THE SWEDISH FOUNDATION FOR STRATEGIC RESEARCH
PRESENTS

INDIVIDUAL GRANTS FOR THE ADVANCEMENT OF RESEARCH LEADERS

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The interviews in this publication were made by Petra Hedbom and Ylva Hermansson, partly within the framework of the project work for their course in Scientific Communication at Stockholm University. The aim of this course is to give people with a scientific education the knowledge and skills needed to present in a comprehensible, objective and ethically satisfactory manner scientific information for those who are not experts.

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THE INGVAR PROGRAM

The research group is not an extinct phenomenon although we live in times when networking and large centres are much in focus. A research group consisting of five to ten research students and post-doctorate students under the guidance of a competent and energetic research leader with time to devote to research is still a driving force in scientific and technological development.

The current budget for a research group of this size, including salaries and overheads, is more than SEK 5 million a year. It has been difficult for young researchers in Sweden to build up an independent group with this kind of power on the basis of their own grants alone. Instead they have been obliged to join up with other more senior researchers, with the risk that new fields of research may not have been covered sufficiently well in Sweden.

The aim of the Swedish Foundation for Strategic Research's INGVAR grants is to place a number of particularly promising young researchers in the driving seat, thus making it possible for them to build up research groups with international impact. We expect that our first twenty-one INGVAR scholars, with the help of an SSF grant of SEK10 million, will develop not only into internationally recognised researchers but also into leaders and mentors for their younger colleagues.

We also expect them to build up research groups that can collaborate effectively with other groups within both universities and industry; as a result of the discoveries they make we would also like to see them establish new companies.

Staffan Normark

Name:
Igor Abrikosov
Born:
1965

Nationality:
Russian
Doctor's degree:
1997
Works at:
Uppsala University

Project title:
Electron Theory of Materials Properties

MATERIAL DESIGN AT THE ATOMIC LEVEL

Igor Abrikosov designs material right down to the atomic level. The search for new compounds that will give us rustless cars, harder-wearing roads or smaller cellphones continues apace. His dream is to be able to determine how resistant to rust a material is with the aid of a computer program alone.

In his mother's footsteps

"Everywhere round us there are many materials of various sorts. Sometimes it is difficult to understand that dynamic processes are continuously taking place in them, even inside the hardest diamond, and I keep on asking myself how the various properties of materials arise," says Igor Abrikosov.

All the materials round us, solids, liquids and gases, are basically compounds of atoms. The way in which the atoms are related to each other is determined to a large extent by the way the electrons in each atom interact. By studying the electronic structure of a material it is possible to get to know its properties. This can be studied in practice by various experimental techniques, but also theoretically with the help of calculations.

"We study material that consists of several different kinds of atoms, and since the relations between them are controlled by many variables, we soon come up against complicated mathematical problems," says Igor Abrikosov.

Igor´s interest in natural science began at an early age, not without influence from his mother, who was a physics teacher. At the age of 12 he knew that he wanted to work with physics in the future. During his secondary school years in Russia he was fascinated by the properties he observed in different materials. How is it that one metal reacts in one way to heat while a similar metal behaves quite differently? His interest in this and similar phenomena stayed with him throughout his school years, so in 1993, when he was invited to begin postgraduate studies, he immediately accepted the offer. After that he became a visiting lecturer at Uppsala, where he is now an Associate Professor.

Metals are heated in computer programs

"In the coming years I would like to do both basic research and applications. I actually want to investigate materials of various types – anything from how a saw can be made more durable or a car more environmentally friendly to how certain alloys can be made more sensitive to magnetic fields."

Igor sees industry and business as natural parts of a link between research and application. Questions from outside give ideas for research and research results make it possible for companies to create new and better products. The research group he is working with at present is co-operating with several large Swedish companies including Volvo and SKB, and he hopes there will be further exchanges.

When Igor and his colleagues want to investigate a material's properties, they use the first-principles simulations. This works by feeding in already known facts about the substance's atomic structure into a computer simulation program, which provides a description of how the materials behave. It is then possible to mix two components in the computer and see how the different types of atoms integrate. By changing the conditions the material in question can be submitted to different kinds of strains, which provides answers to questions like: How easily does a new material begin to wear out in a certain given set of circumstances? The aim is to create models as close to


PHOTO: GENADII GRECHNEV

reality as possible so as to be able to optimise the designs of the experimental tests that follow.

Green trends

New materials are being discovered all the time today, which leads on to an interest in how they function. Metals and semiconductors are what industry is primarily interested in. Increased environmental considerations increase the demands on materials, both existing and new ones. In the SKB project the aim is to find suitable materials for the terminal deposition of nuclear waste; with Volvo the project is the development of more effective catalytic converters. In another of Igor´s projects he is trying to develop more environmentally friendly batteries. Cobalt is used in some types of batteries, but cobalt is potentially toxic, so the aim is to replace it with manganese, which is more environmentally friendly and is also cheaper. Manganese, compounds in turn, needs to be stabilised in a proper structure if it is to function in batteries and Igor is searching for a suitable alloying for this purpose.

"Research results must be applied. The days when we researchers conducted experiments behind locked doors are gone. If research is to move on, there has to be a continuous dialogue between us and those who want solutions. I see myself as a materials consultant. I want to provide solutions for those who ask for them within the widely different fields that our research can support."

Name:
Ernest Arenas
Born:
1962

Nationality:
Spanish
Doctor's degree:
1991

Works at:
Karolinska Institutet
Project title:
Dopaminergic neurons

STEM CELLS IN THE FIGHT AGAINST PARKINSON'S DISEASE

Research into stem cells has given rise to great hopes in the past few years. The visions of what they might be used for in the future are numerous and the possibilities almost endless. One possible area is the cultivation of special types of nerve cells that can help in the treatment of patients with Parkinson's disease.

A popular research field

Imagine being able to cultivate a cell in the laboratory and make it become exactly the cell you need for therapy. It was this dream that made Ernest Arenas leave the Mediterranean coast of Spain in the early 90s and settle down in Stockholm. He was a MD and had just taken his doctor's degree in Barcelona, in the field of neuro-pharmacology, when a scholarship made it possible for him to come to the Karolinska Institute in Sweden. Ernest moved to Stockholm and started to work in a group that was interested in how nerve growth factors work in the nervous system. Two years later he had started his own research group and in 1996 he had begun to look at neural stem cells. The aim was to try to develop a treatment for neurodegenerative disorders like Parkinson's disease. Research into stem cells has developed explosively in the past few years; and you can now read and hear about it every day in the media.

"The whole field of stem cells is bubbling, which is very exciting and positive," says Ernest. "We have to work very hard to keep up with groups all over the world. Research is moving forward very fast." One of the great advantages of working in a popular field, Ernest believes, is that scientists coming from different research areas are now studying stem cells from different perspectives, which results in exciting multidisciplinary approaches to scientific questions.

Nerve cells are cultivated

A person with Parkinson's disease lacks the neurotransmitter dopamine in the brain. Dopamine is vital for our ability to carry out controlled and directed movements. During the ageing process the number of nerve cells that release dopamine decreases in everybody, but in a person with Parkinson's disease this takes place at a much higher rate. The symptoms are disturbances in the pattern of movements such as reduced voluntary movements, rigidity and tremor. It is not known at present whether the problem is caused by increased damage to dopaminergic cells or increased vulnerability or whether they are no longer maintained or renewed. Nowadays, the main form of treatment is pharmacological, based on L-dopa, a substance that is converted into dopamine in the brain. After a long period of treatment, however, negative side effects appear. An alternative to this treatment is to transplant healthy dopamine cells into the brain. Such cells now come mainly from human embryos, which rise both ethical and technical issues since several donors are required to help a single patient. Instead it would be better to cultivate and transplant cells that become just the type of nerve cells that Parkinson patients need. This is what Ernest and his colleagues are trying to do. It is already possible today to cultivate dopaminergic cells from stem cells, but usually many non-dopaminergic cells are also produced at the same time, a kind of unwanted surplus. In addition, dopaminergic cells derived from stem cells in vitro often survive transplantation worse than embryonic dopaminergic cells.

"We will be focusing on the origin and development of dopamine neurons, and those signals required to induce dopamine neurons during development will

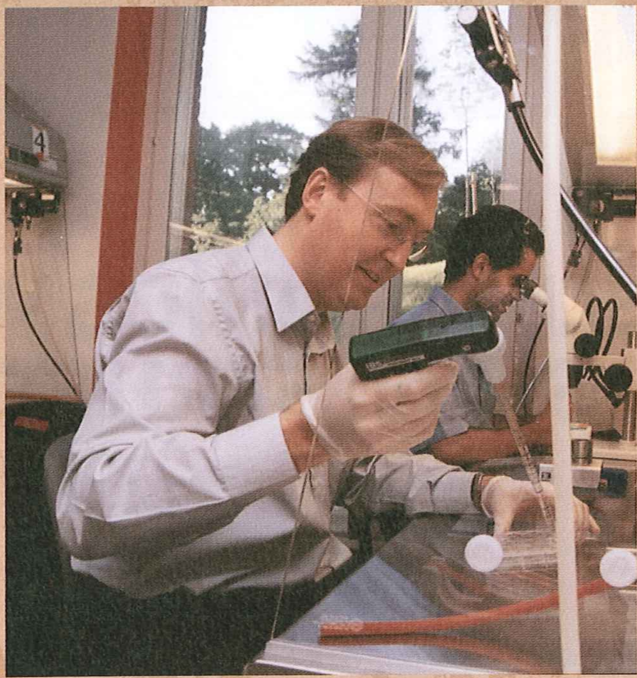
PHOTO: EDUARDO VALENZUELA

be applied to neural stem cells. A good deal of attention in our laboratory is being given to various growth factors and to their significance in the development of dopamine neurons. In the future, when those steps regulating the induction and survival of dopamine neurons will be known, Ernest imagines that it will be possible to develop new therapeutic tools to make the patient's nerve cells regenerate or recover and start to produce dopamine themselves, avoiding perhaps the need for transplantation."

"We have characterised some of the components required for the induction of dopaminergic neurons and that has allowed us to develop a method by which we get as much as 80% of dopamine cells from neural stem cells in vitro, which is the highest number of dopamine neurons achieved so far. We are however at an early stage in our research and I think that it will take several years for this type of therapy to reach the patients."

At present stem cells easily accessible for therapy include bone marrow and skin stem cells. Since those stem cells can be isolated from the patient himself, the problem of the cells being rejected by the body's immune system could be avoided. However, for this type of strategy to be successful, genetic factors influencing disease should not play a decisive role. This and other factors, including the completion of a comprehensive survey of the mechanisms and signals that control the development of these cells is required in order to implement all the potential of stem cells. Ernest points out how important it is to understand the basic biology of stem cells, prior to clinical testing. "We need to understand the mechanisms that control the development of stem cells in order to reduce the risk of undesirable consequences and to exploit all the therapeutic potential of stem cells".

