cost-effectiveness.



A number of methods for producing polymerizable substances from biomass are already being tested at laboratory scale or even pilot plant scale, but in order for bio-polymers to replace polymers from crude oil in more than marginal quantities, the cost needs to be lowered substantially.

“This is not at all unrealistic. After all, reactions that transform crude oil into polymers have been optimized for about 80 years, while production of bio-polymers has just recently been initiated. Thus, it is highly likely that we can find pathways that are significantly smarter than the ones used presently,” Peter Fristrup comments.

## A “non-natural” process

Peter Fristrup’s research is focused on catalysis in the broadest sense, encompassing both chemical catalysis – including heterogeneous and homogeneous systems – and biocatalysis (i.e. enzymes).

The new project has been made possible by Peter Fristrup being awarded the Sapere Aude Research Leader Award by the Danish Council for Independent Research.

“We propose to further expand the scope of the relevant processes by carrying out a combined theoretical and experimental investigation of known transformations. Then we intend to use computational chemistry to quickly screen hundreds of new catalyst compositions. Finally, we will synthesize and test the most promising of these in silico-generated catalysts to identify those with improved reactivity, thus resulting in more efficient utilization of biomass,” explains Fristrup.

“Unfortunately, we are fundamentally looking at a reaction which is “not natural” in the sense that it would not happen spontaneously under ordinary conditions. In order to obtain our desired end-product we need to lose oxygen, which in biomass will be largely in the form of OH-groups. In order to achieve that, we need the system to move upwards in energy level.”

## Raw materials for polyesters

The project will look at catalysis based on transition metals – a group of elements that are especially well suited to act as catalysts. In the case of biomass, the transition metal based catalyst will break the bonds between carbon and oxygen atoms, resulting in two OH-groups being released. As catalyst, a number of transition metals including rhenium, osmium and palladium will be investigated. Depending on the starting molecule and the process design, one may get organic end-products that are suitable for polymerization.

One substance of special interest is 5-(hydroxymethyl)furfural (HMF) which in many regards is comparable to current starting products for making plastics from crude oil. HMF can be converted to 2,5-dimethylfuran (DMF), which is a liquid biofuel that in certain ways is superior to ethanol. Oxidation of HMF gives 2,5-furandicarboxylic acid, which has been proposed as a replacement for terephthalic acid in the production of polyesters.

## Topsoe: “A rational approach”

The studies will include both experimental and computational approaches in an attempt to utilize “the best of both worlds”, says Peter Fristrup:

“The experimental studies will include competition experiments, Hammett studies, and the determination of kinetic isotope effects. In the studies of small-molecule catalysis the computational method of choice will be density functional theory (DFT) in combination with the B3LYP functional. This method is superior to most quantum mechanical methods in terms of speed relative to accuracy and has been successfully applied to a wide range of organic and organometallic systems. However, we are also actively pursuing new computational methods which can potentially be applied to much larger systems.”

Esben Taarning, researcher at Haldor Topsoe A/S, comments: “One major task in this development is to gain insight into the fundamental reaction pathways of important molecules, such as glucose and HMF. The combination of DFT calculations and an experimental approach is a very intelligent and rational way to gain insight into these fundamental reactions.”

**“Reactions that transform crude oil into polymers have been optimized for about 80 years, while production of bio-polymers has just been initiated recently. Thus, it is highly likely that we can find pathways that are significantly smarter than the ones used presently.”**

*Associate Professor Peter Fristrup, DTU Chemistry.*

# A Strong Consortium on Bio-refining

By joining forces with both international and Danish industry and academic partners, DTU Chemistry is expanding its activities in the organic chemistry involved in transforming cellulose and other biomass raw materials into fuel and useful chemicals.

Cellulose is the most abundant organic molecule on the planet and unlike many other bio-materials that can be transformed into fuel or chemicals, cellulose cannot be digested by human metabolism. Its use in bio-refining is therefore not in conflict with human food supply. These facts have triggered vast interest in processes that can upgrade cellulose and similar organic compounds from their present status as agricultural and forestry waste products. A new large-scale project at DTU Chemistry will address the key organic chemistry involved. Partners in the project, which has gained substantial funding from the Danish Council for Strategic Research, are Novozymes A/S, DONG Energy A/S, Arrayjet (UK), PlantProbes (UK), University of Copenhagen, Cornell University (USA), and University of California, Berkeley (USA).

“We see large potential in the consortium. Not only are the partners highly skilled in their respective fields, but the combination of fields covered allows the consortium to address the full scale of research relevant to organic chemistry applications in bio-refining,” says Professor Robert Madsen of DTU Chemistry, adding:

“The processes involved are highly complex, and success in this kind of utilization of biomass will only be possible through an interdisciplinary approach. Excellence in one of the fields involved will not be sufficient to turn a given process into reality”

## Inspired by nature, but improved

While various setups for bio-refining can be imagined, the consortium will focus on processes involving enzymes. The project, starting April 1st 2012, encompasses several families of enzymes.

The main family is glycosylhydrolases, covering enzymes playing a key role as cellulose is broken down into minor chemical “building blocks”, which is absolutely necessary before further refining can take place. Just as in nature when plant materials rot, in a bio-refinery cellulose will most likely be broken down by hydrolysis, a process for which glycosylhydrolases are the chief catalysts.

“However, it is unlikely that the exact same enzymes which do the job in nature will be the best for the task in a bio-refinery. Also, as bio-refining require large quantities of enzymes it is important that they are as efficient as possible,” Associate Professor Mads H. Clausen remarks.

## Specially designed oligosaccharides

The idea is not for DTU Chemistry to provide the enzymes, which will be supplied by Novozymes A/S, the world's leading producer of commercial enzymes.

“The enzymes supplied by Novozymes will be invaluable to the success of the project. Our job will be to study these enzymes in ways

that the company does not have in-house resources to do. Further, we hope to suggest ways to improve the functionality of the enzymes for bio-refinery purposes,” Mads H. Clausen explains.

Cellulose is a polysaccharide – meaning a long chain of saccharide or sugar (in this case glucose) molecules, joined one to another by glycosidic bonds. The main focus of the group at DTU Chemistry is the smaller polysaccharides, called oligosaccharides. These simpler sugars are used as the substrate for characterization of enzymes. Rather than using mixtures of oligosaccharides as substrates, the group believes that tailor-made compounds may improve the process.

“We are going to synthesize a number of well defined oligosaccharides for our partners to test,” Mads H. Clausen promises, while noting that the structures of the compounds are decided through discussions in the consortium.

## Several families of enzymes in focus

The actual synthesis will begin as soon as possible after April 1st 2012 when the project's first two Ph.D. students have taken office. The hiring process is currently in progress. Two more Ph.D. students are to be hired by autumn 2012.

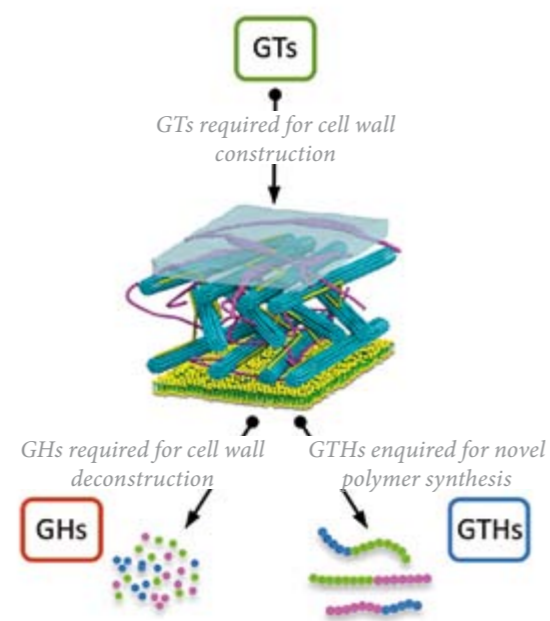


Figure 1. The key roles of glycosyl transferases (GTs), glycosyl hydrolases (GHs) and transglycosylase/hydrolases (GTHs) in biofuel production and bio-refining.

“With these four new positions, research into carbohydrates will involve 11 Ph.D. students and postdocs in the Organic Chemistry Section at DTU Chemistry, thus constituting a significant part of our work,” Professor Robert Madsen states.

While glycosylhydrolases are the most urgent enzymes to study, as the initial breakdown of cellulose by hydrolysis is the prerequisite for all further refining, the consortium will also address two other enzyme families.

One of these families is the glycosyltransferases. These enzymes may become of interest in a future situation where instead of utilizing agricultural and forestry waste products, biomass is grown especially for bio-refining purposes.

## Ready to face fierce competition

The last enzyme family in focus is the transglycosylases, a group of enzymes relevant to production of bio-polymers.

“Right now production of bio-ethanol is high on the agenda, and this application is duly represented in the consortium through DONG Energy, which already has an operational pilot plant running. But a bit further down the road it would be most interesting to produce new types of bio-polymers, as these would have a higher economic value,” Robert Madsen explains.

“Transglycosylases are likely to act as catalysts that will facilitate the production of polymers with new or improved functions. Also, these

enzymes are of high scientific interest as they are currently relatively unexplored,” Mads H. Clausen adds.

Summing up, Professor Robert Madsen has high expectations for the group's involvement in the international consortium:

“International competition to deliver the best solutions for bio-refining is already fierce as the need to replace diminishing oil reserves is becoming ever more evident. In my opinion, tomorrow's winners in the field will most likely be those who are able to construct a consortium strong enough to cover the full technology.”

*The new research project on enzymes for bio-refining is supported by a Danish Council for Strategic Research grant of DKK 18 million. The project will commence April 1st 2012 and run for four years.*

**“We hope to suggest ways to improve the functionality of enzymes for bio-refinery purposes.”**

*Associate Professor Mads H. Clausen, DTU Chemistry*

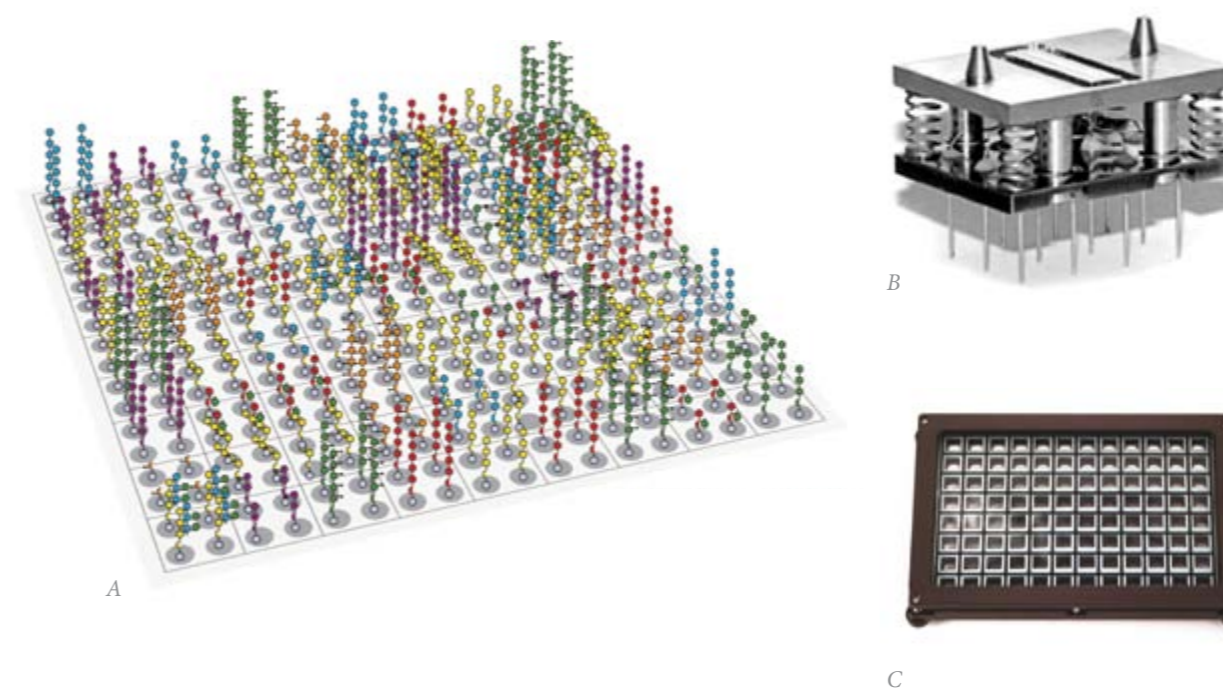


Figure 2. Multiplexed glycan arrays as enzyme assay platforms. Project partners have produced arrays of >100 well defined oligosaccharides (A) using state-of-the-art piezoelectric robots (B). Incubation of arrays in custom apparatus (C) enables massively multiplexed screening. The array shown in (A) contains 324 spots and can be fitted into one 5 mm x 5 mm well of the incubation chamber in (C).



## 3. Physical Chemistry

Recently, it has been realized that the same logic which has driven natural selection in species is reflected all the way down to the molecular level. Learning from the way molecules have been optimized through evolution for specific purposes is a new activity at the Physical Chemistry Section. The research has a dual aim of adding to fundamental understanding, and looking at potential applications for instance in optimizing enzymes for industrial purposes.

The section is built around the Physical and Biophysical Chemistry Group, complemented by X-ray and Protein Crystallography, Analytical Chemistry and Raman Spectroscopy. The section is also involved in the Center for Molecular Movies (CMM) and the Danish Centre for use of Synchrotron X-ray and Neutron facilities (DANSCATT).

The section establishes the basic foundation in physical chemistry needed in all disciplines of chemistry and chemical engineering as well as advanced courses related to the sections research in experimental characterization and computer simulations of chemical structures and reactions.

**Section Coordinator:** Associate Professor Kenny Ståhl

# Survival of the Fittest Molecule

Darwin's classic description of how competition has shaped the natural variation of species is reflected all the way down to the molecular level. Understanding this "molecular evolution" is the first step towards radical improvements in biotechnology – for instance in the search for an enzyme suited to a given task.

**“Metaphorically speaking we are stranded on an island. We know that the golden treasure in the form of a molecule that would be perfect for our task is at the bottom of the sea somewhere. But we are destined to remain very close to the shore.”**

*Associate Professor Kasper Planeta Kepp, DTU Chemistry*

For a sperm whale, the ability to sustain long dives is a highly valuable parameter. While an individual whale with a mutation that reduces its dive duration may of course still be successful in finding nutrition and achieving a normal rate of reproduction, in the longer run it will be whales without this mutation that succeed. And when looking across tens of thousands of years – whales have been around for about 50 million years – even a marginally longer dive duration will prevail. Recently, it has been realized that the same logic which has driven natural selection in species is reflected all the way down to the molecular level.

“By understanding this molecular evolution we hope to find radically new ways of designing useful molecules for given purposes,” says Associate Professor Kasper Planeta Kepp of DTU Chemistry, adding:

“When a biotech company wants to find for example an enzyme for a given industrial purpose it will nearly always start out with a wild type enzyme which does the same type of job in nature. The company will then make tiny changes to the wild type enzyme and hope to find an analogue which is better suited to the given purpose. However, it could very well be that the optimal molecule is quite far from the wild type. But unfortunately we have no idea about how to find that optimal molecule at present.”

## Ever-increasing complexity

For instance, a wild type enzyme for a given purpose could be found in a fungus. While this fungus may live under conditions that have some resemblance to the industrial environment in question, several differences in the two environments will always exist. Thus it is highly unlikely that the wild type enzyme will be optimal in the industrial context.

Should the company want to abandon the wild type enzyme and try to find the optimal molecule by random experiments, it is easy to calculate its chance of success. An average enzyme has a sequence of about 400 amino acids with 20 to choose from in each position. So the number of possible combinations – also known as the sequence space – is  $20^{400}$ . In other words, the chance of a random hit would be astronomically small.

So, how have molecules developed over time? Have they just grown bigger in order to optimize for given purposes?

“There is a bit of truth in that. As in many other areas of life – and in society – there seems to be a tendency for things to develop from something simple to something complex,” says Kasper Planeta Kepp.

This growth has often come in the form of so-called fusion events, where smaller chunks of protein – peptides – have been added to the protein in question.

“However, the growth in protein size is generally not that significant. Instead the evolution is more linked to an increase in the complexity of molecules rather than an increase in size,” says Kasper Planeta Kepp.

## Metalloproteins - nature's tool of choice

Of special interest is a large group of proteins known as metalloproteins. Roughly a third of all proteins contain one or more metal atoms – they are metalloproteins – and they have been found to play a part in a number of key life processes. Iron, copper and zinc are metals that are often found in metalloproteins. The area immediately surrounding a metal atom in a metalloprotein is known as the metal centre. As proteins are large molecules containing 100,000-1,000,000 or even more atoms, the metal centre takes up just a tiny fraction of the protein. But it is often here that we find the key to the function of the particular protein.

“It seems that metalloproteins are nature's tool of choice when faced with complex tasks. We know that metalloproteins play a part in the majority of advanced biochemical transformations,” Kasper Planeta Kepp remarks.

Interestingly enough, the metalloproteins are not “born” with their metals. The metal atoms are added during so-called post-translational modification:

“We are just beginning to discover the importance of this modification. At present about 25,000 basic forms of protein

are known. But when you include post-translational modification the diversity runs up to about 2 million different forms.”

Also, according to Kasper Planeta Kepp, the way we normally describe a protein should be modified:

“We tend to look at a given molecule and say “this is how the protein looks”, but this is in fact a gross simplification. The protein will only look like this under certain conditions. If you change the environment, the protein will also change.”

## An industrially important enzyme

One of Kasper Planeta Kepp's groups' projects concerns a family of enzymes known as laccases, which are metalloproteins. The molecule contains four copper atoms. Laccases are of major industrial importance for applications such as processing wood into paper, removing the bi-taste of cork from wine, and giving an artificial worn appearance to jeans. In nature, laccases are found in the Japanese lacquer tree (which has given the enzyme its name) and in various fungi which use laccases to “digest” wooden surfaces and gain a better grip.

“At some point it would be most interesting for us to collaborate with industry in order to obtain experimental data on the various forms of laccases. However, just now our focus is on increasing fundamental understanding of the enzyme. Laccases are powerful proteins capable of providing a high level of oxidation. Another interesting feature is their relative stability outside the cell. While most proteins are only stable in the protected environment inside the cell, the laccases are resilient to quite dramatic changes in their surroundings. So, the case for using laccases to obtain a better fundamental knowledge of molecular evolution is strong.”

Following three years as a Steno Fellow, Kasper Planeta Kepp became a DTU Chemistry faculty member in autumn 2011.

“So I am still in the process of defining the details of my area of research.”

## “Stranded on an island”

It is clear, however, that the group will address an unusually wide range of fields; from extremely detailed studies involving quantum mechanical computational tools of individual atoms and their nuclei and electrons to studies of protein structures and all the way up to studying cells. The tools will include modelling, simulations and practical production of proteins (in cooperation with DTU Chemical Engineering).

“To my knowledge, no other group is trying to reach all the way from quantum mechanics to entire cells in one, unified quantitative framework.”

The ambitious approach is justified by the complexity of the task ahead:

“Metaphorically speaking, industry and researchers looking to find an optimal enzyme or a similar molecule for a given purpose are presently stranded on an island in the middle of the ocean. If we see the wild type molecule as the island, we know that the golden treasure in the form of a molecule that would be perfect for our task is at the bottom of the sea somewhere. But as the sea is vast and we have no idea where we should look, we have to remain very close to the shore and hope we may find something that is at least useful,” says Kasper Planeta Kepp, who concludes:

“The only way to change this is by obtaining a rational physical understanding of how molecules evolve as they are optimized by nature for a given purpose.”



# Enzymes Tailor-made for Bio-refining

The Chemistry at the Interface to Biology group at DTU Chemistry, the Research Unit for Functional Biomaterials at Roskilde University and Novozymes A/S unite in efforts to find smarter ways to utilize cellulose as a raw material for the production of ethanol and other chemicals.

Cellulose is a major constituent in straw, sawdust, sewage and other waste products from farming, agriculture and forestry. No other biological molecule is as abundant as cellulose, and with crude oil gradually becoming scarcer, interest in exploiting cellulose and other forms of biomass as raw materials for the production of chemicals is increasing. While a bio-refining industry already exists, the partners in a new Danish research project envision plenty of scope for improvements in the methods currently applied.

Initiated by the Research Unit for Functional Biomaterials at Roskilde University, the project aims to develop tailor-made enzymes that catalyze biochemical reactions that can break down cellulose by hydrolysis into small, fermentable sugars and thus make it useful for the production of ethanol and other compounds.

“The hydrolysis of cellulose is a complex process, where different enzymes operate simultaneously. In some cases this will create synergy where the different enzymes enhance each others’ efficiency, while in other cases they may counteract each other. We are trying to establish what would be the optimal “blend” of enzymes for a given task,” says Associate Professor Günther Peters, head of the ChIBi group at DTU Chemistry. The group specializes in modelling biological processes at the molecular level.

## Synergy effect between different enzymes

Given the complexity of the reactions involved, it is not possible to use traditional, deterministic simulations. Instead the group uses the so called Monte Carlo method based on repeated random sampling to compute the enzymatic reactions. The Monte Carlo method (named after the famous casino) is especially useful for simulating systems with many coupled degrees of freedom.

“The development of a stochastic model and in that respect a kinetic model will enable us to study cellulase’s enzymatic properties at a fundamental level. These results will provide key insights needed to take advantage of the synergy effect between the enzymes and to understand in more detail the effect of substrate heterogeneity and product inhibition on the degradation of cellulose,” says Günther Peters.

In these simulations, the ChIBi group at DTU Chemistry will vary different parameters to see how the overall process is

affected. This will reveal which parameters are most sensitive in relation to improving yield. These results may essentially be used to guide cellulase design, and optimize the hydrolysis of various cellulosic substrates.

## Natural enzymes work slowly in industry

In the project, the world’s leading producer of enzymes for industrial purposes, Novozymes A/S, supplies the academic partners with enzymes, which are then characterized by the Research Unit for Functional Biomaterials at Roskilde University.

“We already know that these enzymes are able to do the job, because that’s what they do in nature. For instance, when a dead tree begins to rot, enzymes will start breaking down the cellulose. However, in an industrial context these processes are quite slow – maybe because they have been optimized for the specific task in nature. We try to establish which bottlenecks at the molecular level are causing the processes to be slow,” says Professor Peter Westh, Roskilde University, adding:

“Once we learn this we hope to be able to suggest modifications that will result in more efficient enzyme variation for the task.”

After the characterization, the enzymes are taken into experiments by the group at Roskilde University interacting with the ChIBi group at DTU Chemistry.

**“We are trying to establish what would be the optimal ‘blend’ of enzymes for a given task.”**

*Associate Professor Günther Peters, DTU Chemistry*

## Experiments and simulations interact

The experiments at Roskilde University and the simulations at DTU Chemistry are thus constantly interacting. As the experimental results are obtained, the question is whether they can be mirrored in simulations. If the ChIBi group at DTU Chemistry is able to produce the same results in simulations, the team can say with a high degree of certainty that the process is understood. But if the simulations give different results, a gap in understanding must exist.

While the process of breaking down cellulose by hydrolysis is the prime focus initially, the project will also include later

processes that are needed to turn the intermediate compounds that have been obtained into useful products.

“We will start by looking at ethanol because this is a fairly simple and well understood process. Once we obtain new in-

sights into the processes involved in ethanol production, it will be interesting to expand this knowledge to the production of other, more expensive products,” says Günther Peters.

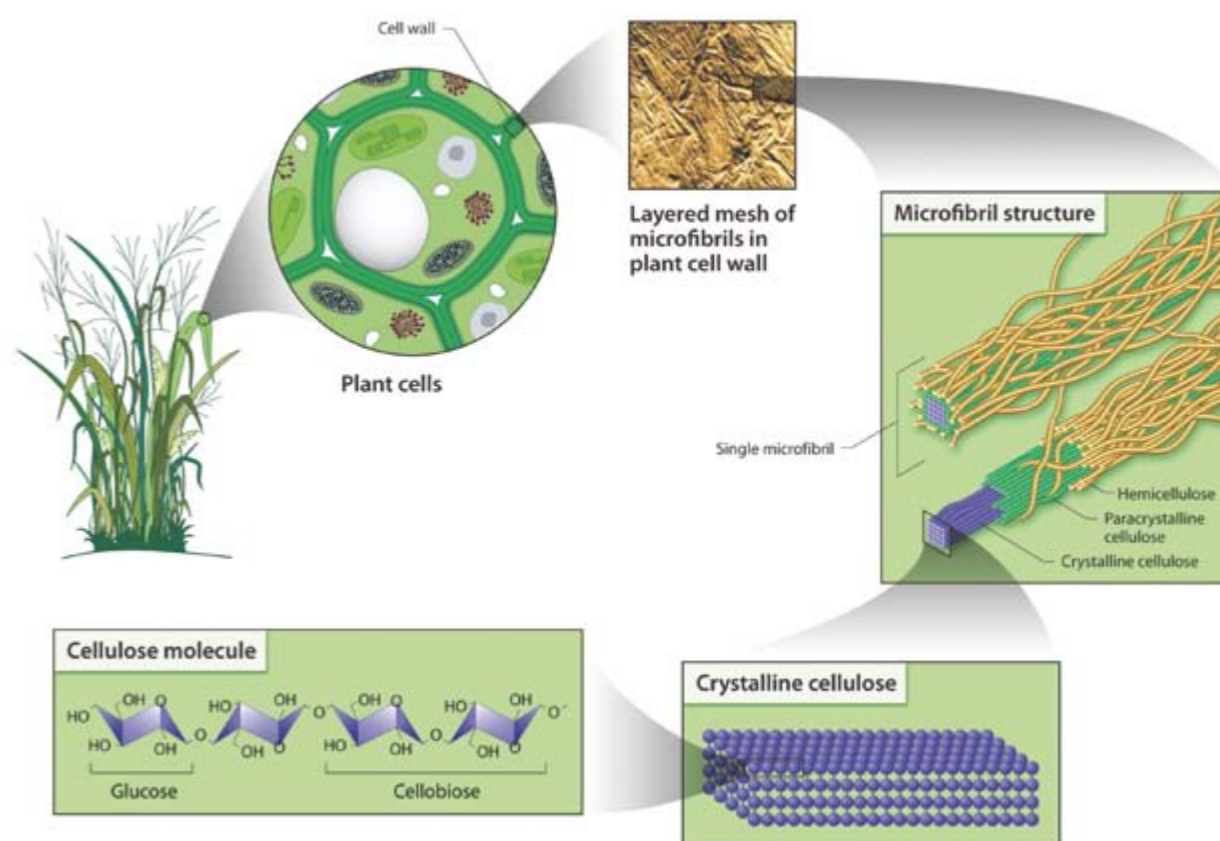
## Cooperation with Novo Nordisk

The Chemistry Interface to Biology group at DTU Chemistry has a tradition for cooperation with Novo Nordisk. The group’s speciality of modelling biological processes at the molecular level will sometimes coincide with projects at the company. Novo Nordisk is one of the world’s leading suppliers of products for the treatment of diabetes, but is also engaged in other fields such as drugs for the treatment of blood coagulation disorders.