Two language teachers

Ernest is convinced that a good leader should communicate openly with his colleagues. But the most important thing for him is to enjoy your work. Many scientists from other countries come to work to the Karolinska Institute for a long period of time. Those bringing along their husband, wife or family have also very good chances to enjoy their stay here, says Ernest.

"As for myself, I was lucky that my wife Carmen came with me. During our years in Sweden both science and family have grown. We now have two daughters, Clara and Julia, seven and five years old."

Besides acting as Swedish teachers for their dad, they are curious about what he is doing.

"My elder daughter asked me the other day about cells and wondered if her little sister had smaller genes because she is smaller."

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Magnus Berggren
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1968
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Doctor's degree:
1996

Works at:
Department of Technology and Science and Department of Physics and Measurement Technology, both at Linköping University.

Project title:
Variable organic processors

GOOD ELECTRONICS WITH A BIOLOGICAL STRUCTURE

Our ability to learn and remember is dependent on the number of nerve cells increasing as we grow up, and on these cells getting better at processing signals that enter the brain. Magnus Berggren copies biology's unique qualities over to electronic components based on organic materials, for example for the manufacture of variable signal processors in biological computers.

The nerve system controls all the functions in the body. It consists of about 100 billion nerve cells, all of which interact with each other in a complex network. While information about the structure of the brain is mainly stored in the genetic make-up, all nerve cells are created by cell division and they organise themselves in an unpredetermined way. Some nerve cells deal with signals from the optic nerve while other are in contact with the auditory nerve or operate so that we perceive touch, smell and so on. This unique quality that biology has is called self-organisation. The data processing itself takes place in the nerve cells´ synapses, which are placed at intersections in between nerve cells. These synapses transmit the information to the next cell in the form of ions, and they can adapt their function according to the stimuli we learn to recognise and remember.

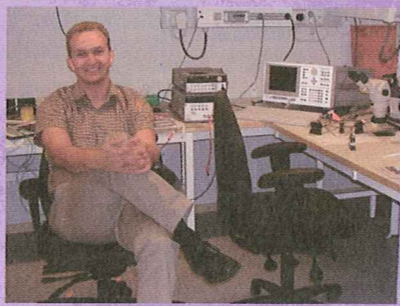
A system as flexible as the nerve system in electronics would be revolutionary. One of the reasons why scientists all over the world have begun to use organic materials in electronic devices is that transformable electronic components can be achieved. Flexible transistors, for example, have been produced, in which the various qualities of the above-mentioned synapses are utilised. Magnus and his colleagues now want to use conducting polymers to create new types of signal processors. Here the components, like the brain's nerve cells, will be able to organise themselves according to the powers of nature and also imitate the synapses´ way of varying their function. As a result they will be able to deal with incoming signals individually. In medical technology today traditional silicon transistors are connected to biological nerve systems, for example when life has to be brought back to nerves after a nerve injury. In these cases problems occur rather often.

What is needed is a station for processing the signals between the silicon system and the biological system – a potential use for our biological processors. In experiments we have seen a connection between electrons and ions in the polymers that does not exist in ordinary semiconductors. The idea now is that an electronic process from the silicon computers should transform the ion signals in the biological processor, which is expected to contain both silicon-based architecture and organic components. These ion signals would then be able to react more easily with ions in the biological system. Another observation we have made is that the biological processor works extremely selectively. By altering the current we can get the ions to react only with specific components. The ions may be compared with the simplest form of a neuronal substance.

Prefers country life to life in the big city

A few years ago Magnus and his family lived outside New York. This was a confusing period.

"You can't really imagine New York until you have been there and seen the city with your own eyes. With the surrounding suburbs included it forms a giant complex of some 40 million inhabitants, and you are amazed that the transportation system works as smoothly as it does. We enjoyed life there, but I think you either have to have grown up



in a big city or be very fascinated by the lifestyle to be able to live there for a long time."

Nowadays they live in a residential suburb in Vreta Kloster near Bergs Slussar outside Linköping. Magnus's wife Karin has also a nature science background and she works as a secondary school teacher, in chemistry and biology, in a small village school. The fact that they have to commute to work every day is more than compensated by the calm and peaceful atmosphere that country life offers.

"Our daughters Linnea and Elin, eight and six years old, have lots of parks and countryside to play in, while Karin and I can relax properly when we are at home. Erik is two years and just started at kindergarten. I've become something of a carpenter and have built a fence and a garage for the house. Now I'm building a veranda so we can enjoy our coffee outdoors in the summer. It's a very relaxing hobby but not the easiest one in the world," he says with a laugh.

Inspired by photosynthesis and the eye

This isn't the first time that Magnus has used organic polymers as active material in electronic components. Earlier, together with chemists at Chalmers Institute of Technology he produced light-emitting diodes in which organic polymers with varying optic properties were combined to get different colours, from infrared to violet. By changing the current across the diodes they could even get them to change colour.

During a project at Bell Labs at Murray Hill, USA, he copied biological photosynthesis. By absorbing energy of one wavelength and letting it decline in energy content, as energy is transformed in plants, he succeeded in producing extremely low-threshold lasing light. This was something quite new and revolutionary.

After his stay in the United States he was given the chance to help start a company, Thin Film Electronics, TFE. He and his colleagues were now inspired by substances like rhodopsin, which is found on the retina. Rhodopsin can switch between two different states, and it translates light from the eye to ionic signals in the optic nerve. This turning moment is a type of memory/signal transfer function.

"The conducting polymers we use function along the same principles. One position which the polymer adopts at a certain current represent a one, while the other position represents a zero after a change in the current. In this way it is possible to store digital information in the polymers, creating plastic memories that are much smaller, cheaper and more economical than the memories that are based on present-day silicon technology. The company has now expanded and has about fifty or so employees who will develop computer memories in a large laboratory in Linköping that will be completed in August this year.

Electronic paper

Besides being a lecturer at Linköping University, Magnus is also employed as a researcher at Acreo, a company in Norrköping. There he is developing a completely new technology that aims at making paper electronic. With the aid of ordinary printing techniques conducting polymers are applied to the surface of paper.

"Like plastic memories we are utilising the ability of polymers to change their state from one physical state to another. We are also inspired by the bistable functions of chameleons, octopuses and butterflies that are connected with various absorption properties. With the aid of an electric current we can change the polymers from one state to another and so determine which parts of the paper will be activated and what colour will be shown."

It is hoped that this research will create new applications for traditional paper. So far mobile figure displays like those in clock radios have been produced; other potential applications are, for example, electronic daily newspapers or computer processors that contain paper electronics.

The technology bodes well for the future

Up to now this technology, using organic material as an active medium in components, has led to many new products, of which transistors, light-emitting diodes, lasers, plastic memories and electronic paper are but a few. The future goal, as previously mentioned, is new signal processors in biological computers that can be used as translators between biological systems and silicon electronics, but it is believed that the technology can also be useful for various types of hardware using recognition electronics such as sensors or perception memories.

"So far this field is purely visionary and up to now we have only been working from the phenomena we have observed in the lab. If we are to develop this technology further, and get a clearer picture of possible applications, we must understand what mathematical algebra best describes the phenomena. It's an unbelievably stimulating situation, because at the same time as I can use my knowledge of materials physics and electronics, I get the opportunity to read up on neurophysiology and neurochemistry. It's great to feel that one is developing all the time."

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1965

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Doctor's degree:
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Project title:
New methods for radiography

AN OLD INVENTION IN A NEW FORM

Developing and improving systems for radiography is Mats Danielsson's goal. He aims to make it possible to use smaller doses of radiation. It is especially important to minimise the risk of damage in health care, where many examinations are carried out. "We must take care of people," says Mats.

A 100-year-old invention

X-ray radiation is used today in a multitude of different fields; diagnostics in health care is one of the very biggest ones. X-ray examinations are in many cases the only way of discovering tumours or damage in bones and tissue. But there are problems involved. The doses of radiation caused by radiography can affect biological material. At the same time good image quality can be decisive for detecting breast cancer, for example, at an early stage. Much of the research in this field is therefore devoted to achieving equally good or even better resolution with a smaller dose of radiation. Mats and his research group have developed an X-ray system for mammography, which is the examination performed on women to detect breast cancer. Some 600 000 examinations are carried out annually in Sweden, so it is desirable to reduce the radiation dose at the same time as the image quality is enhanced by means of more effective equipment.

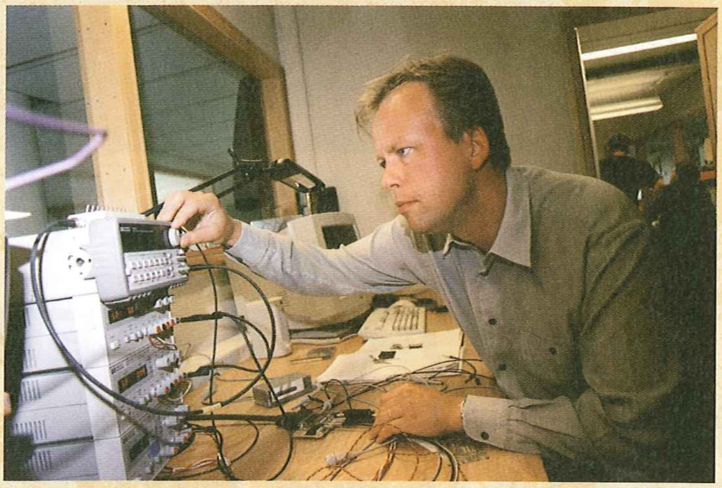
"When non-living material is radiated, it is unnecessary to worry about the dose," Mats explains, "but when it is people, it is important to keep the dose as low as possible. We have been able to lower the dose by developing a very sensitive detector."

From film to digital sensor

X-rays were discovered just over 100 years ago when Wilhelm Conrad Röngten found that very low-frequency radiation, in contrast to visible light, could partly pass through human tissue so that it could be used to photograph what was inside the human body. Ever since then this method of registering, storing and showing information has consisted of photographic film. In recent years this has begun to be replaced by digital technology. Instead of the radiation leaving an impression on a film when it has passed through its subject, it goes to a digital sensor. Besides reducing the dose of radiation, digital processing is better from several other points of view; above all it is easier to handle. Working with film requires complex equipment for developing the film and the plates take up a lot of storage space. Using digital technology, the images also appear directly, which gives the doctors quicker answers. In Sweden over 50 per cent of traditional X-ray equipment has been replaced by digitalised equipment, which makes it the leading country in this field in the world. But mammography has up to now proved to be difficult to digitalise. These examinations make greater demands on both safety and resolution.