“The level of cooperation will always vary depending on which projects are ongoing, but we do have mutual interests in modelling,” says principal scientist Ole H. Olsen of Novo Nordisk’s haemostasis biology unit.

Currently Novo Nordisk (Ole H. Olsen), Lund University (Assistant Professor Ingemar Andre) and the Chemistry Interface to Biology group at DTU Chemistry (Associate Professor Günther Peters) are supervising a Ph.D. project focusing on the structured and functional characterization of protein complexes in the blood coagulation cascade.

“The project has just started recently. Right now the project is mostly in our field, but we appreciate the opportunity of including Günther’s capacities more at a later stage,” says Ole H. Olsen.



US DOE. 2005. Genomics:GTL Roadmap, DOE/SC-0090, U.S. Department of Energy Office of Science. (p. 204) (<http://genomicscience.energy.gov/roadmap/#page=news>)

# How Weak Bones Grow Stronger

A new drug for treatment of osteoporosis approaches the market. It is expected to help millions of people world wide. A research group at DTU Chemistry was engaged in the first stages of the long journey.

**“Quite possibly we have set an unofficial world record as the smallest research group that has ever discovered a new drug.”**

*Associate Professor, D.Sc. Jens E. T. Andersen, DTU Chemistry*

Having passed the clinical testing in the final phase (phase III) of a pharmaceuticals way to the market only paper work should remain, before the pharmaceutical corporation Servier can present a novel drug for treatment of osteoporosis. World wide are estimated that more than 100 million people suffer from osteoporosis (porous bones).

“Obviously, the really good news is that so many people are able to benefit from an improved treatment, but to our research group it is also very satisfying,” says Jens E.T. Andersen of the Analytical Chemistry group at DTU Chemistry.

The story began in 2003, when Jens E. T. Andersen was approached by Stephan Christgau who was CEO at the time for the start-up company Nordic Bone A/S. Since 1910 it has been known that the chemical similarity between strontium and calcium allows for strontium to replace calcium in bones. Much later it was realized that high doses of strontium could even strengthen bones that were damaged by osteoporosis. When Nordic Bone approached the analytical chemistry group, was the first strontium-based prescription drug for treatment of the disease, strontium ranelate, due to be launched to the market (by Servier, in 2004). Nordic Bone’s idea was to discover an alternative drug that was also based on strontium, but with a different carrier molecule than ranelate which is insoluble and cannot be processed into a pill. Strontium ranelate is sold as a powder which needs to be suspended in water.

“The taste of this suspension may not be to everyone’s liking but in a pill you would have a better control of the dose; plus it would generally be a more comfortable way for the patient to administer the medicine,” Jens E. T. Andersen sums up.

## An unusual board meeting

The group at DTU Chemistry soon came up with about 20 candidates for the new drug. All had strontium as the cation and a small organic molecule as the anion.

“When I first heard of the idea, I thought we could solve this in a few weeks. It sounded to me like a simple acid-base reaction,” Jens E. T. Andersen smiles.

But things proved not to be all that simple. For some drugs candidates were problems of sedimentation impossible to get around. Also, the group was challenged by Nordic Bones’ desire to find a drug that could be administered in not more than one pill a day – calling for a high content of strontium.

After an intense three month period pointed the needle towards strontium malonate as the best candidate. The molecule has a 46 % content of strontium, which is very high and enough to satisfy the only-one-pill-a-day demand. In comparison, the strontium content of strontium ranelate is 34 %. Also, strontium malonate proved to have a number of other appropriate chemical properties in relation to pill production.

On top of that, the taste was pleasant – a fact which was established in a far from academic fashion.

“Well, the board of Nordic Bone A/S tasted the product. I should say that this was against my recommendation, as the product had not yet undergone any clinical testing for toxicity and other possible side-effects,” says Jens E. T. Andersen, adding:

“But anyway, they liked the taste and fortunately, it was later shown in clinical trials that strontium malonate is safe!”

## An unofficial world record

Stephan Christgau (today working with Novo Seeds) and his colleagues at Nordic Bone in collaboration with Jens E.T. Andersen

### Osteoporosis

Osteoporosis (“porous bones”) is a disease in bones that leads to a reduced bone mineral density (BMD), which in turn leads to an increased risk of fracture. The form of osteoporosis most common in women after menopause is referred to as primary type 1 or postmenopausal osteoporosis. Primary type 2 or senile osteoporosis occurs after age 75 and is seen in both women and men at a ratio of 2:1. Finally, secondary osteoporosis may arise at any age and affects men and women equally. This form results from chronic predisposing medical problems or disease.

Osteoporosis is estimated to affect 200 million women world wide (World Health Organization Technical Report, University of Sheffield, UK, 2006). According to a US study (National Osteoporosis Foundation, Washington DC, USA, 2002) osteoporosis afflicts 55 per cent of Americans aged 50 and above. Of these, approximately 80 per cent are women.

were able to develop a high-yield synthesis of anhydrous strontium malonate.

In the following efforts, the Analytical-chemistry group at DTU Chemistry was able to characterize the crystal structure of the compound. Among other methods applied by the group were inductively-coupled mass spectrometry (ICP-MS), single-crystal X-ray crystallography and dual energy X-ray absorptiometry (DEXA).

The Danish company Clausson-Kaas in Farum was commissioned to produce the first batches of strontium malonate for trial purposes. Following the initial toxicological tests of the product, Nordic Bone changed its name to Osteologix A/S, and the company commenced the extensive statutory, preclinical trials in animals. Upon completion of these toxicological studies, the clinical phase I-III trials were initiated. Osteologix later became Osteologix, Inc. and changed its focus to the U.S. market. In 2010, the company was granted its patent for synthesis and application of strontium malonate. By August the same year, announced Osteologix that it had granted Servier an exclusive license to develop and commercialize strontium malonate outside the U.S.

Today, Jens E. T. Andersen can sum up the products’ journey:

“From we set out, it took seven years before it was patented, and

ten years will be a fair guess on the time to market. To date, approx. 130 million DKK has been invested in phase I and phase II trials while much more has been invested for the phase III trials. All triggered by the initial efforts we made in collaboration with Nordic Bone.”

Besides himself, the efforts at DTU Chemistry has involved collaboration with Assoc.Prof. Kenny Ståhl (Crystallography), one PhD student (today PhD) Anders C. Raffalt, two master thesis students and four laboratory technicians.

“Quite possibly we have set an unofficial world record as the smallest research group that has ever discovered a new drug,” says Jens E. T. Andersen.

**“Jens E. T. Andersens group provided essential contribution in the early phase of the project by producing and evaluating a number of strontium salts.”**

*Stephan Christgau, former CEO of Nordic Bone A/S (today with Novo A/S)*

## A series of scientific articles underway

The Danish legislation on Intellectual Property Right at the time – 2003 – made it impossible for DTU to secure royalties or other forms of future income from the discovery. Still, according to Jens E. T. Andersen the project has benefited to DTU Chemistry in a number of ways:

“First of all, Nordic Bone and later Osteologix have supplied us with samples worth a fortune. Without the project we would never have had access to this kind of material. Also, the project has helped us to obtain a much higher level of knowledge on bones. This has given us a platform for further research.”

The Analytical-chemistry group applied modern methods of quality assurance of the research that were a key factor in the success of developing a new synthesis that could be patented. A very fruitful collaboration with Professor Jens-Erik Beck Jensen at Hvidovre Hospital allowed detailed studies of the relation between strontium doses and bone-strengths of animals treated with strontium malonate.

Due to confidentially agreements that were needed to protect the pending patenting process publication of some of the groups’ scientific finding has been delayed. But since the patent was obtained in 2010 will these restrictions no longer be valid.

“The delay has not really harmed our research because we have had many other projects going on. Probably we could not have published our findings on strontium malonate much faster anyway. However, as soon as we can we will start publishing a series of scientific articles around the subject,” promises Jens E. T. Andersen.

*A summary of Ph. D. Anders C. Raffalt’s thesis “Effects of strontium malonate [NB S101] on the compositional, structural and biomechanical properties of calcified tissues in rats and dogs” can be found in chapter 4.*



# 4. Ph.D. Defences 2011

## ZEOLITE CATALYZED PRODUCTION OF SYNTHETIC FUELS



Full title: "Towards a Methanol Economy: Zeolite Catalyzed Production of Synthetic Fuels"

Supervisor: Rasmus Fehrmann

The project was funded by Haldor Topsøe A/S, the Danish National Research Foundation and DTU

One possible scenario for a future energy system with less dependence on fossil fuels is "the methanol economy", where methanol acts as the main energy carrier and building block in the chemical industry. Methanol is currently produced from fossil-based syn-gas (mainly based on natural gas) but may also be produced from various other sources, including methanol synthesis and electrochemical reduction from carbon dioxide.

This project focuses on methanol-to-hydrocarbons (MTH) reactions, where methanol is converted in a one-step process to a mixture of different hydrocarbons over a solid acid catalyst – typically a zeolite or zeotype catalyst.

Zeolites are crystalline inorganic materials composed of silicon atoms, bridged through oxygen atoms to form an ordered structure containing micropores of molecular sizes throughout the entire crystal, leading to a massive internal surface area.

MTH reactions over zeolite catalysts were discovered in the early 1970s by two

groups of researchers at Mobil Oil. These findings were published in the open literature in 1976 and 1977. During the oil crisis at the time, great efforts were put into developing this reaction, since it offers an alternative to the ordinary petrochemically derived gasoline. As oil prices later dropped, these efforts diminished, but in recent years attention has returned to them.

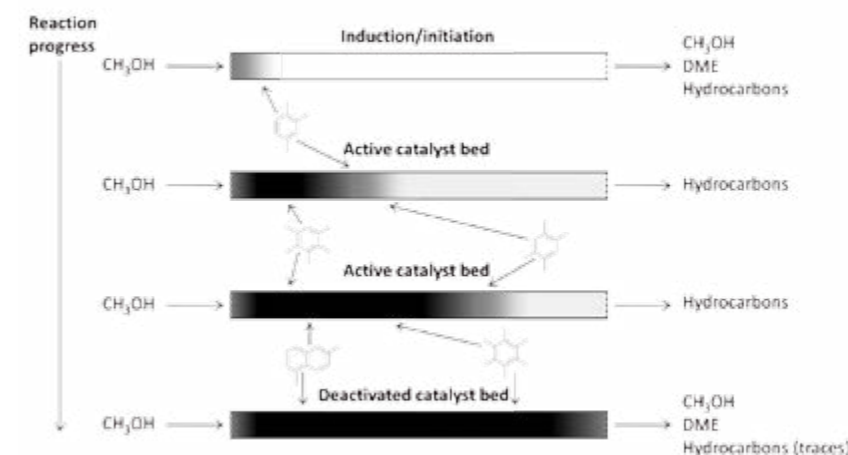
In this project, a series of experiments concerning co-conversion of ethane and methanol over a commercial H-ZSM-5 zeolite impregnated with gallium and/or molybdenum was carried out. Isotopic labelling studies performed with  $^{13}\text{C}$  labelled methanol and unlabelled ethane showed that in the very first minutes of the reaction, large numbers of carbon atoms from ethane are incorporated into the products.

Conversion of methanol, ethanol, 2-propanol, and 1-butanol to hydrocarbons over various zeolite catalysts was also studied. When 2-propanol or 1-butanol is converted over H-ZSM-5, the total conversion capacities of the catalyst are more than 25 times higher than for conversion of methanol and ethanol.

Finally, the direct zeolite catalyzed production of hydrocarbons from other

oxygenates such as glycerol, methyl lactate, and acetic acid was studied. The incorporation of the carbon atoms from oxygenates into the hydrocarbon products was confirmed by isotopic labelling experiments. More than 25 different oxygenates are converted over H-ZSM-5 as 10 % solutions in methanol, and the effect of the H/C atomic ratio of the dehydrated reaction mixture and the specific functional groups in the reactant on the catalyst lifetime, product selectivity, and formation of coke was addressed.

**This project focuses on methanol-to-hydrocarbons (MTH) reactions, where methanol is converted in a one-step process to a mixture of different hydrocarbons over a solid acid catalyst - typically a zeolite or zeotype catalyst.**





## ZEOLITE CATALYSTS FOR BIO-REFINING



Martin Spangsberg Holm, Ph.D.

Full title: "Conversion of Oxygenates over Zeolite Catalysts: Structure-Activity Relations"

Supervisor: Rasmus Fehrmann

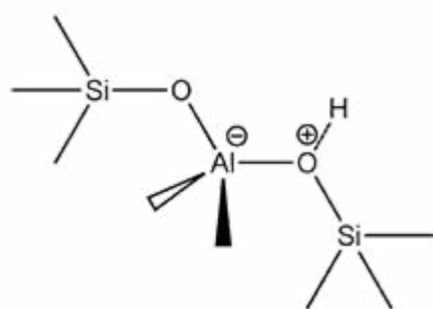
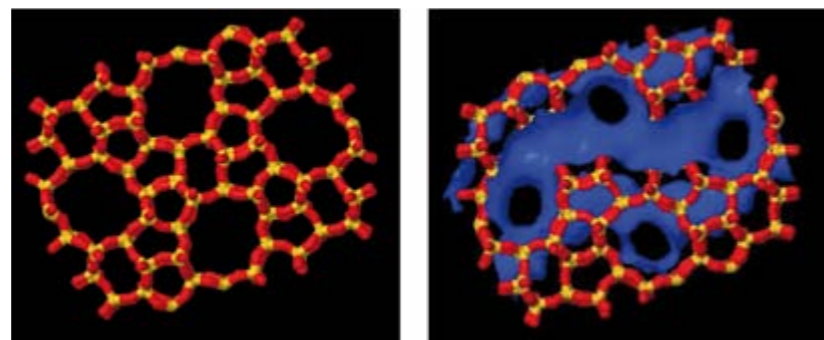
The project was funded by the Danish National Research Foundation, DTU Chemistry and Haldor Topsøe A/S

The thesis was selected as the best Ph.D. thesis at DTU in 2011.

Biomass is currently the only viable non-fossil resource for liquid hydrocarbons that can be used as an additive to conventional liquid transportation fuels. One example produced on an industrial scale is bio-ethanol through fermentation. Also, the production of commodity chemicals rather than fuels could represent an economically attractive utilization of biomass.

In this project, pathways for bio-refining based on catalysis are considered.

As with current oil refineries, the utilization of biomass will require a dedicated and flexible processing apparatus. A wide range of possible designs and concepts for bio-refineries can be imagined. The present project focuses on refineries that transform biomass into useful "platform chemicals". The term refers to compounds which have a suitable chemistry to allow multiple transformations into numerous useful products.



Lactic acid (methyl lactate) was chosen as an example of a platform molecule. Known transformations of lactic acid include dehydration, decarbonylation and reduction, which form useful products that can be further upgraded or sold directly. Lactic acid is also an additive in food and cosmetic products. A further, particularly interesting utilization of lactic acid is polymerization into polylactic acid (PLA) which has similar properties to conventional plastics such as polyethylene (PE) and polyethylene terephthalate (PET). The main advantage is that PLA is non-toxic and biodegradable. PLA has been adopted for use in surgical and pharmaceutical applications where the devices are not intended to be removed from patients. This example shows that in some cases, a bio-refined product can be a superior choice even if it does not outperform conventional products in all property aspects.

In the project, lactic acid was produced using a zeolite catalyst. Zeolites are naturally occurring microporous aluminosilicates made of tetrahedrally

coordinated silicon atoms bridged by oxygen. The organization of the framework forms pores, and channels extend throughout the entire crystal giving rise to the microporosity – and even to nanoporosity. Due to the fact that the majority of the total surface area is present within the zeolite shape, selective catalysis arises, since only molecules small enough to enter the zeolite pores will be able to reach the catalytically active site.

In the project, dealuminated zeolite Y and Sn-Beta (tin incorporated in zeolite Beta) gave near quantitative yield of methyl lactate from C3-sugars. Sn-Beta further proved applicable in the transformation of hexoses into methyl lactate. A reaction path involving retro aldol- and aldol condensations of the sugars is proposed to rationalize the results.

In this project, pathways for bio-refining based on catalysis are considered.

## CATALYTIC PRODUCTION OF BIO-DIESEL



Anders Theilgaard Madsen, Ph.D.

Full title: "Catalytic Production of Bio-diesel"

Supervisor: Rasmus Fehrmann

The project received financial support from the Danish Research and Innovation Council (RTI) under the innovation consortium "Waste-2-value"

It has become increasingly evident that humanity faces unprecedented challenges in terms of future energy resources. The most critical feedstock in the chemical industry and refineries is oil, and transportation fuels constitute the largest part of oil consumption. This means that a global shift towards renewable feedstock is necessary, and biomass is the

only renewable carbonaceous material available (apart from carbon dioxide). Its use as a base for sustainable fuels and chemicals in the future is therefore indispensable. Current EU policy mandates a share of 5.75 % energy content derived from bio-fuels, rising to 10 % in 2020.

This project focuses on one group of bio-fuels, commonly referred to as bio-diesel. The term normally refers solely to fatty acid alkyl esters, although wider definitions are sometimes seen.

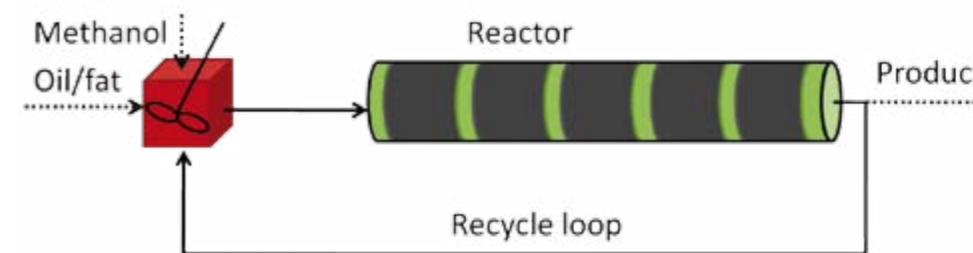
Efficient, economical and environmentally sound chemical production usually requires the aid of catalysis to run at acceptable rates. Production of bio-diesel is already growing – triggered by the EU directive and other policy initiatives – and a number of catalytic methods have been established. Two methods have been used industrially for a number of years; namely transesterification (and esterification) of fats and oils with methanol to form fatty acid methyl esters (FAME), and hydrodeoxygenation (HDO) of fats and oils to form straight-chain alkanes. Both methods are investigated here.

In the experimental part of the project, a range of acidic catalysts for FAME production were tested in a model fat mixture of methanol, lauric acid and trioctanoin. Sulphonic acid-functionalised ionic liquids showed extremely fast conversion of lauric acid to methyl laurate, and trioctanoate was converted to me-

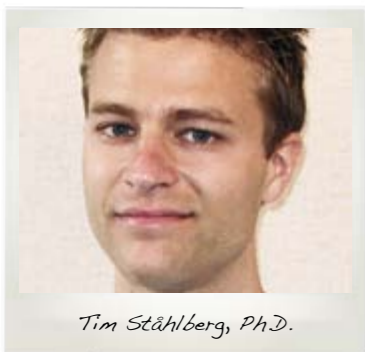
thyl octanoate within 24 hours. A catalyst based on a sulphonated carbon-matrix made by pyrolysing (or carbonising) carbohydrates, so-called sulphonated pyrolysed sucrose (SPS), was optimized further. A number of functionalised, organic bases have been tested for their activity in transesterification of trioctanoate with methanol, especially guanidines. The activity for trioctanoate conversion was promising.

As for the HDO method, reaction routes and activity in batch hydrodeoxygenation was strongly dependent on the supported noble metal catalyst and temperature used for the conversion to alkanes. Generally, platinum and palladium were the most active metals and have the highest selectivity for decarboxylation reactions.

This project focuses on one group of bio-fuels, commonly referred to as bio-diesel. The term normally refers solely to fatty acid alkyl esters, although wider definitions are sometimes seen.



## IONIC LIQUID CATALYSIS FOR BIO-REFINERIES



Tim Ståhlberg, Ph.D.

Full title: "New Catalytic Systems with Ionic Liquids as Reaction Media for the Synthesis of Renewable Chemicals"  
 Supervisor: Anders Riisager

The project was funded by DTU

Biomass is a ubiquitous renewable source of carbon that currently accounts for a small part of global chemical production. It has an annual production of up till  $10^{11}$  metric tons of which carbohydrates constitute 75%. Thus, the potential for biomass to replace fossil resources as the latter become scarcer is enormous.

While utilization of biomass in bio-refineries could be based on renewable platform chemicals identical to the current chemicals produced from crude oil, this project focuses on an alternative chemical infrastructure based on platform chemicals less common today, but readily derived from biomass. These can be, e.g. lactic acid from glucose, 5-(hydroxymethyl)furfural (HMF) from fructose (or glucose), furfural from xylose and 1,3-propanediol from glycerol.

HMF, a furan derivative formed by the triple dehydration of hexoses, may either act as a platform chemical in its own right or serve as an intermediate for production of 2,5-furandicarboxylic acid (FDA), which is believed to be a possible replacement for terephthalic acid in polyethylene terephthalate (PET), a polymer of large industrial importance.

In relation to green processes, ionic liquids – commonly defined as salts that are liquid below  $100^{\circ}\text{C}$  – are interesting alternatives to conventional molecular solvents due to their negligible vapour pressure, non-flammability and unique dissolving abilities for polar compounds and polymers. Certain ionic liquids have dissolved as much as 25 wt% of crystalline cellulose, and a few of them have proven to be highly advantageous in the production of HMF from fructose and glucose.

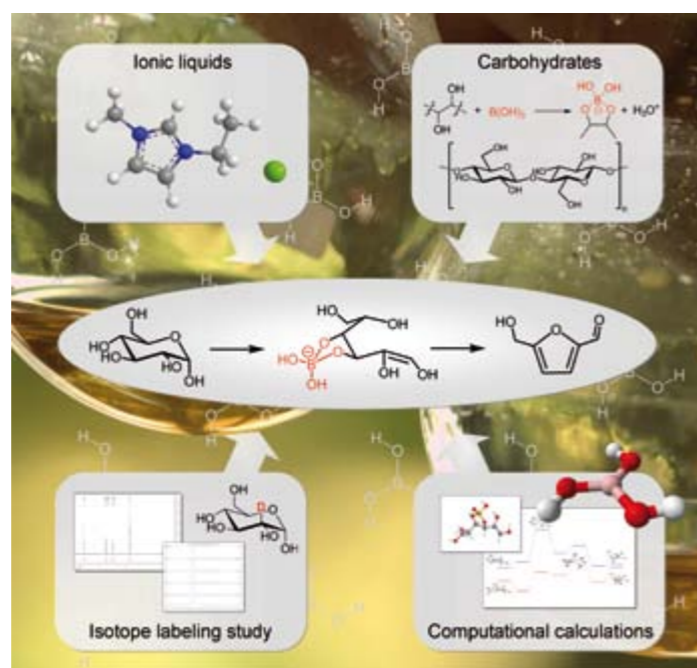
In particular, the ionic liquids [EMIm]Cl and [BMIm]Cl form HMF with high selectivity from fructose and, with the addition of an appropriate catalyst, also from glucose.

In this project new catalytic systems for the synthesis of HMF and its further oxidation to FDA in combination with ionic liquids have been developed. Feedstock has included hexose sugars as well as sucrose, and polymers of glucoselike cellulose and starch.

Enzymatic isomerisation of glucose to fructose in an ionic liquid/water system has also been demonstrated. Finally, an assessment of a process in ionic liq-

uids was made where chemistry, as well as technological and economical parameters, was taken into account. The assessment concludes that an ionic liquid-based process for HMF production from glucose is potentially viable but highly dependent on the number of recycles of the ionic liquid and the price of the feedstock.

**While utilization of biomass in bio-refineries could be based on renewable platform chemicals identical to the current chemicals produced from crude oil, this project focuses on an alternative chemical infrastructure based on platform chemicals less common today, but readily derived from biomass.**



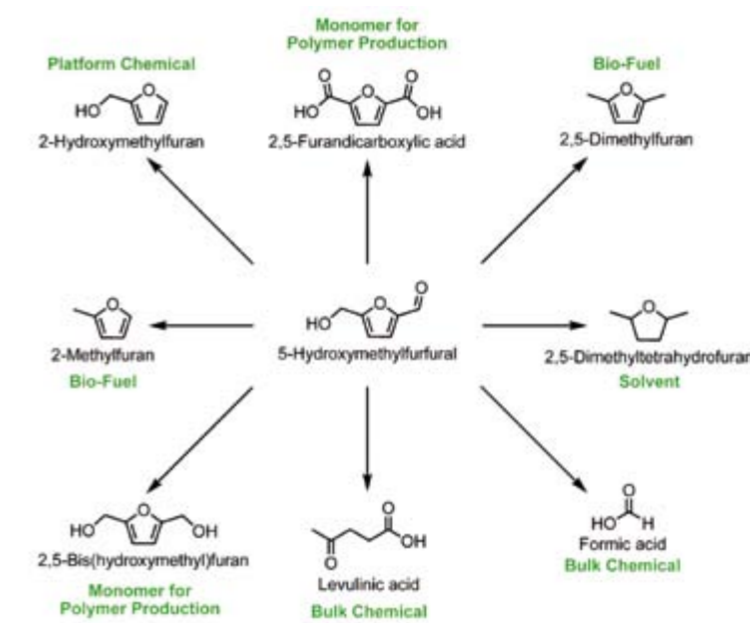
## POLYMER BUILDING BLOCKS FROM BIOMASS



Thomas Søndergaard Hansen, Ph.D.