Sensitive sensors

It is hoped that, by creating a detector of silicon, Mats and his colleagues will be able to reduce the dose of radiation in mammography by a fifth. One of the reasons for this improvement is that there is no intermediary stage where the information is processed. A comparison can be made with an ordinary photograph – the more sensitive the film, the less light is needed for a sharp image. The silicon detector makes it possible for each individual photon from the X-ray radiation, several thousand per second, to be detected. Thus the different X-rays can be assessed individually. The amount of information is related to the energy con-



tent of each photon. Those that have less energy have a higher contrast content, are more clearly distinguishable from the background and carry more information. The photons that carry a great deal of information can be processed differently and be given more attention when the images are interpreted. A year and a half ago Mats and his research assistants founded a company called Mamea, in which the new silicon detector is marketed by Sectra, a company in Linköping, under the name Sectra Microdose Mammography. These researchers are pioneers in their field, and their equipment for mammography will be tested clinically in the autumn of 2001.

From the forest to the big city

Mast's interest in physics was awakened at high school in Nässjö, leading him to move later to Stockholm and the Royal Institute of Technology. After taking his university degree he began post-graduate studies in particle physics. After his doctor's degree Mats went to California, where he spent two years at the University of California at Berkeley. During this period his interest in more applied research grew.

"Particle physics is very exciting, but it can also be very abstract. It wasn't something you could discuss with just anyone over a cup of coffee," he says with a grin. X-rays are something that affects more people, they have an inkling of what it involves. It feels great to see one's ideas realised, like in the clinical trials this autumn."

Cooperating with industry inspires him as well, and combining this with university research has gone well so far, he thinks.

"You have to enjoy working with a group if it's going to function properly. That's the prime factor for performing well."

Another important factor in Mats´s life is his family. His wife and two sons, Oscar and Arvid, five years old and five months old respectively, are a source of inspiration and he gives them as much of his time as possible.

Vinyl discs in focus

One way of further reducing radiation doses is to focus extra important X-rays. Ordinary cameras and microscopes use a refractive principle, that is, glass lenses, to focus the light. In radiography the rays have not been focused in the same way and until a few years ago it was generally believed that this was impossible. It was one of Mats´s research students, Björn Cederström, who first realised that it was possible to make saw-toothed refractive lenses. An advanced saw-toothed pattern is cut with micrometric precision and the X-rays are allowed to pass through it. It was evident that when the light tried to pass the notches, it did so in such a way that the effect when the rays emerged on the other side was the same as for a lens – they were focused.

"After considering various materials, we contacted a manufacturer who constructed special LP discs of vinyl for us. These discs with their saw-toothed pattern are placed next to each other, forming a "crocodile bite". By altering the size of the bite you can control the size of the lens. A big bite gives a broad lens and a small bite a small lens. This new lens is planned to be used in an upgraded version of the existing detector system. In the literature it is known as "the crocodile lens".

"Finding solutions to advanced problems using simple methods is something I want to go on with. It was wonderful for Björn to go round to conferences among all the world's high-tech apparatuses and demonstrate his discs!"

When asked if any particular kind of music was most suitable, Mats reveals with a grin that the discs he uses are in fact silent ones.

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1966
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Doctor's degree:
1995
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Project title:
The Mediator – structure and function

THE MEDIATOR – ESSENTIAL FOR THE REGULATED EXPRESSION OF GENES

A human genome contains about 40 000 genes. A key component in the molecular machinery, which controls gene expression, is the Mediator complex. Claes Gustafsson is going to explore the Mediator's function in detail, which will be of significance for our understanding of gene activation as well as the development of new drugs, which can directly influence gene expression.

"The Mediator is a large protein complex that transmits information from factors that control the genes´ activity to a protein that reads the DNA strands called RNA polymerase. In this way the Mediator plays an important role in keeping cells healthy or if they develop abnormal activity from some gene and become unhealthy.

Today we know that the thyroid gland hormone, oestrogen and vitamin D enter cells and via their receptors bind to the Mediator. The Mediator then contacts the RNA polymerase, which start reading the genes that are regulated by the respective factor. It is now thought that almost all gene expression, at least in part, is controlled through the Mediator.

"If we could determine in detail how the Mediator interacts with its various factors, we would be able to create drugs that specifically reinforce or break these contacts. Already now the interaction between the thyroid gland hormone receptor and the Mediator is an important target when we are trying to develop new medicines to treat thyroid gland diseases such as goitre.

Life is fun for Claes

Claes was born in Borås but moved to Göteborg to study medicine. His never-ending curiosity and need to decide himself about his working hours made him start to do research.

"First of all one gets an enormous feeling of freedom from being able to think about one's own questions all day long, the ones you really want to find the answers to. Second, I know how incredibly exalted I feel when I get the smallest little result. I can rush to the phone and ring my friends and colleagues, long before the results are definite. It's probably the need to feel the same kick again and again that drives me on."

Claes is a positive person with a good sense of humour. At the same time as he is very focused on his work, he has the ability to let life be fun. Planning is all very well, but you shouldn't be a slave to your obligations. Last year he moved house from Göteborg to Tullinge, a suburb of Stockholm.

"My job at the Institute for Medical Nutrition at Novum came quite unexpectedly, so we had to find somewhere to live quite quickly. When there were only a few days left before we started work, our search for a home ended with us buying a house in the middle of the night. We didn't even know what colour it was," he says with a smile.

In spite of a chaotic period at the beginning of his life in Stockholm they love being there. His daughters Hanna, 5, and Amanda, 2, have found new friends at their day nursery, while Claes and his wife Mia have good workmates who help them solve their everyday problems.

"Now that we're settled in, we can start to live properly. That feels really good."

Vital to determine structure

The Mediator's function is a field of research that is attracting increasing numbers of researchers all over the world. Claes and his colleagues are in a good position because they already have extensive experience in protein purification and can study protein complexes that other groups might have difficulty in isolating.

"We have also chosen to work on a special kind of yeast cell called Schizo-

PHOTO: MARIA FALKENBERG

saccaromyces pombe. Its cells grow rapidly and have a stable, easily studied Mediator complex that is also very similar to the human system. I think our choice of this particular yeast as our model system has given us a competitive edge."

To be able to understand more easily how the Mediator works Claes and his colleagues will study how the complex changes shape in its contact with various molecules. A problem that arises in this context is the Mediator's enormous size.

"Instead of producing the whole of the Mediator's structure, we and a group of researchers in Germany are going to concentrate on a small part that we believe is important in its contact with the RNA polymerase.

A travelling family

Both Claes and Mia research and travel a lot in their work. A few years ago they spent two years in the United States at Stanford University, a stay that led to many useful contacts. Together with colleague, Prof. Nils-Göran Larsson at the Dept. of Medical Nutrition, Claes has also begun to investigate the mechanisms of gene expression in mitochondria, the powerhouses of the eukaryotic cell. Based on the discoveries made in this area, the have also founded a company, MitoTech AB.

"We are going to try to develop medicines that affect energy production in mitochondria. You learn a lot running a company. And hopefully our know-how will be needed when the competition for results gets keener in the world of research."

When the holidays come round, Claes and Mia are fed up with travelling and are happy to stay at their holiday cottage in Falkenberg.

"It's a wonderful place to be in the summer. The kids have plenty of room to play in and we are close to relatives and friends. It couldn't be better."

Strategic projects

Apart from the fact that the Mediator is not by any means the only factor that regulates which genes are to be activated, results indicate that Mediator complexes called tissue-specific complexes will be found in various organs and with varying characteristics.

"The human body has an enormous variety of proteins, all of which are unique and need their own special functions and structures to be determined. Sweden used to be one of the leading countries in protein biochemistry, but today much of that competence has disappeared. That is why our project is also of strategic importance, and we are convinced that we in a couple of years will know the Mediator's structure and function. But it will take much longer for a complete understanding of how gene expression is regulated."

Name:
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1964

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1995

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Controlled electron transmission

SMALL-SCALE TECHNOLOGY WITH A LARGE CAPACITY

Developments in high technology aim at making components smaller and smaller. Computers and cell-phones are shrinking in size, yet at the same time they have to be more and more powerful. Is it possible to manufacture electronic equipment on the smallest imaginable scale without the functions being affected? One solution is to make the small big instead of making the big small.

Small systems and large molecules

Electronics basically deals with the ways in which electrons can move between molecules. In our present-day society we often try to make electronic equipment faster, smaller and better. The electronics we use is primarily based on circuits of semi-conductor material. A semi-conductor is characterised by its ability to conduct electric currents under certain conditions and to insulate under other conditions. The deciding factors can be additives of other substances in the semi-conductor; by altering them we can control its conductive power. The ability to control when and in what amount the current shall flow through a system has made it possible to develop the advanced electronic equipment that we have today, and we have generally speaking learnt the behaviour of electric currents. But just as the laws of nature that apply on earth cease to operate when we go out into space, the traditional laws of physics cease to apply when electric circuits are greatly diminished, being replaced by those of quantum physics. This breach of the law means that it is no longer possible to be really certain how electrons will behave, which makes it difficult to control the current. So Leif Hammarström has become interested in the ways in which electrons move between molecules.

For several years Leif had been studying artificial photosynthesis, trying to imitate the photosynthesis of plants in synthetic systems. He had been fascinated by the way in which energy from light can be transformed in order to initiate various reactions. In the photosynthesis that occurs continuously in plants, light meets chlorophyll molecules and its energy is transferred to them. When the chlorophyll disposes of this energy, which it always does sooner or later, this is used to initiate reactions. This process involves moving electrons, exactly as in an electric current, but on a considerably smaller scale than is used in technical contexts.

"I was curious about how, instead of making our technology smaller and smaller, we might be able to utilise nature's own method of transporting electrons and blow up the small instead of diminishing the big. This is called molecular electronics and it has become a major field of research in recent years.

Colour-controlled electrons

One of the problems of quantum physics is that electrons can start to move in another direction than expected, which makes it more difficult to predict and control the flow of current. When Leif looked more closely at parts of plant cells that are central for photosynthesis, he was fascinated by their ability to maintain a balanced and precise system, with very little leakage, when individual electrons are transported between molecules and across membranes – exactly what is required in modern technology.

"When a molecule absorbs light, the electrons in it will move from a state of low energy, a basic state, to a state of higher energy. In other words, the electrons are excited. They very quickly return to a somewhat lower energy state and finally lose a lot of energy, returning to the basic state."

A great deal of energy is emitted bet-

ween the next to lowest and the lowest state, often in the form of light radiation. Between the highest and the next to highest state, however, the difference in energy is not so great, and the higher state is very short-lived. Together with his research team Leif began to investigate the possibility of getting the higher state to emit an electron during its short life. He began by looking at porphyrin, which has a molecule similar to that of plant chlorophyll and hemoglobin in human blood. The porphyrin molecules were allowed to react in a solution together with another molecule that easily accepted a free electron from the porphyrin.

"We succeeded in getting a controlled transmission of electrons. When we used red light to excite it, it took 100 picoseconds for an electron to move across to an electron receiver – but it went a hundred times faster if we radiated it with blue light, which contains more energy. This opens up new possibilities to control reactions so that a molecule reacts in different ways if it receives light of different colours."