Full title: "Catalytic Routes to Renewable Polymer Building Blocks"  
 Supervisor: Anders Riisager

The project was funded by DTU



Concerns about fossil fuel depletion and global warming have sparked a profound research effort into the development of alternative renewable and carbon neutral technologies. Despite intensive research activity, few technologies in renewable chemicals have yet been implemented on an industrial scale.

This project is focused on catalyzed bio-refining processes that may produce platform chemicals – meaning intermediate products which may be processed further into either fuels or chemicals – from biomass. The main emphasis is on building blocks for polymers, but some bio-fuel applications are also considered.

5-hydroxymethylfurfural (HMF) has been identified as a possible platform chemical for the production of numerous industrially valuable bio-based chemicals. Especially interesting are oxidized derivatives of HMF, which are suited for polymer production. HMF is derived from the consecutive dehydration of hexose sugars, a process that has been known for years. However, no industrial production methods are currently able to compete with today's petrochemicals.

In this project, three methods for production of HMF were developed.

The first method relies on the power of microwaves for efficient control of the reaction parameters in the aqueous dehydration of fructose to HMF. The second method takes advantage of the synergy between boric acid and salts for the promotion of HMF synthesis from aqueous fructose, glucose and sucrose solutions. The third method uses only salts and the inherent promoting effect of hot saline solutions on the dehydration of aqueous fructose and mixed fructose/glucose solutions.

Also, two methods for the oxidation of HMF to 2,5-diformylfuran (DFF) and 2,5-furandicarboxylic acid (FDA) respectively were developed. The first method is a modification of an existing oxidation protocol relying on CuCl and (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) radicals for the oxidation of alcohols to aldehydes. The protocol has been modified to afford excellent DFF yields and to proceed with high selectivity toward DFF in previously non-suited solvents by introducing nitrogen containing promoters (NCPs). In the second, slightly different protocol, HMF is oxidized to FDA by a combination of CuCl and tert-butyl hydroperoxide.

The project took part in the "Bio-Petrochemicals" collaboration established by DTU Chemistry, DTU Chemical and Biochemical Engineering and Novozymes A/S. In May 2010, the collaboration filed a patent application entitled "A method of producing 5-hydroxymethylfurfural". Some of the results leading to the patent application have been described in this project.

**This project is focused on catalyzed bio-refining processes that can produce platform chemicals - meaning intermediate products which may be processed further into either fuels or chemicals - from biomass. The main emphasis is on building blocks for polymers, but some bio-fuel applications are also considered.**

## ZEOLITES AS MOLECULAR SIEVE CATALYSTS



Karen Thrane Hejholt, Ph.D.

Full title: "Mesoporous Molecular Sieve Catalysts"

Supervisor: Rasmus Fehrmann

The Ph.D. project was funded by Haldor Topsøe A/S, the Danish National Research Foundation and DTU

Zeolites are porous crystalline aluminosilicates. The porous structure gives zeolites a large internal surface which makes them suitable in relation to catalysis. As the pores are tiny – they are so-called micropores – they can also act as molecular sieves which only allow certain molecules to reach the catalytically active sites. Zeolite catalysts are in wide use in the petrochemical and other industries.

In the project, new zeolite and zeolite-type materials for catalytic applications have been developed and characterized. Primarily the porosity of the zeolites was modified, and metals were added to the framework. The obtained materials were used as solid acid catalysts, as an inert matrix for stabilizing metal nanoparticles, and as an anchoring material for molecular metal oxide species.

Even though zeolites are remarkable materials in relation to catalysis, the presence of micropores may in some cases limit catalytic performance, particularly when diffusion in the micropores become significantly slower than the cat-

alytic reaction. Introduction of so-called meso-pores (2-50 nm) is suggested as a possible solution, since meso-pores can function as an auxiliary system supporting the intrinsic micropore system. Mesoporous zeolites are used in the petrochemical industry for cracking large hydrocarbons into the gasoline range.

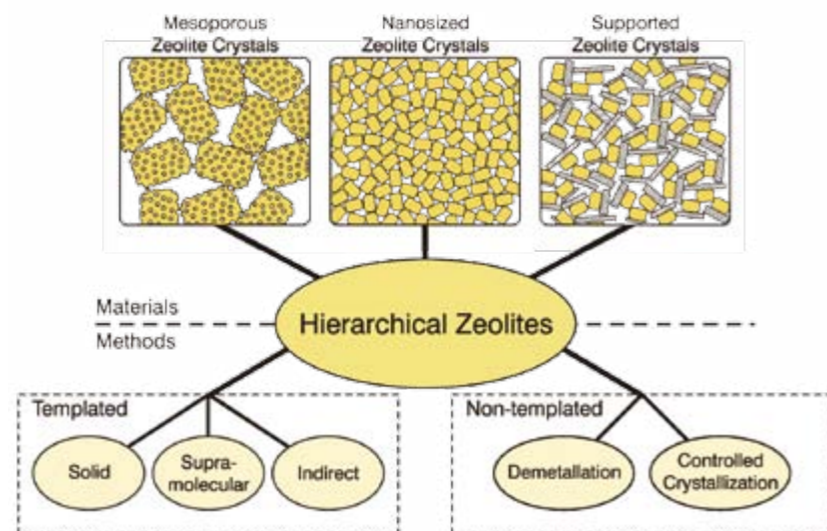
In the project, nano-sized and mesoporous zeolites were prepared to investigate the effect of inter- or intracrystalline mesopores on catalytic lifetime in the conversion of methanol to hydrocarbons. It was found that the mesoporous zeolite with intracrystalline mesopores displayed a significantly longer catalytic lifetime compared to the nano-sized zeolites and the conventional counterpart.

Zeolites can be used not only as catalysts but also as a size-selective matrix – a molecular sieve. It was shown that it is possible to encapsulate 1-2 nm diameter gold nanoparticles by silicalite-1 or ZSM-5 zeolite crystals, thereby forming a sintering-stable and substrate size-selective oxidation catalyst. Both in situ and ex situ calcination experiments indicated that the gold nanoparticles embedded in the crystals were highly stable towards sintering. The catalytic tests proved that

the embedded gold nanoparticles were active in selective aldehyde oxidation and were only accessible through the micropores.

Furthermore, preliminary work was done using mesoporous ZSM-5 zeolites as support material for anchoring molecular CoMo<sub>6</sub> species for application as potential bi-functional catalysts in simultaneous hydrodesulphurisation and hydrocracking. It was revealed that the anchoring improved activity compared to an impregnated counterpart.

**In the project, nano-sized and mesoporous zeolites were prepared to investigate the effect of inter- or intracrystalline mesopores on catalytic lifetime in the conversion of methanol to hydrocarbons.**



## HIGH TEMPERATURE PEM FUEL CELLS



David Aili, Ph.D.

Full title: "Proton Conducting Polymeric Materials for Hydrogen Based Electrochemical Energy Conversion Technologies"

Supervisor: Niels J. Bjerrum

The project was funded by DTU

Polymer Electrolyte Membrane (PEM) fuel cells have been commercially available for a number of years but have issues around their durability which make them feasible only for some niche applications. New HT-PEM (High Temperature PEM) cells are able to operate at temperatures ranging from 150 till 200 degrees C, which makes them interesting for applications relevant on a much broader scale. Ultimately, it will be possible to have individual dwelling houses equipped with its own micro heat and power plant fuelled by natural gas or biogas.

This project is focused at phosphoric acid doped PBI (poly[2,2'(m-phenylene)-5,5'-bibenzimidazole] polymer fuel cell materials. By using phosphoric acid (H<sub>3</sub>PO<sub>4</sub>) as carrier medium instead of water – used in traditional PEM cells – temperatures above 100 degrees C can be tolerated. Phosphoric acid is stable at temperatures well above 200 degrees C. Secondly, PBI, as opposed to many other polymers, sustains temperatures up till

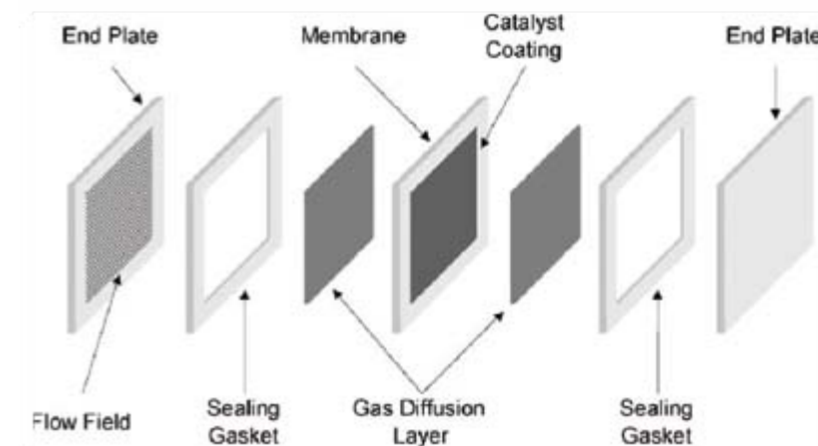
200 degrees C without deformation or loss of internal strength. The resulting phosphoric acid doped PBI membrane achieves a high level of conductivity.

The approaches in this project mainly include chemical modification of conventional PFSA materials with phosphoric acid or inorganic proton conducting particles such as zirconium phosphate or boron phosphate. A novel methodology for the preparation of homogeneous Nafion (DuPont)/PBI polymer blends was also developed. The miscibility behaviour between Nafion and PBI was investigated using different Nafion counter cations. It was demonstrated that NH<sub>4</sub><sup>+</sup> could be used as compatibilizer in the Nafion/PBI system to give homogenous solution cast blend membranes covering the entire composition range. The strong intermolecular coulomb interactions gave the polymer blends improved mechanical characteristics.

High content of phosphoric acid is the key to achieve the desired high proton conductivity of the membrane in a HT-PEM cell. However, the mechanical strength of PBI membranes is strongly correlated to its phosphoric acid con-

tent due to the strong plasticising effect of the dopant. Consequently, the doping level of the membrane has to be a compromise between sufficient mechanical strength for the membrane electrode assemblies' preparation and maximized proton conductivity. In this project, PBI membranes were cross-linked, either by post-treatment with divinylsulfone or by thermal curing, in order to improve their mechanical characteristics at high acid doping levels. In addition, the cross-linked membranes also exhibited radical-oxidative stability which should improve their long term durability. The feasibility of the cross-linked membranes was demonstrated in fuel cell tests at temperatures up to 180 degrees C.

**This project focuses on phosphoric acid doped PBI (poly[2,2'(m-phenylene)-5,5'-bibenzimidazole] polymer fuel cell materials.**



## WATER ELECTROLYSIS AT ELEVATED TEMPERATURES



Full title: "New Construction and Catalyst Support Materials for Water Electrolysis at Elevated Temperatures"  
Supervisor: Niels J. Bjerrum

The project was financially supported by the Center for renewable hydrogen cycling (HyCycle), Denmark, and the WELTEMP project under the EU Seventh Framework Programme

Hydrogen has been known as a fuel ever since its discovery. Since the only combustion product is water, hydrogen is one of the cleanest fuels available, which is one of the main reasons why hydrogen has been suggested as a substitute for fossil fuels. However, significant amounts of elemental hydrogen are not found on the Earth's surface. So rather than an energy source, hydrogen should be seen as an energy carrier, which means that its generation is as important as its transportation and consumption in terms of efficiency and performance.

This project looks at production of hydrogen through proton exchange membrane (PEM) electrolysis of steam at elevated temperatures. This method has several advantages over low temperature electrolysis, but places increased demands on the dimensional and chemical stability of components against corrosion. Materials used in low temperature PEM electrolyzers cannot be used in systems operating above 100°C and new

candidates need to be found.

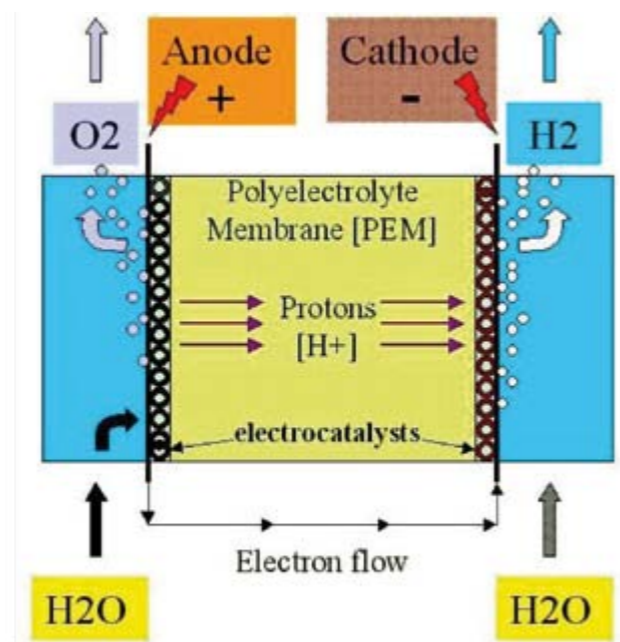
The project is focused on developing bipolar plates, gas diffusion layers (GDL) and catalyst support materials for the anode compartment of PEM electrolyzers.