The next step is to bind two different types of electron receiver to the porphyrin molecule. On one side they want a receiver that prefers negative charges, which would accept electron with a low energy content. On the other side they will bind a more demanding molecule that only accepts electron with a great deal of energy. By radiating the porphyrin with light of various wavelengths they hope to be able to steer the electrons in a particular direction.

"Red light contains little energy and would be able to steer the electron to the receiver that is easily manipulated, whereas blue light contains a great deal of energy and would steer the electron to the other one. By letting a laser beam switch between red and blue at short intervals it would be possible to create an optoelectronic switch with a reaction that takes only a few femto or picoseconds.

Many strings to his bow

In conventional electronics approximately 10 000 electrons are needed to mark a one or a zero, that is, to decide whether or not there will be a signal. In molecular electronics a single electron is enough to give a signal. By understanding how this can be controlled we will get closer to finding a solution to the problem of hoe electronics can be both smaller and faster.

"A legitimate question is whether we really need better and faster electronics that we have today. But I think that interest in having smaller and more powerful computers will continue for a long time, and there will always be new kinds of problems to solve."

Medical spare parts to be operated into the body are examples that Leif mentions when discussing what very small electric circuits could be used for, but also to make more advanced calculations and why not smaller replacements for today's cellphones and laptop computers?

Besides spending time with his wife and their two children, Leif likes playing music – everything from renaissance to experimental pop. His instrument is the classical guitar, but he likes singing too. And as he likes to get to the bottom of things, he has written some music.

"A fugue is the most complicated thing I've tried – apart from being a trainer for my six-year-old son's football team."

Name:
Anders Karlsson
Born:
1964
Nationality:
Swedish

Doctor's degree:
1992
Works at:
Department of Microelectronics and Information Technology, Royal Institute of Technology, Stockholm

Project title:
Quantum information technologies

QUANTUM INFORMATION TECHNOLOGY – A NEW WAY OF THINKING

If computers, cellular phones and broadband are to be more efficient, the microelectronic components in them must be made even smaller. Shrinking the size and one enters the micro world where quantum mechanics rule. Anders Karlsson is, among many things, studying how one by sending information in the form of single light particles can improve optical communication.

"Quantum effects have for long been associated with problems since they give rise to noise that limits the capacity of electronic and fibre-optic systems. We want to turn the question around and instead utilise the effects that distinguish quantum mechanics from classical physics and let the quantum particles work for us. This field of research is called quantum information technology and is a mixture of applied physics, electronics and information technology."

Popularisation is important

Anders Karlsson has long been fascinated by physics and technology. He holds a chair as Professor of Quantum Photonics at the Department of Microelectronics and Information Technology at the Royal Institute of Technology Kista (Stockholm). He also occasionally writes articles in popular-scientific magazines such as the Swedish *"Forskning & Framsteg"* (direct translation Research & Progress).

"My main goal, apart from my research, is to show students how exciting and fun physics is. Another aim is to raise interest among the general public, and that's where popular science enters."

If more young people are to choose the natural sciences, it is important to get them interested as early on as possible. Media plays an important role.

"There ought to be more television programmes like *"Hjärnkontoret"* (Swedish Science show for children) that discuss everyday phenomena that most people have probably wondered about. Why are there bubbles in soft drinks? How does a CD player work? Me, my wife Dana and our daughters Gabriella (10) and Alexandra (7) always follow that programme with interest."

Individual light particles are detected

Quantum mechanics forms the basis of several of the great inventions of the 20th century like microelectronics, lasers and nuclear power. This theory describes the behaviour of the smallest units of matter – atoms, electrons and light particles, photons, and is based on the fact that all energy is divided into small fixed chunks of energy, called quanta. Previously it was impossible to carry out controlled experiments with individual quanta, but for instance in optics, after the laser was invented, great progress was made in the 1960's and 1970's. Today there are also sources of light that can transmit individual photons. Anders Karlsson and his colleagues have taken this technology a stage further.

"We can now measure individual photons, and that's like measuring the light from a 100W light bulb some 50 kilometres away. Measurement technology as sensitive as this is useful not only for physics, but it also has a broader range of applications in fibre-optic communications, biology and medicine."

Quantum coding for secure communications

In his research Anders Karlsson wants to make use of various quantum effects to improve information technology. He is now working, among other things, with his team to develop a technique for fundamentally secure information transmission, called quantum cryptography. This technique could potentially be use-

ful in the fibre-optic telecommunications network

"Since we use light one the level of a single or a few light quanta, it is the laws of quantum mechanics that sets the scene. For instance, one can create photon twins, two light quanta, where the photons twins will always behave the same way as each other, irrespective of the physical separation. The twin-like behaviour of quantum particles, in fact, can be made stronger than is allowed by any perceivable model of classical physics; a fact even the late Albert Einstein had troubles accepting. Such photon twins can be used for secret communication, or cryptography. When an encoded message is sent, you first send a code key, a long table of random data bits (zeros and ones) in which each data bit is encoded on two entangled (twin) photons. One of the twin photons goes to the person who is sending the message and the other to the recipient. If someone tries to eavesdrop, listen in on the twin photons, the fragile quantum connection between the photons is disturbed. This means that the information from the code key is not the same for the sender as the recipient, and the eavesdropper can be detected.

"Quantum cryptography could potentially provide a good alternative to some of today's cryptography systems if a larger degree of security is seen needed".

Indeed, already today some start-up companies have announced a prototype for a commercial quantum cryptography system. The US research agencies, military and civilian, are financing projects in this field, but also the European Union has funding allocated to this area. Anders is the total project co-ordinator of one of the European projects on quantum information.

"Generally speaking, it is good that Sweden finally now is a full member in the European Union. This opens many doors for international cooperation in research and other areas."

Tokyo, Paris, San Francisco – a mixture of influences

The department where Anders work has been collaborating for some twenty years with the Nippon Telegraph and Telecommunication-NTT basic research laboratory, which also have a research effort in quantum mechanics for applications in information technology.

"My family and I have lived in Tokyo on a few occasions. I find the people there being open and easy to get along with, and I like the Japanese culture and the language. At home we enjoy Japanese cooking and for a time I also had Karate as a hobby."

Apart from Japan, Anders also has worked at Stanford University outside San Francisco. During the last two years he also had a part-time position at the Ecole Polytechnique in Paris, where he lectured on semiconductor physics.

"France has a very strong research in the field of quantum optics, so it is both fun and stimulating to work with people there. And it gives plenty of opportunities to keep my French alive."

Research beyond quantum information

Fibre-optic communication would be revolutionised if optic components could be connected in similar way as done in electronic integrated circuits. This research area is called optoelectronics and is also part of Anders´s research work.

"One solution would be so called photonic crystals in which light propagation can be controlled, by using artificially made optical materials on the nanoscale level, in a similar manner as electric currents are controlled by semi-conductors. This would make the optical components smaller, faster and more efficient than what is used commercially today."

In contrast to the relatively industry oriented optoelectronics, quantum information technology is so far more of at the basic research level.

"The media often describe quantum information technology in too much product oriented terms. For instance, it will take many years before, so called, quantum computers are on the market and "Pentium" becomes "Quantium". But that is relatively uninteresting, because basic research in itself gives us better insight into physics, which in turn leads to new and often un-foreseen applications. Already the detection of very small amounts of light and the precise control of light propagation is of great interest for optical communication.

Name:
Maria Kempe
Born:
1965
Nationality:
Swedish

Doctor's degree:
1995
Works at:
Department of Cell and Molecular Biology, Biomedical Centre at Lund University

Project title:
Polymers for biomedical applications

POLYMERS MANUFACTURED BY MORE EFFECTIVE METHODS

Polymer is a Greek word meaning "many parts". DNA molecules, regulating proteins, and small parts of proteins, peptides, are just a few examples of polymers that all consist of several types of building blocks. We are now living in the age of plastics and the production of synthetic polymers is growing continuously. Marie Kempe is developing new effective methods for manufacturing biomedically useful polymers.

"Humans learnt at an early stage how to use natural polymers such as wool, cotton, wood, and rubber. During the 19th century we also began to produce synthetic polymers in the form of plastics. But it wasn't until the 20th century that peptide synthesis became possible."

In the beginning, peptide syntheses were carried out in solution, which was a very demanding and time-consuming method. Each new building block, an amino acid, was connected to the peptide chain in activated form or with the aid of a special coupling substance, a coupling reagent. After that it was necessary to purify the peptides from the solution by a long process in order to get rid of the excess starting material, reagents, and by-products.

"In the 1960s the Nobel Prize winner R Bruce Merrifield invented peptide synthesis on solid phase. This was a revolutionary discovery and is the technique used today. The amino acids are also in this method coupled to the peptide chain with the aid of a coupling reagent, but the peptide is now bound to an insoluble support material in the form of plastic beads. This avoids the long purification procedure between each step; instead the plastic beads can be filtered simply with their anchored peptides. Other advantages of solid-phase synthesis are that it is an easily automated process and that it gives a better yield. This higher yield is obtained by driving the reaction to completion by the use of excess coupling reagents. After the coupling, excess reagents can then easily be filtered off."

Owing to the increased need for new solid phases, Maria is devoting one of her projects to the development of new polymer support materials. These are to be used for the solid-phase synthesis of long peptide sequences, which can be difficult to produce, small organic molecules, and various pharmaceutical candidates.

"So far one of the supports, CLEAR, has been commercialised. This is a new type of polymer, which is highly crosslinked and thereby mechanically stable.

Synthetic receptors manufactured

Many peptides function in the body as hormones, binding with a large number of rather weak bonds to their respective receptors. When artificial peptide hormone receptors are prepared, the configuration and electronic properties of the natural receptors are imitated to make the binding to the hormone possible. Maria Kempe is now going to produce synthetic receptors for the synthesis, purification, and analysis of various peptide hormones, antibodies, and an HIV protein. Potential applications are for the development of new drugs, clinical analyses and food testing, or for administrating drugs in the body. To produce recognition elements specific for the desired molecules, they will use two different methods.

"Besides preparing peptides with a high binding capacity for specific molecules by solid-phase synthesis, we have developed a more direct and effective method for receptor synthesis. This is a molecular casting technique called molecular imprinting. The molecule that the receptor should be selective for, its ligand, acts as a mould when producing the receptor. This is done by synthesising a synthetic polymer, of plastic, around it. The ligand is then washed away, leaving

PHOTO: HENRIK KEMPE

a cavity in the plastic where the ligand fits in."

"The artificial receptor that is formed in this way is called a molecularly imprinted polymer, MIP. It has high chemical and mechanical stability and can, after regeneration, be used repeatedly to bind its ligand without losing its selectivity or binding capacity."

Using this molecular imprinting process Maria has produced a receptor for the peptide hormone oxytocin. Oxytocin, which is secreted from the pituitary gland in the brain, has two functions. It operates at the end of pregnancy, when it stimulates the contractions of the uterus before childbirth, and it stimulates the smooth muscles in the mother's breast so that the milk is transported from the glands to the suckling child.

With an interest in string instruments

Maria Kempe comes originally from Malmö. After having studied chemical engineering at Lund Institute of Technology she stayed on and took a doctor's degree focusing on molecular imprinting technology. After that she continued to study peptide synthesis at the University of Minnesota in the United States. Her varied interests were woven together in biochemistry.

"I have been interested in medical questions for a long time and thought about studying to become a physician initially. But it wasn't clinical work that attracted me most and when I realised I wanted to do research, biochemistry seemed to be a natural choice. Now I keep in touch with medicine through my research discoveries instead, from projects that I myself have chosen to work on in my own research group. That suits me down to the ground."

Besides playing golf Maria is deeply interested in music. Her instrument is the violin.

"I have played in the Malmö Youth Symphony Orchestra, the Lund Youth Orchestra and the Lund University Academic Orchestra. What is fun when you play with other people, apart from getting to know a lot of people, of course, is that everybody's efforts are woven together into something big. I like listening to classical music at home – what it is depends on the mood I happen to be in at the time.

Milk is tested for antibiotics

Today both consumers and food manufacturers are showing increased interest in controlling the quality of food products. They want to be sure that they do not contain any outside substances like industrial contaminants, pesticides, veterinary drugs or growth hormones. If it is to be possible to carry out effective tests directly at the factory, or even in the farmyard, the tests must be adapted for the non-expert.

"Today's antibody-based tests need to be improved. That's why I and some of my colleagues are developing a method to be able to determine in a simple way whether milk contains antibiotics. This is a EU-financed project that also involves researchers from other fields such as microtechnology and foodstuff quality control. Milk is an important product in the European Union and the importance of minimising the spread of antibiotics that can cause allergies among people has now been understood. It is also vital to minimise the risk of the emergence of antibiotic-resistant bacteria.

This method is based on polymers that have been made selective for various kinds of antibiotic molecules. These polymers, which are synthesised by the molecular imprinting process, are packed in a cartridge, which in turn is placed in the measuring instrument that has also been developed in the project. If a polymer binds to an antibiotic molecule, this is detected by means of fluorescence.

As robust imprinted polymers are used as the recognition element, this method has great advantages over conventional methods. The synthetic polymers are far more mechanically, thermally and chemically stable than biological antibodies. So Maria hopes that their method will be more reliable.

"The content of antibiotics in milk is just one of the applications of this method. Diabetics, for example, would find it very useful to be able to measure in a simple way the glucose content in their blood."

Name:	Doctor's degree:	Project title:
Anna Kidiyarova-Shevchenko	1997	Gigahertz electronics
Born: 1969	**Works at:** Department of Microelectronics and Nanoscience at Chalmers University of Technology, Göteborg	
Nationality: Russian		

SUPERCONDUCTORS TO HELP THE MOBILE SOCIETY

Today, when almost everybody uses a mobile phone, the base-station receivers run into a problem supporting both increased number of services and increased number of users. Anna Kidiyarova-Shevchenko is going to make solutions of the problem more efficient.

"Instead of silicon semiconductors, which are in most digital base stations today, we are going to use superconducting material. Superconductors can conduct current without resistance, which provides signal transmission more than 100 times faster than semiconductors. Due to this fact, serial algorithms implemented on superconducting electronics can be used instead of over-complicated parallel algorithms realised in silicon."

Anna Kidiyarova-Shevchenko has been working at Chalmers in Göteborg since 1998. She has chosen the niche field of mobile telephony since it is a rapidly growing area of research that she believes would require advanced electronics in the nearest future.

"In cellular mobile networks the signals from handsets are corrupted by the interference between them. Removing of the interference is a very complicated task that requires very fast digital signal processing. For the future scenario with increased number of users, the problem became vital for conventional electronics. We are convinced that superconductors are the solution to the problem."

Ice-cold environment vital

The only way of getting the present semiconductor receivers to function faster is to reduce the silicon components. This is virtually impossible, however, since they are already very small. Apart from the manufacturing costs skyrocketing, quantum mechanics also sets limits.

A problem with superconductors, however, is that they have to be cooled down to a very low temperature to become resistance-free. But the disadvantages of this manufacture-demanding process are outweighed by the fantastic capacity that is achieved.

"We shall use two different systems: a low-temperature one based on niobium which begins functioning at -269 °C, and a high-temperature one based on yttrium barium copper oxide (YBCO). The high-temperature system has superconducting properties at the somewhat higher temperature of -253 °C. This system is not fully developed yet, but when it will be the digital operational frequency will be raised from 30 gigahertz, which is the maximum frequency for the low-temperature system, to 150 gigahertz. This level of frequency is unique and cannot possibly be achieved by conventional semiconductor technology, which has a current operational frequency for digital systems of about two gigahertz."

Russia in her mind

Being a researcher in Moscow is not easy. Science has low status in society, which makes it difficult for researchers to finance their projects. On top of that, being a woman and daring to invest in higher education with career opportunities demands extra courage and self-confidence – something that many Russian women lack. Anna is proud of what she is today and exalted by the technology available in Sweden. Chalmers with its resources is a world-class research centre, she says, but she still misses her home country.

"Not until now, when I am living in a foreign country, I do realise how much I value my family and my friends. What I miss most of all is everyday socialising at dinners and telephone conversations. Now my phone is silent and a few weeks ago I missed the birth of my niece. But

I had to choose between meeting my family and having a job that I enjoy. Research came first."

She is living now in a house in Särö, south of Göteborg. The fantastically beautiful countryside gives her a feeling of freedom that helps her to enjoy life. But her native traditions are kept alive with Pelmeni, a ravioli-like dish, and Pirogi, pastry filled with cabbage, boiled egg and fried onions.

"Those tastes are so closely connected with a host of memories that I feel as if I were at home with my parents for a while. "That's a cheap trip to Russia," she says with a smile.

Apart from going back with her family to Moscow once a year, she has discovered large parts of Europe over the past few years.

"The best thing about travelling is that you get to experience different atmospheres, cultures and histories. Every place you visit raises one's consciousness of what a myriad of environments there are all round the world. Florence in Italy is the town I like best, because it is so rich in Italian history. When you arrive there, you feel as though you have been taken back in time and you forget everything else."

Future visions

Superconducting material has a great potential for use in levitating express trains, computers that control nuclear reactors or weather forecasting, to mention but a few areas.

Privately Anna thinks that she will stay in Sweden for a long time. Her daughters Anastasia (13) and Kseniya (5) also like living here, as does her husband Alexander. Do you want your daughters to be researchers?

"Yes, that would be great, but I don't want to push them in any way. I'm trying to teach my elder daughter some maths and physics, but she is more of the artistic type. She paints really lovely pictures."

So, what do you think about best illustration for your project? She laughs.

"You'd better ask Anastasia about that!"

Name:
Jörgen Larsson
Born:
1963

Nationality:
Swedish
Doctor's degree:
1994
Works at:
Lund Institute of Technology

Project title:
High temporal resolution X-ray studies

INVESTIGATING HOW MOLECULES MOVE

All round us there is constant change. Molecules and atoms move about, attach themselves to each other and disengage. We are aware of some of these changes, as when ice turns into water. But there are others that we do not see – at any rate properly yet.

An eventful life

There are a great many things we cannot see with the naked eye but which are going on all the time, with or without our knowledge. In the end it is a matter of how atoms and ions bind together and how they behave in relation to their surroundings. If we are to be able to observe individual atoms and how they move in relation to each other, we have to be able to measure events that last as little as 10^{-13} seconds and movements across distances as little as 10^{-10}. Rapid events have been studied mainly with the aid of short-pulse lasers, within the visible range. This is done in very small structures with what is called X-ray diffraction. But these techniques are inadequate when exact moments are to be studied in order to find out what happens in the middle of a process, because it is only possible to see what happens before and after. It is these intermediate stages when changes take place that Jörgen is investigating.

A maths-interested boy

Jörgen was born in Småland and grew up in Skåne. When it was time to go to university, he moved to Lund, which is still his home base.

"I began to get interested in science when I was at high school. I liked maths best but it seemed boring just to work with calculations, so I chose Engineering Physics."

His university education gave him the breadth he was looking for and after his degree project, which was about atomic physics, he decided to stay on and take a doctor's degree. The Hubble telescope had just gone up into space and started operating. This made Jörgen curious and gave him inspiration, because this great telescope made it possible to see what hitherto had not been visible: vacuum ultraviolet light. This type of light cannot penetrate the atmosphere, so before the Hubble telescope it could not be studied.

After taking his doctor's degree he spent a year at Imperial College, London, where he studied atoms in strong laser fields. These laser pulses last 10^{-13} seconds and generate from one to ten TW, which corresponds to the amount of energy that up to 10 000 nuclear power stations like Barsebäck generate in the same time. In the high fields that arise then short-wave radiation is generated at odd multiples of the laser light's frequency. Many thoughts passed through Jörgen´s mind when he was doing this work about how it might be possible to utilise these short and short-wave laser pulses in various applications.

Rapid events and short distances

In his current project Jörgen will develop laser-based methods that can be used to observe atomic structures in solid material and to understand how laser radiation per se affects material. What interests him are the small changes that take place in the atoms.

"If we can find a technique that works, we will be able to observe and even control specific chemical processes in solid material to a considerably greater extent than at present," says Jörgen Larsson. "This will help us to understand the properties of various kinds of material and why they react in the ways they do."

To do this we can use X-ray diffrac-

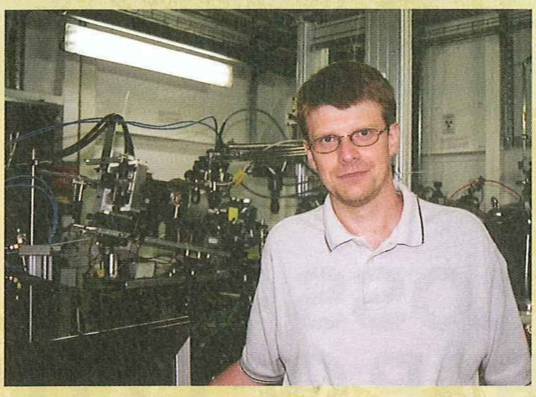


PHOTO: OLA SYNNERGREN

tion, by which a specimen is radiated with X-rays and, by studying the rays´ diffusion, get a picture of the structure of the specimen. If we want to study dynamic processes over a short period of time, the X-ray sources used must be considerably more short-pulsing than those in use today. The most intensive X-ray source in Sweden at present is the synchrotron source of light, MAX II, which happens to be in Lund. With this and by the use of fast detectors it is possible to study processes that last only $5 \cdot 10^{-13}$ seconds. In a synchrotron light source the electrons circulate at a speed close to the speed of light. By adding a magnetic field it is possible to get the electrons to change course and when they do so they emit energy in the form of light. What is unique about this type of light radiation is that it consists of wavelengths from a very wide spectrum, from long-wave visible light to short-wave X-rays. The divergence of this radiation is also minimal. Depending on how the rays spread, it is possible to read the specific pattern the atoms in the radiated material have. X-ray radiation has a wavelength of a few nanometers, which is about the same as the distance between two atoms in a randomly selected molecule. By making use of the advances that have been made in accelerator and X-ray physics in recent years, it will soon be feasible to produce electron pulses and hence X-ray pulses that are shorter than 1 ps. These techniques can also be used to investigate how laser-generated shock waves move through material and how these waves affect the atomic structure.