First, different types of commercially available products were tested as possible metallic bipolar plates and construction materials for high temperature PEM electrolysis – including stainless steel and nickel-based alloys, as well as titanium and tantalum. Corrosion resistance was measured under relevant simulated conditions. It was found that stainless steels were the least resistant to corrosion under strong anodic polarization, whereas nickel-based alloys showed higher corrosion resistance. Tantalum-coated stainless steel showed outstanding resistance to corrosion in selected media, while passivation of titanium was weak, and the highest rate of corrosion among all tested materials was observed for titanium at 120°C.

Further, a novel SiC-Si compound was investigated as a potential catalyst material. Active iridium oxide was deposited

on the SiC-Si in-situ by the Adams fusion synthesis. The prepared catalysts were electrochemically characterized by cyclic voltammetry experiments at 25, 80, 120 and 150 degrees C. The investigations showed that even a support material with poor electrical conductivity contributes beneficially to the electrocatalyst's active surface area, increasing its utilization. Results demonstrated potential perspectives of using low conductive ceramics as a catalyst support which means that further research in this field will be of high interest.

**This project looks at production of hydrogen through proton exchange membrane (PEM) electrolysis of steam at elevated temperatures.**



## NANO-PARTICLES IN BIO-MOLECULAR ELECTROCHEMISTRY



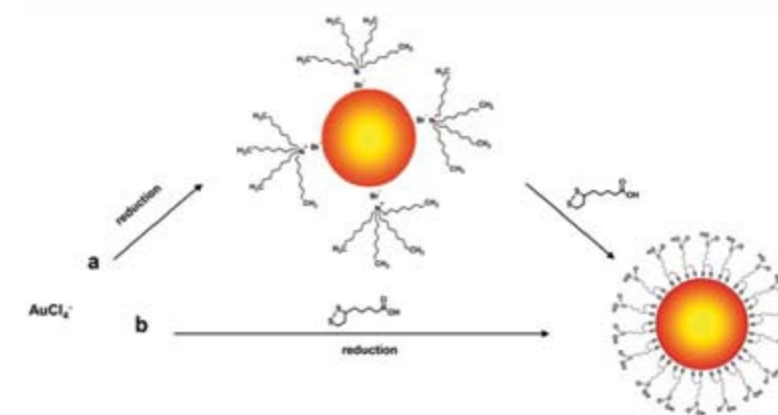
Full title: "Metallic Nanoparticles and Indium Arsenide in Molecular and Biomolecular Electrochemistry"  
Supervisors: Jens Ulstrup and Qijin Chi

The project has received financial support from the Lundbeck Foundation and from Copenhagen Graduate School for Nanoscience and Nanotechnology

The main focus of this bio-nano-technology project is the fabrication and study of hybrid structures which combine the properties of biological macromolecules with those of inorganic nano-scale structures. The project has exploited two different approaches to the study of such structures.

The first approach is to combine molecular scale gold nano-particles with proteins containing metal atoms (metalloproteins) into "hybrid" structures. The second approach deals with the design and construction of chemical and biochemical detection devices based on semiconductor nano-wires.

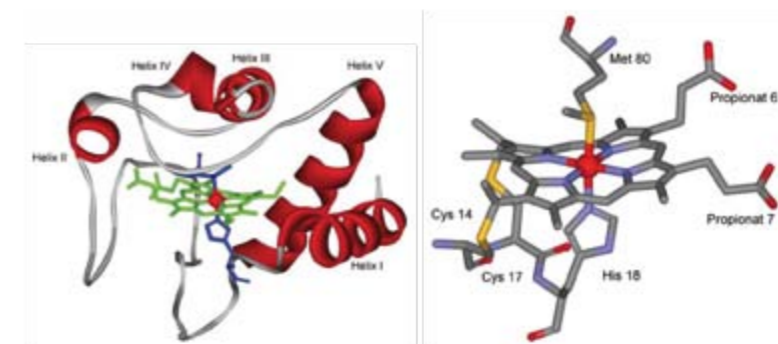
The redox protein heme protein (horse heart) cytochrome c and the blue copper protein (*Pseudomonas aeruginosa*) azurin were the metalloproteins used in the "hybrid" structure approach. Gold nano-particles of a size comparable with that of the two proteins were synthesized and coated by molecular layers chosen specifically for the immobilization of



the two proteins. As something really novel, water-soluble 1:1 stoichiometric nano-particle – cytochrome c "hybrid" structures could be prepared and characterized in solution by UV spectroscopy. The interfacial electrochemical electron transfer kinetics of the "hybrid" structures were also studied using atomically flat single-crystal Au(111)-electrodes. An enhancement of more than an order of magnitude was observed for both the nanoparticle-cytochrome c and the nano-particle-azurin hybrid structures compared to the analogous reference systems without the gold nano-particles. Indium arsenide nano-wires were used in the second approach. Indium arsenide was characterized electrochemically as an electrode material using macro-scale single-crystal electrodes. Building of densely packed self-assembled monolayers of thiol based molecules on indium arsenide was carried out using cysteine as a probe molecule. The results were verified by electrochemical reductive desorption. In order to fabricate small

devices based on field effect transistor design, a UV mask that allowed for the contact of individual nano-wires was designed, and successful contact was verified by measuring the current-voltage characteristics. The indium arsenide based nano-wires will be combined with metalloproteins such as cytochrome c and azurin, as well as other metalloproteins and metalloenzymes into new hybrid types in future work.

**The main focus of this bio-nano-technology project is the fabrication and study of hybrid structures which combine the properties of biological macromolecules with those of inorganic nano-scale structures.**



## FERREDOXINS CONTAINING HETEROMETALLIC CLUSTERS



Full title: "Ferredoxins Containing Heterometallic Clusters – Synthesis and Characterization"

Supervisor: Hans E. M. Christensen

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



Metal containing proteins – metalloproteins – account for almost half of all naturally occurring proteins. They are involved in a variety of important biological processes. Metalloprotein design and engineering offers the opportunity to improve the existing functional properties of natural metalloproteins or to impart new ones to them.

The project focuses on one group of metalloproteins, iron-sulfur proteins. Widespread in nature, small in size with simple and structurally similar metal centres, but functionally very diverse, iron-sulfur proteins are ideal templates for metalloprotein design.

A wild type (WT) iron-sulfur protein, *Pyrococcus furiosus* ferredoxin (*Pf. Fd*), and its D14C variant were used as starting materials for the synthesis of two sets of artificial ferredoxins. The first set contains a  $[\text{ZnFe}_3\text{S}_4]$  cluster and the second a  $[\text{AgFe}_3\text{S}_4]$  cluster.

The two starting materials as well as the two sets of artificial ferredoxins were characterized, a multidisciplinary ap-

proach being used for the latter. Mass spectrometric data showed that the proteins were synthesized in a form containing the reduced cluster  $[\text{ZnFe}_3\text{S}_4]^+$  and that a good separation was achieved during the purification procedure. Both ferredoxins containing  $[\text{ZnFe}_3\text{S}_4]$  clusters were electrochemically characterized and the formal potentials determined for the  $[\text{ZnFe}_3\text{S}_4]$  cluster in WT *Pf. Fd* and in the D14C *Pf. Fd* are -206 mV and -254 mV vs. SHE, respectively. EPR spectroscopy has confirmed the presence of the  $[\text{ZnFe}_3\text{S}_4]^+$  cluster in both WT and D14C *Pf. Fd*.

The  $[\text{AgFe}_3\text{S}_4]$  cluster was synthesized for the first time inside a protein. The WT *Pf. Fd* and its D14C variant containing the  $[\text{AgFe}_3\text{S}_4]$  cluster were synthesized, chromatographically purified and characterized using UV spectrophotometry, intact metalloprotein mass spectrometric analysis, cyclic voltammetry and EPR spectroscopy. Mass spectrometric analysis of the purified samples showed that the proteins are synthesized in a form containing the reduced clus-

ter  $[\text{AgFe}_3\text{S}_4]^+$ . Stability studies of these novel ferredoxins have shown that they are much more inert towards oxygen exposure than other ferredoxins containing heterometallic clusters, especially the D14C *Pf. Fd*.

**The project focuses on one group of metalloproteins, iron-sulfur proteins. Widespread in nature, small in size with simple and structurally similar metal centres, but functionally very diverse, iron-sulfur proteins are ideal templates for metalloprotein design.**

## STRONTIUM MALONATE FOR OSTEOPOROSIS TREATMENT



Full title: "Effects of strontium malonate [NB S101] on the compositional, structural and biomechanical properties of calcified tissues in rats and dogs"

Supervisor: Jens E. T. Andersen

The project was funded by DTU

Strontium is known to have a positive effect on bone by concomitantly increasing bone formation and decreasing bone resorption, thereby providing a sustained skeletal benefit. Strontium ranelate (SrR) has been shown to reduce the risk of both vertebral and non-vertebral fractures in patients with postmenopausal osteoporosis. Strontium malonate (SrM) is currently being developed as a novel pharmaceutical for the treatment and prevention of osteoporosis.

In this project, SrM was tested in three animal studies: a 4-week study in dogs, a 26-week study in rats and a 52-week study in dogs. Femurs, vertebrae, skull-caps and teeth from the treated animals

**In this project, SrM was tested in three animal studies: a 4-week study in dogs, a 26-week study in rats and a 52-week study in dogs**

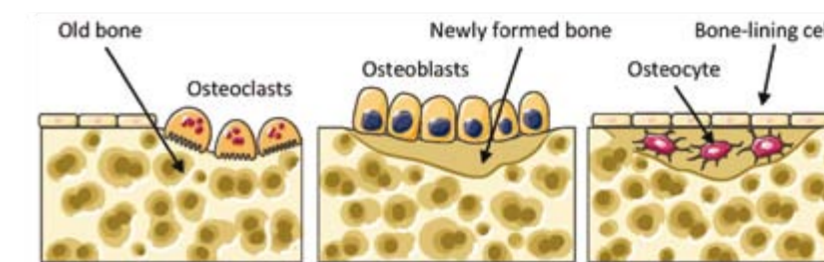
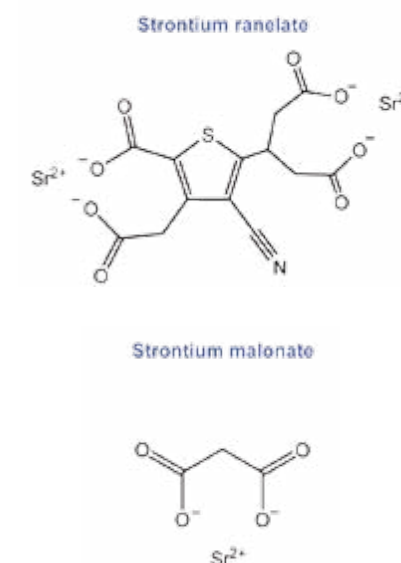
were examined for treatment-related changes in concentrations of strontium (Sr), calcium (Ca), magnesium (Mg) and phosphorus (P) using inductively coupled mass spectrometry (ICP-MS). Bone mineral density (BMD) was determined using dual energy X-ray absorptiometry (DEXA), and the biomechanical properties of the bones were assessed using bending and compression tests.

Treatment with SrM resulted in a dose-dependent increase in Sr content in all analysed tissues. The highest concentrations were found in rat incisor, where the Sr level in the highest dose group corresponded to a 450-fold increase compared with placebo. A strong correlation between serum Sr and incisor Sr was also observed. In dogs, the highest concentrations of Sr were found in skullcap after 52 weeks of treatment, with an average in the highest dose group corresponding to a 350-fold increase compared to placebo. The trials suggested that the initial incorporation of Sr proceeded by a faster mechanism than the long-term incorporation. In both rats and dogs, long-term treatment was associated with decreased concentrations of Ca and P in the mineralised tissues.

A simple stoichiometric model was proposed for incorporation of Sr into the hydroxyapatite (HAp) matrix of bones and teeth. The model showed excellent agreement with the analytical data and

demonstrated that at least a part of the perceived loss of Ca and P was caused by the increased weight of HAp following adsorption and incorporation of Sr.

Measurements of BMD using DEXA was found to be heavily influenced by the presence of Sr in the mineralised matrix, and a linear correction of 9 per cent was determined for a 1:10 molar ratio of Sr:HAp. The corrected BMD was found to be strongly correlated with bone strength, indicating that the increase in corrected BMD following SrM treatment was associated with concomitant increase of bone strength.



**Figure 2.4** In bone remodelling, osteoblast activity is coupled to prior osteoclast activity. After bone resorption by osteoclasts, osteoblasts start laying down new bone. Some osteoclasts remain inside the newly formed bone and are converted to osteocytes, which are connected to each other. The resorption process takes place within a matter of weeks, while bone formation takes several months. Unless there is remodelling imbalance, net changes in the amount of bone are minimal. Figures were produced using Servier Medical Art [78].

## ROBUST HIGH TEMPERATURE OXYGEN SENSOR ELECTRODES



Anders Lund, Ph.D.