The future

Time-resolved X-ray diffraction technology is a relatively new field. In the world today, Jörgen thinks, there are only a dozen or so groups researching in this field. He himself has been in it from the start and believes that there will be rapid developments now.

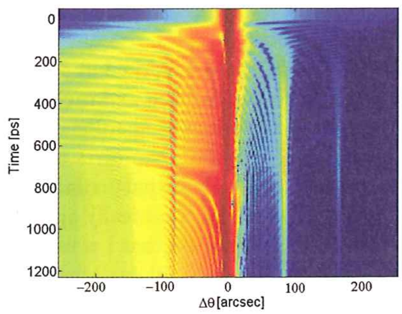
"In five-six years time I think it is reasonable to believe that we will have developed many of the analysis methods and that they will be available for use. I really think that we will also have begun to be able to diagnose and control both physical and chemical processes."

Today they are collaborating with the Department of Nuclear Physics at Lund Institute of Technology with the aim of improving a material used to encapsulate nuclear fuel rods, a zirconium alloy. The life of the fuel rods is limited by the fact that the outer material oxidises too quickly. If we manage to find out exactly what happens between the atoms, it will be easier to counteract oxidisation, thus making the storage capsules better and more durable.

"It feels great to have as long a period as six years with a secure financial situation," says Jörgen. In this field we usually think in terms of two to four-year periods. It means that I will be able to let my present research team of two postgraduates grow and establish a stable work situation.

Jörgen likes living and working in Lund. Apart from his year in London he has also worked for a few years at the university at Berkeley, California.

"Right now I don't long to move abroad. But I like travelling and I do quite a bit when I travel round doing my experiments."



Numerical simulation of a two-dimensional X-ray reflection curve. The reflection is shown as a function of both time and the angle of the crystal relative to the X-ray radiation.

Name:
Nils-Göran Larsson
Born:
1959
Nationality:
Swedish

Doctor's degree:
1992
Works at:
Department of Medical Nutrition, Novum, Karolinska Institutet

Project title:
Mitochondrial biogenesis

ENERGY LOSS – THE DEATH TRAP OF CELLS

Nils-Göran Larsson is searching inside cells for common causes of many of our widespread diseases: Parkinson's disease, Type II diabetes and heart disease.

The sky is blue and the sun is slowly warming the air on this morning at the Karolinska Institute at Solna. He is casually dressed and seems relaxed.

"I've always wanted to be a scientist. But I thought I ought to get a proper education first, so I became a pediatrician. Neither of my parents went to university, so going to university was something new for me.

Nils-Göran was born in Kristinehamn and you can still hear a faint Värmland accent when he speaks although he left his hometown a long time ago to start medical studies. He first worked as a doctor in Göteborg.

"That was when I worked at a children's clinic in Göteborg and met children who had serious congenital diseases in which the mitochondria in the heart and muscles in particular had impaired functions. That really opened my eyes and I realised that I would be able to do useful work although the research in that field had not really got going."

After ten years on the west coast as a doctor and researcher he set off for California and Stanford University, with its fantastic research climate, as he saw it.

"I was lucky enough to work with David Clayton, who had long experience of mitochondria studies. He taught me how best to create an environment where solving scientific problems was always in focus. This was how I wanted to work – long-term efforts to solve important biological problems.

After his stay in the United States he and his family moved back to Stockholm where he now lives in a house in Sollentuna. He spends a lot of his leisure time with his children, Erik (10), Siri (8) and Björn (6). They are the future. But Nils-Göran also likes to look back into the past.

"In recent years I've been reading a lot about the history of the Second World War. Its interesting to find out about the process that led to such an enormous human disaster and which until quite recently explained the political situation in Europe. If you know about the past, I think it's easier to understand today's society.

Function and effect of mitochondria

Nils-Göran Larsson has now been working for more than 10 years trying to understand what happens in the human body if the cells´ energy-producing capacity is damaged or completely destroyed. And this is where the mitochondria play the leading role.

Mitochondria are small components inside the cell. The mitochondrial respiratory chain produces the bulk part of cellular energy. Another important function that the mitochondria fulfil is to control programmed cell death, apoptosis. In normal cases this is a vital process ensuring that defective cells are broken down and disappear. But when cell death takes place in an uncontrolled way, tissue damage can occur.

Nils-Göran Larsson and his colleagues have now seen that there may be a connection between damage to the cells´ mitochondria and premature cell death in the brain.

"This may be a contributory cause of the development of diseases like Parkinson's. We also know that damaged mito-


PHOTO: ANDERS KALLERSAND

chondria can give rise to similar processes in cells in, for example, the pancreas, where the insulin-producing cells are destroyed, leading to diabetes. But our project also includes studies to determine the role that the mitochondria play in the normal ageing process."

Cells starved of energy

"In experiments mice have their mitochondrion function eliminated and the effects of this, if any, are documented. It is not possible to directly manipulate the genome of mitochondria, mitochondrial DNA, and we therefore chose to knock out a gene in the cell nucleus controlling mtDNA maintenance."

So as to be able to follow the process even more successfully the group uses a refined method that makes it possible to eliminate mitochondrial function in a single type of cell such as heart-muscle cells, insulin-producing pancreas cells or nerve cells.

"With the help of this method we can very exactly study the molecular consequences of reduced energy production in selected tissues. This makes it easier to understand the underlying mechanisms."

Compensation for survival

When cells have their energy supply reduced or completely eliminated, they try to compensate for the losses of energy by producing more mitochondria. But all the mitochondria that are produced will lack a breathing chain.

"The result is an enormous accumulation of mitochondria in the cells which cannot at any rate satisfy the need for energy. The cells end up in a vicious circle."

One experiment studied the long-term effects of this loss of energy. Mice had their mitochondrial function eliminated in the parts of the brain that are important for learning and the memory – in the hippocampus and the cerebral cortex. To begin with no change was noticed in the mice, but when they were five months old those areas of the brain suffered extensive cell death.

"It seems as though the cells cannot compensate for an impaired mitochondrial function in the long run. Loss of mitochondrial function causes cell death in a variety of tissues. If we can learn how to control the mitochondria´s ability to induce cell death, we would be on the right track for treating diabetes or Parkinson's disease.

Their own company

Nils-Göran Larsson and his colleagues now want to find out which genes which regulate mitochondrial mass in the cell. They are studying mice with an eliminated mitochondrion function in the heart, brain, skeletal muscles or pancreas so as to pinpoint a small number of genes that are active in all cases. With further experiments in the pipeline they hope to identify a few interesting genes for further animal studies.

Nils-Göran Larsson has started collaborating with his colleague Claes Gustafsson at the Department of Medical Nutrition at Novum. They met during their post-doctoral period at Stanford University. Claes is a protein biochemist and he is trying to identify the proteins that read the mitochondria's own DNA. They have recently started a company, MitoTech AB, together with another researcher, Claes Wahlestedt.

"Our company will try to develop medicines that affect the energy production of the mitochondria. The whole project is a long-term one, but I believe that the first results will appear quite soon."

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Project title:
Double-directional mobile radio channels

MORE ANTENNAS GIVE INCREASED INFORMATION FLOW

Many new wire-borne services have arisen as a result of the development of broadband services. If the wireless networks are to be able to offer services of the same quality, their information speed will have to be raised considerably. Andreas Molisch and his colleagues, with the aid of a new method, are going to utilise radio channels more effectively.

"When data is transmitted today in the form of radio waves, a system is used that has one antenna in the transmitter and one in the receiver. So that the waves do not interfere with each other, all radio users are separated, for example, by allocating each signal its own frequency band. A certain information speed demands a specific number of frequencies that has to be increased if you want to increase the amount of data transmitted per second by those traditional methods. Today there is a lack of frequencies within the range that can be used at present for radio communication, so an expansion of the bandwidth is expensive in many ways. Thus an increase in information speed using today's technology means that the whole system will be more expensive, which the users of wireless services will have to pay for in the long run."

A new method has now been developed called MIMO (Multiple Input, Multiple Output). Attempts are being made to increase information speed by utilising each frequency more effectively. MIMO has more antennas in both transmitter and receiver, so in contrast to the present system it can accommodate more signals in a frequency band. The transmitter sends information in parallel with the various antennas, and this information can then be separated at the receiver end, in part thanks to its numerous antennas.

"This means faster information transmission with fewer frequencies. This system can also be cheaper because the companies do not have to pay for such a large frequency spectrum."

The MIMO system has been pioneered at Bell Labs in the United States. In comparison with the old system, which at a certain bandwidth has a spectral efficiency of 1–5 bits/second/Hz (bps/Hz) for cellphones and 10–12 bps/Hz for stationary systems, it has been possible to attain a spectral efficiency level of 20–40 bps/Hz using the MIMO system.

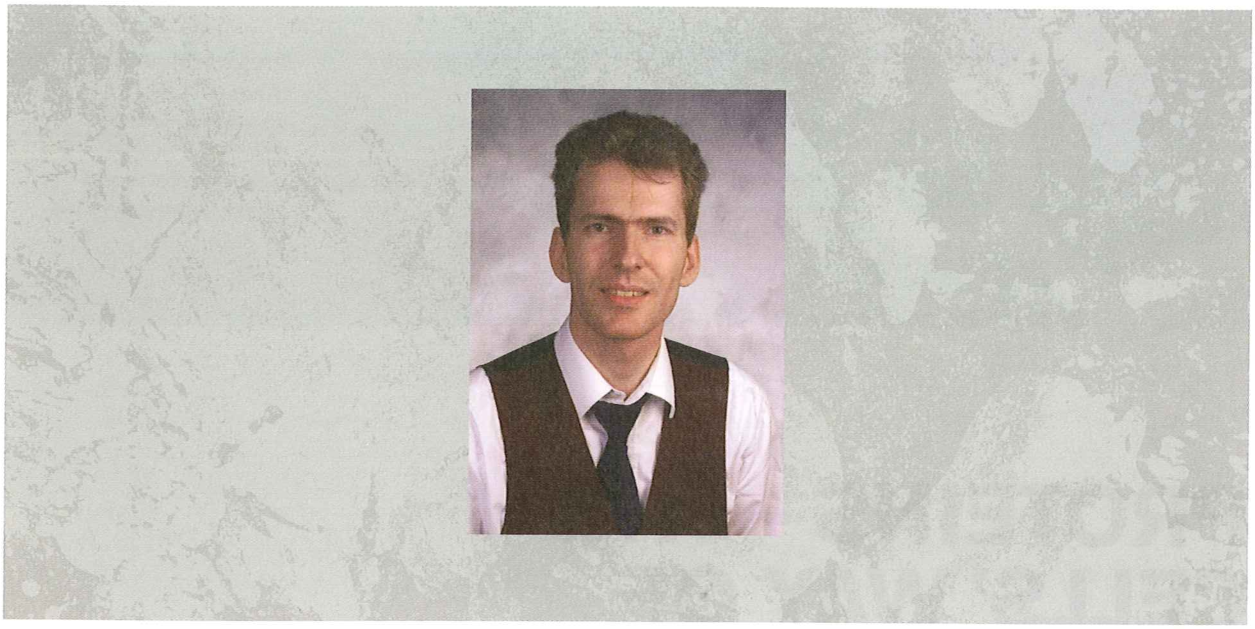
"That level of efficiency cannot theoretically be attained with traditional systems.