Full title: "Robust High Temperature Oxygen Sensor Electrodes"

Supervisor: Steen Skaarup

The project was funded by the Programme Commission on Sustainable Energy and Environment, The Danish Council for Strategic Research

Oxygen sensors are used to monitor the oxygen partial pressure in for example industrial furnaces, boilers, gas turbines and in food packaging. The solid state oxygen gas sensor was introduced in the 1960's and is widely applied in combustion engines to measure the air-to-fuel ratio and minimize the emission of pollutants. They typically operate at temperatures above 500°C. The main components are a piece of oxide ion conducting ceramic material and a set of electrodes which are catalytically active towards oxygen reduction/oxidation. Platinum is the most widely used electrode material, but it is expensive and the platinum electrode may, under certain conditions, suffer from poisoning, which is detrimental for an oxygen sensor.

This project evaluates various materials as candidates for robust oxygen sensor electrodes. Three types of porous platinum-based electrodes and one porous electrode based on perovskite-structured strontium and vanadium-doped lanthanum chromium oxide (LSCV) were in-

vestigated. The porous electrodes were applied on yttrium-stabilised zirconium oxide (YSZ) substrates in collaboration with the company PBI-Dansensor.

At an oxygen partial pressure of 0.2 bar, the response time of the sensor electrode was determined by oxygen reaction kinetics. At oxygen partial pressures below 10-6 bar at 700°C, the mass transport processes dominated the response time. The response time increased with decreasing oxygen partial pressure and inlet gas flow rate.

A series of porous platinum electrodes were impregnated with ionically conducting gadolinium-doped cerium oxide (CGO). The addition of CGO was found to decrease the polarisation resistance of the oxygen reaction by up to an order of magnitude compared with a single phase platinum electrode, by increasing the effective triple phase boundary (TPB) length.

The response time of a composite LSCV/YSZ electrode was around an order

of magnitude longer compared with that of the platinum-based electrodes. Even though the response time is longer for a composite LSCV/YSZ electrode it may be applied as an electrode for oxygen sensors used in industrial processes. Furthermore, the platinum-based cermet and the composite LSCV/YSZ electrodes have a longer effective TPB length and are therefore more robust compared with a single phase platinum electrode. The increase in the effective TPB length did not have any significant effect on the response time at low oxygen partial pressures, where the response becomes critical.

**This project evaluates various materials as candidates for robust oxygen sensor electrodes.**

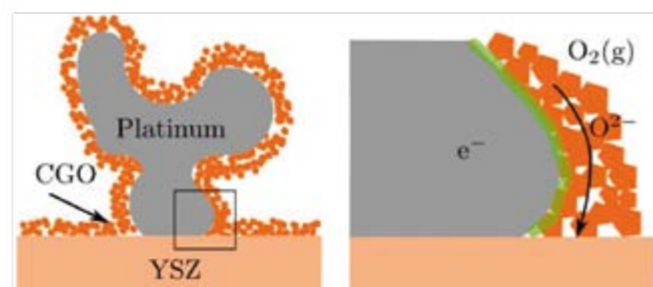


Figure 2.6: A cross section of an impregnated electrode for which a layer of CGO is formed on the platinum surface. CGO grains may facilitate transport of oxide ions to the electrolyte. The active area is highlighted with green colour.

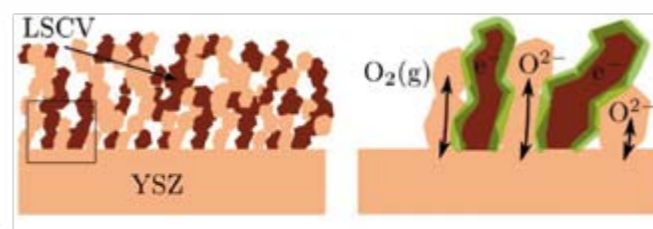


Figure 2.8: A cross section of the LSCV/YSZ composite electrode. YSZ grains facilitate transport of oxide ions. The active area is highlighted with green colour.

## ENZYMES INVOLVED IN NUCLEOTIDE METABOLISM AND IRON-SULFUR PROTEINS



Monika Nohr Lovgreen, Ph.D.

Full title: "Structure and Characterization of Proteins and Enzymes Involved in Nucleotide Metabolism and Iron-Sulphur Proteins"

Supervisor: Pernille Harris

The project was funded by DTU

Evolution is constantly on-going and studying evolution is of interest to provide substantial, fundamental knowledge on how organisms function and evolve. This project studies an intermediate step in a reaction which is connected to the evolution of a fundamental life process, namely base pairing in DNA.

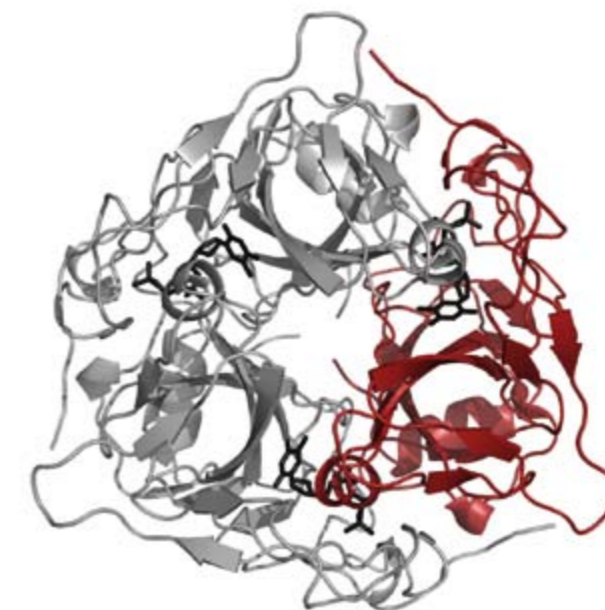
While the study should be seen as a small contribution to improving our understanding of evolution, practical applications in the future cannot be excluded – for instance the project included studies of the bi-functional enzyme dCTP deaminase-dUTPase (DCD-DUT) from *Mycobacterium tuberculosis*. The infectious disease tuberculosis, caused by the bacteria, killed an estimated 1.7 million people in 2009, and enzymes involved in deoxyribonucleotide synthesis provide potential drug targets. Structures and inhibition mechanisms of these enzymes are important in the design of specific inhibitors that leave the human host unaffected.

Enzymes are proteins that catalyze biochemical reactions. They are also of vital

importance, as they catalyze the majority of reactions involved in metabolism and are also involved in transcription, DNA replication and DNA repair. The three-dimensional structure of an enzyme is related to its function, and structure determination is thus a valuable method for discovering shared features among members of molecular families.

This project has determined three-dimensional enzyme structures by use of X-ray crystallography. Before the method can be applied, successful protein crystallization is required. This can be an immense task involving numerous crystallization conditions, and meticulous bookkeeping of the results is important. A database programme – MyCrystals – was developed for the task. The program is available online.

Other enzymes in focus in this work are metalloproteins. Ferredoxin from *Pyrococcus furiosus* (Pf) is hyperthermostable and contains a single  $[\text{Fe}_4\text{S}_4]$  cluster with incomplete cysteinyl coordination. Studies of the D14C variant ferredoxin, in which the cluster coordinating



aspartate has been changed to cysteine, may contribute to the understanding of cysteine ligation and its effects on protein function and stability.

Conversion of  $[\text{Fe}_4\text{S}_4]$  to  $[\text{Fe}_3\text{S}_4]$  is a preceding step in the formation of heterometallic clusters, in which an externally imposed metal ion is part of the cluster  $[\text{MFe}_3\text{S}_4]$ . Formation of novel metalloproteins presents an opportunity to engineer new or improve existing functional properties with relevance for a wide range of applications in the pharmaceutical and biotechnological industries. In the project expression and purification of D14C  $[\text{Fe}_4\text{S}_4]$  Pf Fd as well as cluster conversion to  $[\text{Fe}_3\text{S}_4]$  and subsequent purification was obtained.

**This project has determined 3-dimensional enzyme structures by use of X-ray crystallography.**

# Master Theses 2011

## Kasper Torp Madsen

"Towards a Fluorinated Cyclooctyne for Click Chemistry"

## Louise Kjærulff

"Natural Product Chemistry of Marine Bacteria"

## Mathilde Søndergaard

"Synthesis of New Peptide Thioester Linkers based on Backbone Amide Activation"

## Jesper Jonasson Madsen

"Stochastic Computational Modelling of Heterogeneous Biocatalysis"

## Pernille Mansgaard Simonsen

"Solid-phase Synthesis of Anti-cancer Peptides"

## Anja Stausgaard

"Improved TaqMan Assay for Detection of Neisseria Gonorrhoeae"

## Yavuz Köse

"Preparation and Characterization of Catalysts for Proton Exchange Membrane Fuel Cells"

## Annemette Hindhede Jensen

"Ceramic Coatings of Materials for Water Electrolysis"

## Osman Görmez

"Analysis of Dextran-HMCV1 Conjugates with Respect to Degree of Labelling"

## Thomas Adam Gade Jensen

"Inorganic Proton Conductors for Fuel Cells and Electrolysis"

## Jerrick Jørgen Mielby

"Production of Nitriles by Selective Oxidation and Ammoxidation Catalysis"

## Christian Engelbrekt

"Formation Mechanisms and New Applications of Green Metallic Nanostructures"

## Teis Lübcke

"Investigation of the Interaction between Metallic Ions and Vesicles with Tentative Implications to Alzheimer's Disease"

## Elena Fernandez Laborda

"Possible Analytic Methods to Determine Physical, Chemical and Biochemical Parameters to Evaluate the Effect of Dye Label"

## Stine Møller Hansen

"Synthesis of Amphiphilic Cyclic Peptides"

## Stig Helmer Jensen

"Ensemble Based Virtual Screening in Nicotinic Acetylcholine Receptor Homology Models"

## Mette Terp Petersen

"Ruthenium-catalyzed Tandem Reactions via Ring-closing Metathesis and Isomerization of Double Bonds"

## Christian Kistrup Hansen

"Raman Spectroscopy for Food Analysis"

## Niels Theis Bendtsen

"Development of New Catalysts and Support Materials for Steam Electrolysis"

## Carsten Brorson Prag

"Development of Oxygen Electrode Catalyst for Middle Temperature Steam Electrolyzer"

## James Atwoki Mugabi

"Optimization of Chemical Vapor Deposition of Tantalum"

## Remi Jacob Thomsen Mikkelsen

"Synthesis of Doxorubicin Derivatives on Photolabile Solid Support"

## Thomas Flagstad

"A Bull-couple-pair Strategy for the Synthesis of Structurally Diverse Small Molecules using Multi-component and Cyclisation Reactions"

## Casper Lykke Hansen

"Synthesis of Tetrahydro- $\beta$ -Carbolines via a Metal-catalyzed Isomerization/N-alkylaluminum Cyclization Sequence"

## Helene Kolding

"Flue Gas Cleaning by Ionic Liquids"

## Xintai Wang

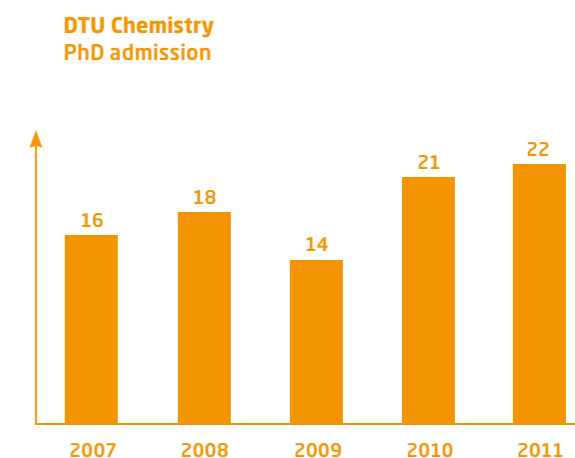
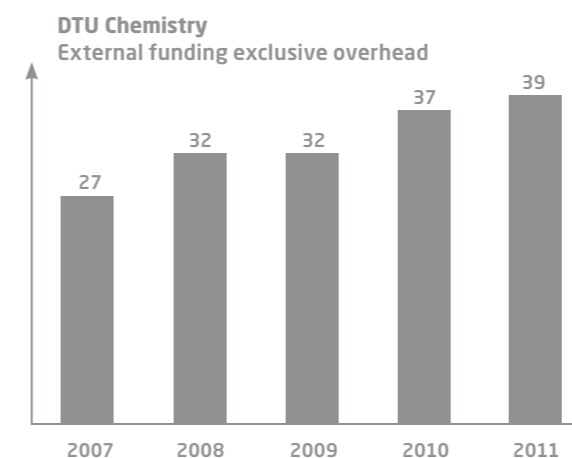
"Assembly and Electronics of Ferrocene based Molecules"

# Funding 2011

DTU Chemistry's position as a leading research institute was solidly maintained in 2011.

During the year our external funding has increased to more than 37 million DKK (exclusive overhead) and the startup of new Ph.D. projects was 22. Both figures represent an upward trend.

Also within education a high level of activity was maintained, a total of 24 students completed their bachelor degree (B.Sc.) and 26 students completed their Master degree (M.Sc.) at DTU Chemistry.