Even if the capacity is reduced a little when the system is tested outdoors, we are convinced that it will function better than the present system. We shall find out how information transmission can be optimised by studying the radio channels´ characteristics."

A refined system by analysing and modelling radio channels

If the MIMO system is to be tested and developed, statistical models will be required showing how radio waves behave in different environments. The mathematical descriptions of radio channels, so-called propagation models that exist today are based on transmitters and receivers with one antenna. That is why it is not possible to use these models to simulate the MIMO system. Instead Andreas and his colleagues first have to develop new propagation models that are suitable for MIMO.

When a radio wave is transmitted, it meets on its way from the transmitter to the receiver various objects that reflect and disperse it in various directions. All these partial signals lie within the same frequency range but can carry separate information streams. At the receiver the signals, which are now coming in from



different directions with different delays, are received by one antenna each.

"In the usual system reflections create problems because the waves can interfere with each other at the receiver antenna, which means that information is lost. But the MIMO system works better when signals come from several different directions. What we need to know now is which direction we should send the waves so that they deliver the information in the best possible way in different environments. We also want to find out what the resulting waves´ amplitudes, delays and arrival directions will be. These affect the receiver's ability to separate all the incoming signals from each other."

To get as many different parameters as possible, Andreas and his colleagues will carry out measurements in various environments, in both cities and rural districts. On the basis of these measurements they will then prepare propagation models that can be used for developing the MIMO system. These measurements will also provide information about the effect of the environment on the system's capacity.

"The idea behind these experiments is that the systems developer will discover new ways in which the capacity and range in various environments can be improved on the basis of the measurement results and the propagation models."

Dancing to music

Andreas was born in Vienna and studied at the institute of technology there. After having taken a doctor's degree in electrical engineering he started working in a research group that was studying mobile radio channels. Two years ago he visited Lund Institute of Technology and met Professor Per-Ola Börjesson there, who is now one of his colleagues in the MIMO project. Andreas divides his time between Lund and AT&T Labs in the United States, where he is running a project on mobile radio channels.

"In my various projects I'm studying both wave routes between transmitter and receiver and how the receiver receives signals and processes the information. These two areas are usually kept strictly apart, but I think it is important to try to have as broad a research project as possible. That's when you discover the interesting connections."

He is an inquisitive researcher with a somewhat unusual hobby.

"I love dancing and have been practising and competing in dances like tango and slow waltz for thirteen years now. It's a very good way of getting exercise as well as being great fun when you feel that you and your partner are on the same wavelength. As I like listening to classical music and have played the piano for quite a few years, this hobby suits me perfectly. My two interests, music and dance, are combined in a very happy way."

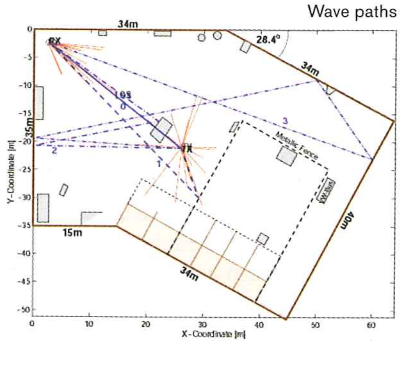
Flexible electronics a necessity

Andreas and his colleagues can foresee two main applications for the MIMO system.

"One application is in cellphones. These are dependent on the transmission of information functioning well during movement, which means that the system has to be able to adapt to changes in the environment. But cellphones do not yet make very high demands on data capacity. The other field in which the system could be useful is when laptop computers are connected to the Internet via wireless connections. In the future there will be outlets for wireless net connections in more and more places, for example at airports or railway stations. Here there will be a need not so much for coping with movement but for a considerable data capacity.

"The flexibility that is required places great demands on the electronics in the system. But when that problem is solved, new, higher quality wireless services will be available."

Wave paths



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Project title:
Structural intermediaries of membrane proteins, soluble proteins and photochemical systems

PROTEINS – THE CELLS' WAY OF COMMUNICATING

Nobody would believe that a New Zealander could feel at home in Sweden because of the weather. Nor that he would because he grew up on a farm. Richard Neutze, who has changed both his field of research and his continent, enjoys living in Göteborg.

Richard Neutze came to Sweden almost four years ago. He had left his home country, New Zealand, two years before, to go to Oxford and do research in biophysics. After that he continued doing research at Tubingen in Germany. As a boy he was fascinated by the universe, wondering if it had a boundary or not. These thoughts led him to study physics, but now he has changed direction.

"I took my doctor's in physics and it wasn't until my thesis was completed that I decided to change course and study biology."

The reason was that Richard thinks there is more to discover in biology. Different fields are beginning to move together more and more and the technologies used to study biological systems often stem from what has been discovered in physics. As an example Richard mentions nuclear magnetic resonance spectroscopy (NMR), with the aid of which small biological systems can be studied. After Richard had moved to Uppsala four years ago, he began to look more closely at various types of proteins found in cell membrane. With his background in physics he thinks he has quite a few advantages that help him to see applications that would not be so evident to a biologist.

"Instead I have the disadvantage that I lack parts of biology, but I'm learning something new every day and this switch is very stimulating."

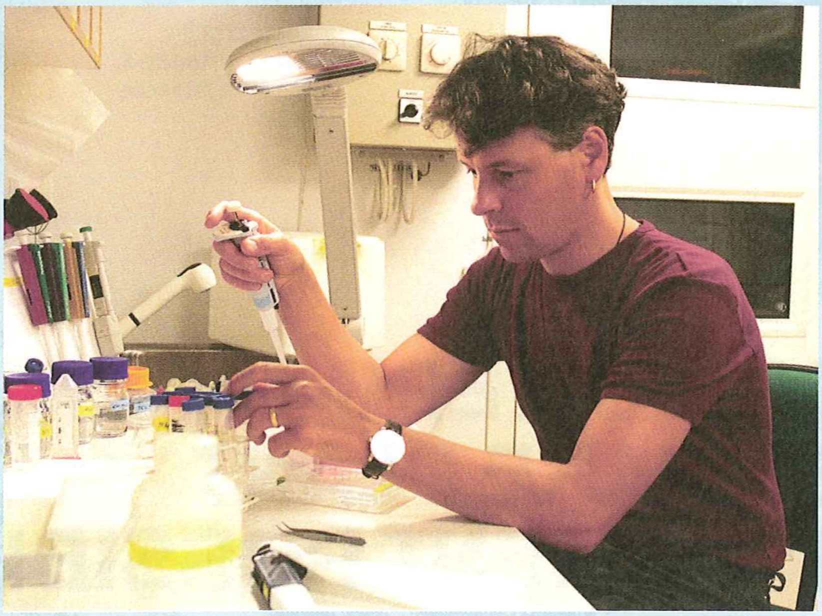
After having worked for three years on protein crystallography at Uppsala, Richard moved last autumn to Chalmers. His main goal is to establish a crystallography lab in Göteborg. He also hopes to be able to develop the methods that are used to study proteins. In addition he looks forward to deepening his own knowledge of biomedicine.

"I believe that the boundaries between scientific fields will soon not be as sharp as they are today. As a researcher I believe that you really benefit from interdisciplinary thinking."

Important proteins

Proteins in membrane have several functions. One of the more important of these is to transport ions from one side of the membrane to the other. This ion transport is the basic mechanism by which all living organisms (bacteria, plants and animals) transform energy from one source, like light or food, into useful chemical compounds. This transformation is essential for the organism to be able to carry out vital functions. To be able to better understand how energy transformation in a cell takes place Richard and his group have studied a protein called bacteriorhodopsin. Bacteriorhodopsin is the light-driven proton pump that has the simplest known structure. It functions as a pump that absorbs energy from a single photon and uses it to take ions in a controlled way in and out of the cell. These proteins are found in a bacterium that lives in water with an extremely high salt content, as in the Dead Sea, for example.

There are also other families of membrane proteins that can mediate signals in and out of cells. Certain bacteria, for example, use the wavelength of light to decide in which direction they should swim. To manage this they have two proteins in their membrane, sensorrhodopsin I and II. When the sensorrhodopsin



molecule is hit by light, it changes its structure, which in turn transmits a signal into the bacterium that stimulates it to swim in a certain direction. The structure of these proteins is repeated in several other membrane proteins and is used as a model for studying the mechanisms. Now Richard wants to try using the same methods to study similar proteins. He has become interested in a large group of proteins with a structure that is very like that of the bacterio- and sensorrhodopsins but that deal with signalling within the cells. They control a number of important functions in the body including vision. The methods used are crystallography or X-ray diffraction. The equipment is called an X-ray synchrotron and when experiments are to be carried out, Richard and his team go to Grenoble in France, where Europe's most powerful X-ray synchrotron is found. They spend a few intensive days a year there, carrying out their experiments. The specimen that is radiated consists of a complex of millions of identical copies of one and the same protein in a crystal. When the X-rays strike the protein crystal, the light is spread in different ways depending on its structure, and by means of a detector it is possible to get a picture of the protein's structure.

"It's a nervous business to go off to another country and carry out a large number of experiments in one go," says Richard. "You're nervous until you get back home and can decide whether the results you have obtained provide valuable information." Both during his work in Sweden and when he is doing experiments in France, Richard says, he gets a lot of help from his colleagues, both those in the home lab and his collaborators out in the world. Together with two Swedish groups, for example, he has begun to study other types of proton pumps that transport protons across the membrane with the aid of light or energy from food.

"By studying what happens at the atomic level when the charges move between the molecules or signals are sent through the cell we can place our discoveries in a medical context. Both processes are decisive for all living material and the results we have got from X-ray crystallography have helped us to understand many of the basic events that take place in all types of cells."