DTU Chemistry staff and external participants at the Department's Ph.D. Symposium, November 2011 at Rungstedgaard.

# Acknowledgement

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

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

DTU Chemistry has wide cooperation with industry. 2011 saw a number of new projects with Danish and international industry initiated. Among the department's industry partners are:

Lundbeck A/S

NovoNordisk A/S

Leo Pharma A/S

Arla

QuantiBact A/S

CP Kelco A/S

Vattenfall A/S

Danish Power System ApS

Amminex A/S

Daka a.m.b.a.

Danisco

Dong Energy A/S

Dinex

Eastman Chemical Company

Grundfos A/S

Haldor Topsøe A/S

Wacker Chemie

LAB S.A.

Novozymes A/S

OK a.m.b.a.

Arrayjet

PlantProbes

Teknologisk Institut

Maersk Oil

Ferring

Veloxis

Clauson-Kaas



# Support Units

Innovating research, teaching, communication and consulting require the support of professional services. DTU Chemistry's support units consist of Workshop, Glassblower, IT, Communication, External Funding, Reception, Administration, Laboratory Technicians.

They are all strong partners for our research teams, teachers and students supporting them throughout all phases of their work from education to research projects and innovation.





# Highlights

## “Magic chemistry can save the world”

Life on Earth could hardly be sustained in the years to come, had it not been for the discovery of organic catalysis based on so called transition metals, according to Nobel Laureate (2010) Ei-ichi Negishi of Purdue University, USA.

DTU Chemistry was proud to host a guest lecture by Professor Negishi at August 29th 2011. He has contributed to a set of methods that facilitate synthesis of a wide range of useful chemicals in medicine, agriculture and electronics. More specifically, the applications include pharmaceutical antibiotics that work on drug resistant bacteria, agricultural chemicals that protect crops from fungi, and electronic light-emitting diodes used in the production of extremely thin monitors.

Still, according to the Nobel Laureate, only a fraction of the perspectives inherent in the field have been exploited today:

“We are looking at a world subject to shortages in both food supply and energy supply. All projections point to a worsening of these problems. We can only meet these challenges by improving our ability to recycle. To that end making use of efficient catalysts for breaking down and assembling organic compounds will be absolutely essential.”

The specific technique mentioned in the Nobel Prize committee’s motivation regarding Ei-ichi Negishi is palladium-catalyzed crosscoupling. However, he remains fascinated by the full range of transition metals:

“We already know of many reactions in traditional chemistry which can be easily reversed. For instance sulphur can easily be oxidized to sulphur oxide and sulphur oxide can be easily reduced to sulphur. However, you need to change the regime from one of oxidation to one of reduction in order to reverse the reaction. With transition metal catalysis you can reverse your reaction without changing the regime!”

“I can’t find a better word than “magic” to describe this!”



### Professorial Appointment to Rasmus Fehrmann

On September 1st 2011, Rasmus Fehrmann was appointed Professor in Ionic Liquids. The appointment is a natural result of his long career at DTU. Since achieving his Masters title from the university in 1973, Rasmus Fehrmann has been at DTU Chemistry, only interrupted by short periods as a visiting professor abroad.

The appointment also marks an enhanced focus at DTU on ionic liquids. As shown by Rasmus Fehrmann and his colleagues, ionic liquids have a large potential to act as alternative solvents which are less environmentally harmful compared with many traditional industrial solvents. Unlike practically all other solvents, ionic liquids have the significant advantage that they are unable to vaporize. Even if heated they remain unvaporized and ready to be used again and again.

The research in ionic liquids at DTU Chemistry has been exceptionally rapid over the last decade. No less than six patents have been filed, all of them with Rasmus Fehrmann’s participation.

### Extraordinary Ph.D. Thesis on Catalysis Honoured Twice

A Ph.D. Thesis on “Conversion of Oxygenates over Zeolite Catalyst” by Martin Spangsberg Holm of DTU Chemistry received two prestigious awards in 2011. It was also selected by EFCATS, the European Federation of Catalysis Societies, covering 25 European countries, as the best Ph.D. Thesis during the latest two years. And DTU also selected it as the best thesis in 2011. The results of Martin Spangsberg Holm’s work have been published in *Science*, in *Journal of American Chemical Society* and in various scientific journals on catalysis. Further, a patent has been filed for. The project was supervised by Professor Rasmus Fehrmann. Martin Spangsberg Holm today works at Haldor Topsøe A/S.

### Award for Student of Ionic Liquids

Masters student Helene Kolding of DTU Chemistry was one of the recipients in 2011 of donations from the Oticon Foundation. The foundation gives 20 donations annually for Masters students in the technical and natural sciences at Danish universities.

In her Masters thesis, Helene Kolding is investigating carbon dioxide absorption in ionic liquids. DTU Chemistry has a strong engagement in this field, which may result in a completely novel approach to the removal of carbon dioxide at coal fired power plants.

The thesis is co-supervised by Professor D. Rogers, University of Alabama, USA. The DKK 100,000 donation from Oticon Foundation allowed Helene Kolding to include a stay as visiting student with Professor Roger’s group.



### Molecular Movie Scientist goes West

Under fierce competition Thomas Scheby Kuhlman, Ph.D. student at DTU Chemistry, has won a so called “EliteForsk” (Excellence in Science) scholarship from the Ministry of Science. The 300,000 DKK grant allowed him to include a stay as visiting researcher at Stanford University in his project. The stay was associated with the Linac Coherent Light Source (LCLS), operated by University of California. The LCLS, inaugurated in 2010, is among a few international facilities to have opened a range of exciting opportunities within Thomas Scheby Kuhlman’s field of interest which is femto-second chemistry (one femtosecond is 10<sup>-15</sup> second).

While a chemical textbook equation will traditionally show reactant(s) on the left hand side and end product(s) to the right, sub-reactions in-between are left to the readers’ imagination. However, even simple reactions often involve a set of sub-reactions occurring at the femtosecond time scale and so complex that they are not fully understood and it would, if at all possible, take vast amounts of modelling and computer calculations to describe them. But with the LCLS and similar facilities it will, for the first time, be possible to make so called Molecular Movies that show the reactions as they occur.

### Olympic Spirit at the Department

The cream of chemistry talent at Danish high schools gathered at DTU Chemistry for three days in spring 2011. Competing for the honour of representing Denmark at the international Chemistry Olympics, 14 young “athletes” were challenged to solve a series of both theoretical and practical exercises.

Denmark took part in the international event for the 30th time in 2011, and hold proud traditions with four gold medals, 16 silver medals and 44 bronze medals. It is a long-standing tradition for DTU Chemistry to take part in the selection process.

### Turning on the Charm

The annual Open House event at DTU, held on 3 March in 2011, attracted no less than 1,600 visitors, and DTU Chemistry was dressed for the occasion. Wearing white “Chemistry and Technology” coats, the department’s students were keen to address potential students. Several staff members also took part in practical demonstrations of the power of chemistry.

### Chemistry as seen by DYNAMO Magazine

The international year of chemistry prompted a special issue of DTU’s magazine “Dynamo”.

Featuring articles on a range of topics from NMR spectroscopy, X-ray crystallography and nanochemistry to the production of novel polymers by bio-refining, the issue brought the work at DTU Chemistry to the attention of a broader audience. Further, the issue carried a comprehensive interview with Chemistry Nobel laureate (2010), Professor Ei-ichi Negishi on the role of chemistry in the world today.

### Students’ Initiatives Awarded

Masters student Andreas Hougaard Laustsen, DTU Chemistry, not only achieves high grades in exams, he is also strongly engaged in outreach activities that bring chemistry to broader attention.

These merits were honoured by McKinsey & Company. The international consultants granted Andreas Hougaard Laustsen “The McKinsey Award 2011”. Each year the DKK 10,000 award is given to five DTU students who have shown exceptional analytical skills, initiative and leadership. Both Andreas Hougaard Laustsen and Lasse B. Olsen also received the Carlsberg Mindelegat Scholarship. They were each granted 75,000 DKK to their master-project in chemistry.

### Outreach at National TV

In 2011 the Danish national TV channel, DR2, initiated a series of science shows under the title “The Danes’ Academy”. A special programme, dedicated to the international year of chemistry, was featured on November 29th 2011.

No less than three members of DTU Chemistry’s faculty starred in the programme, which lasted two hours in total.

Professor Rasmus Fehrmann lectured on the challenges and possibilities inherent in transitioning from fossil fuels to bio-fuels at power plants. Associate Professor Pernille Harris showed how X-ray techniques can unravel the motion of atoms in enzyme processes relevant to a range of applications from the production of detergents to drug discovery. Finally, Associate Professor Christian Adam Olsen spoke on potential future drugs that may either inhibit or raise the activity of selected enzymes in the body as a novel treatment for a range of diseases.



# Highlights

## Power Chemistry

Chemists from three DTU departments joined forces to celebrate the international year of chemistry through "Chemistry Open House". Besides of course DTU Chemistry, also DTU Chemical Engineering and DTU Systems Biology contributed to present the full range of chemistry applications: pills to cure your headache, insulin for treatment of diabetes, production of beer, food additives, enzymes for washing powder, lotions for baby skin, concrete for giant bridges, oil recovery. In other words, the event brought the role of chemistry in modern society to the attention of the general public.

## Ph.D.'s Reach Out - on Video

The 2011 version of DTU Chemistry's Ph. D. symposium was added extra spice as the departments' Ph. D. students presented their projects in 90 second video clips. The format urged the Ph. D. students to grasp the essence of their projects much like they would need to if they were interviewed for television. The clips were also made available at YouTube. Initiated in 2010, the Ph. D. symposium is an annual event where industry and other stakeholders are given the opportunity to meet the departments' researchers and learn how projects are making progress. The 2011 event was held at Rungstedgaard conference centre at 15 November. The video presentations are available at the YouTube section at [www.dtu.dk](http://www.dtu.dk)

## Visual Chemistry & Technology Appetizer

All educations at DTU are to be presented by a short film, and Chemistry & Technology was chosen for the debut. The film is targeted at a young audience, i.e. future students. The film can be found at [www.kemi.dtu.dk](http://www.kemi.dtu.dk)

## Interacting with High Schools

Each year hundreds of students from high schools and similar institutions visit DTU Chemistry. The program will always include lectures involving both spectacular exercises and opportunities for studying chemical processes through spectroscopy. Recently, the department has also initiated visits by its students to give lectures and demonstrations at high schools.

## Celebrating 40 year anniversary

In November DTU Chemistry celebrated Associate Professor Rolf W. Berg's 40 year anniversary. Many colleagues came to congratulate Rolf W. Berg enjoying old and new stories from a lifelong employment.

## Sapere Aude Research Leader Award

Associate Professor Peter Fristrup received 8.6 million DKK from the Danish Council for Independent research, Sapere Aude. Peter Fristrup, 33, being the youngest researcher to receive the award this year. He is going to lead the research project on sustainable chemical reactions for conversion of biomass for the next four years. "It's a great honor to be selected among the best young researchers in Denmark," says Peter Fristrup about the award.

## Scientist honored for efforts to Danish industry

Associate Professor Anders Riisager from the Centre for Catalysis and Sustainable Chemistry at DTU Chemistry received 200,000 DKK from the Reinholdt W. Jorck and Wife's Foundation for his commitment and efforts to Danish industry. The award is a recognition of Anders Riisagers efforts to Danish industry. It is also meant as an inspiration to continue the good work within research, teaching and publishing.



# Publications in 2011

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

DTU Chemistry researchers produced 116 refereed international journal articles indexed in ISI's databases in 2011.

In addition, the department's participation in conferences resulted in more than 40 conference meeting papers and abstracts published in journals and proceeding books together with a large number of scientific project reports.

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

For a complete list of DTU Chemistry publications in 2011, please see:

[www.kemi.dtu.dk/publications](http://www.kemi.dtu.dk/publications)



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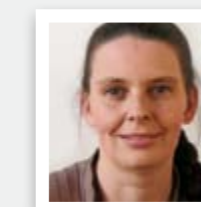
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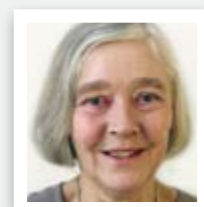
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Tove Rønne, Service Assistant

### Administration

Mia Trolle Borup, Center Coordinator  
Maria Bundgaard, Chief Secretary  
Mette Hansen, Ph.D. Administrator  
Lillian Karen Holm, Receptionist  
Bente Hviid, Administrative Assistant  
Jette Nilsson, Assistant Head of Administration  
Charlotte Malassé, Special Advisor, Communication  
Anne-Jette Olsen, Teaching Administrator  
Majken Kramer Overgaard, Special Advisor, Funding  
Kirsten Munkgaard Thomsen, Senior Clerk\*  
Patricia Wagner, Project Administrator  
Susanne Helmark, Graphic Designer

### Trainees

Mads Andersen, Laboratory Technician  
Said Alam, Industrial Technician  
Andreas Graff Pedersen, Industrial Technician  
Debbie Natascha Englundh Jakobsen, IT Supporter  
Troels Varming-Petersen, Industrial Technician

### Other Staff

Jesper Steffens Pedersen, Student Worker\*  
Louise Hededal Svendsen, Student Worker

\* From 1 January, 2012, DTU Energy Conversion