Problem-solving at sea

One of the main reasons why Richard left Uppsala for Göteborg was that his wife Helena also lives and works there. But the move also meant a change of work for Richard, so he was able to start his own research group. He likes living in Sweden even though he has to put up with a somewhat lower average temperature than in New Zealand.

"I have a farming background and grew up on a farm. When I came to Sweden, I found out that almost all Swedes´ grandparents were farmers. Farming society has certain sets of cultural values that suffuse the whole of society, which gave me a sense of belonging. I didn't get that same feeling during the years I was in England, which in other respects is usually regarded as our home country."

Richard, who has studied leadership training in New Zealand, also looks forward to developing as a leader. He was involved in a project in which youngsters lived on a boat together to learn how to cooperate and solve problems. In his free time he has a sailing boat which he likes to use, though not mainly for problem solving.

"Sweden is really a fantastic place to sail in."

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1964
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Doctor's degree:
1995

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Project title:
Control of flowering in annuals and perennials

EARLY FLOWERING TREES MAKE PLANT IMPROVEMENT POSSIBLE

A great deal of our food, like cereals, rice, maize and fruit, has been improved over the years by crossing different flowering crops with each other. Trees, on the other hand, have not been possible to improve since they do not flower until after ten to twenty years. Ove Nilsson is now making use of a weed, Thale cress, to get aspens to flower earlier, which is of great interest for plant improvement.

"People have always dreamt of being able to control the flowering of plants. They would then be able to make sure that flowering took place when the weather is at its best, or get it to occur earlier so as to get more harvests per season. Flowering is also a prerequisite for plant improvement."

One example of what traditional plant improvement has achieved is our cereals. To start with, two sorts of cereals were crossed with each other, both of which had desirable characteristics. After generations of crossing and selection we have today cereals that not only produce more seed but are also smaller, more stable and more resistant to different kinds of diseases than the original grasses. By selecting for different flowering times it has also been possible to make them more frost-resistant.

"In the past few years transgenic technology has come to agriculture. Almost all maize, soya and cotton cultivated in the United States today has been changed by transgenic methods. Maize has been developed that is poisonous for pests but not for humans, and "Frankenstein" tomatoes that do not rot. Some plants have also been made herbicide-resistant, which has resulted in a reduced use of herbicides and a trend towards more environmentally-friendly insecticides and pesticides."

In forestry, on the other hand, neither traditional plant improvement nor transgenic technology have come so far because it has taken too long to develop flowering trees.

"But more recently transgenic technology has made great progress in forestry as well. Our aim is now to investigate, with the aid of the new technology, how flowering is regulated, partly to make tree improvement possible and partly to make the improvement of agricultural plants more effective.

The weed that became famous

When Ove was a biologist with an interest in molecular biology, he was offered a postgraduate scholarship. It was to study with Sweden's first plant-molecular biologist, Olof Olsson, and Ove accepted the offer at once. He left Göteborg for Umeå and the University of Agricultural Sciences, SLU.

"Together with hormone physiologists from SLU we introduced a growth-hormone gene from a bacterium into aspen trees. This meant that we could influence the trees´ development and after a time we were the first research group in the world to produce a transgenic tree that had had its growth altered. This was really a push in the right direction.

But to be able to use his new knowledge Ove felt that he needed to learn more about molecular genetics and various model systems in plants. The weed Thale cress was, and still is, the most fully developed model system.

"The reason why we use Thale cress, *Arabidopsis thaliana*, is that it is a small plant that doesn't need much space to grow in. It also flowers early, sometimes as early as two weeks after the seed has germinated. As a self-pollinating plant it is easy to cross it both with itself and with other plants. It also has a very small genome with a very small amount of unimportant gene material, and it is now the first plant in the world to have been completely sequenced."

PHOTO: MIKAEL LUNDGREN

Ove moved on to Detlef Weigel at the Salk Institute in La Jolla, just north of San Diego.

"Detlef Weigel had previously isolated a gene he called LEAFY which was necessary for Thale cress to flower. All plants have a LEAFY gene and from the cells where it is active flowers are formed, while cells that lack the active gene develop into leaves or shoots. When I went to see him he had just put a LEAFY gene into a tobacco plant, with the result that the plant flowered after only a few weeks instead of after four months. This was fascinating and I knew that I wanted to try putting the gene into aspen trees."

Against all odds this gene transfer functioned at the very first attempt and the aspen began to flower after a few months instead of after eight to twenty years.

"Our scientific article had an enormous impact in the American media and in Europe as well. This was the first time it had been possible to show a direct application from research into Thalia cress, which many people had thought was of no use except for pure basic research. Today we can see that research into Thalia cress has led to a large number of very important commercial applications.

Bass singer and a hiker

Apart from being part of the recently started company SweTree Genomics, Ove is also one of the bass singers in the Chamber Choir called Sångkraft. In May this year it gave a jazz concert with music by the composer Gene Puerling, and last summer they won the big choir competition Choir of the World in Wales. Music is central in Ove´s life and when he is not singing himself he likes to go to listen to the Umeå Symphony Orchestra or an opera at the Umeå Opera House.

"Umeå is a good-sized town. Although it has a rich cultural life it's not too big, so transport isn't problem. The only negative side is the climate. Even though I've got more or less used to it I still get the Arctic blues when spring and early summer don't make an appearance."

Despite his Arctic blues he is attracted by the Swedish mountains.

"I've hiked in many parts of the Swedish mountains, but one of my favourite places is Ammarnäs in the Vindel Mountains. It's a beautiful little village where the road comes to an end in one of Sweden's relatively unknown wildernesses."

Identifying genes that control flowering

For four years now Ove has been a research assistant at SLU in Umeå. Instead of directly studying the LEAFY gene in Thale cress, he is concentrating on the genes that control its activity. This is where flower formation really starts.

"Nearly all the LEAFY gene's regulating genes, in contrast to the LEAFY gene itself, are affected by outside environmental factors such as light, temperature and access to nutriments. But there is a group of genes that seem to control the flowering time of Thale cress in the absence of flowering-inducing factors in the surroundings.

They are the genes that that control the formation of the growth hormone gibberellin. This is similar to the conditions in the aspen, whose flowering is not controlled by surrounding factors either but is only activated when the tree has reached a certain age. Quite a large part of my studies will therefore be devoted to studying gibberellin regulation of flowering in Thale cress and comparing this with conditions in aspen"

Thale cress flowering is dependent on the length of the day insomuch as it flowers early during periods with long days, while during periods with short days it flowers late. Besides studying the gibberellins they will use Thale cress plants that have grown during short days and thereby regulate their flowering in a way that is like the way in which aspen flowering is controlled. They can then also compare the two plants´ genes, with the aim of discovering if aspen flowering is controlled in the same way as Thale cress is.

"We also want to identify completely new aspen genes that might control the flowering time. To be successful with this we have, in the big Poplar-EST project, isolated and sequenced a large number of aspen genes that are active in various tissues. The specimens are taken from various parts of the trunks, leaves, shoots and flowers. In this way we can get a large number of activated genes that can be compared with the genes of interest in Thale cress. So far we have sequenced 50 000 genes in aspen and identified 13 000 other ones. Among them we hope to be able to ring in a number of interesting genes whose activity is on or off during the period up to or at the development of the flowers. These genes may be involved in regulating when aspens flower and may explain why aspens do not flower until after 8–20 years.

So far LEAFY-induced flowering in aspen has been rather abnormal and resulted in half-sick plants. This is probably due to the fact that from the start it is not the LEAFY gene that determines when the tree will flower but rather where the flowers will be formed.

"If we manage to identify the genes that control LEAFY instead, we believe that the trees will be healthier and have more normal flowering. Then large-scale tree improvement will be possible."

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Project title:
Hormone regulation of bone tissue

NEW OESTROGEN-LIKE PREPARATIONS WILL REDUCE THE RISK OF POROUS BONES

Osteoporosis is one of the diseases that is increasing most in the western world. Claes Ohlsson is going to investigate how the three hormones oestrogen, somatotropin (growth hormone) and thyroxin affect the skeleton.

Sahlgrenska University Hospital is enormous. And if your lab and your clinic are at one end of the building complex and your office is at the other end, it feels even bigger. Claes Ohlsson sits down at his desk, slightly out of breath, but quickly collects himself.

"Brittle bones or osteoporosis as it is also called means that the amount of bone tissue decreases. So the skeleton becomes brittle and patients often suffer from fractures of the hip and vertebrae."

The risk that Swedish women will suffer from osteoporosis is amongst the highest in the world, and at the age of 80 half of all women will have developed the disease. Its development is connected with the renewal of bone tissue.

"Bone is not a static tissue but is renewed throughout life. Two different types of cell interact: osteoblasts are the cells that build up the bone, while osteoclasts are those that absorb and remove bone tissue. The level of activity of these cells is regulated by oestrogen, somatotropin and thyroxin, and it is when osteoclast activity gets too high that osteoporosis can occur."

Increased risk after the menopause

As well as protecting the soft parts of the body, bone tissue also plays a part in regulating calcium in the body. The older one gets, the more difficult it is for the body to absorb and use calcium. This leads to the important calcium balance between blood and bone tissue being more easily upset, which results in more fractures.

The greatest increase in the risk of fractures comes with the menopause, when the oestrogen content decreases greatly in women. The osteoclasts, which are normally inhibited by the oestrogen, become more active and the bone tissue becomes thinner. Other factors contributing to osteoporosis are physical inactivity, a poor diet and smoking. Being fat, on the other hand, protects bone from osteoporosis.

"When you are fat, the skeleton is continuously and more heavily stressed. The bone gets stronger and can take greater strains. So if a heavily-built person falls over, it doesn't put so much extra strain on the skeleton, as it does with a person who is very thin. So if old people were not so thin, they would manage better."

Doctor in research

Claes Ohlsson has always worked both as a physician and as a researcher. As a clinical doctor he is well acquainted with the ways in which all the organs of the body work and can more easily draw conclusions and parallels from his research work

"It's important not to be blinded by one's own little field but to be open to new ideas and make use of information in many fields. That's how you get the interesting angles on things. There are not so many doctors in training today who are planning to go into research, which is a great pity. We need greater variation among researchers."

Claes collaborates with many doctors and researchers and looks after four postgraduate students himself. He had already established his research team in Göteborg when he went to the United States for post-doctoral studies in 1996. So for two years he had to try to keep in

touch with his colleagues at home in Sweden.

"I guess I've got to be something of an e-mailaholic, because I can't stop sending mails once I've started. It might be a bit stressful for my colleagues when they see that one was written in the middle of the night at the weekend," he says with a grin.

But he also points out that communication is vital for the progress of research.

Reduced risks of side-effects

Many women today take oestrogen pills during and after the menopause. The problem with this medicine is that it has proved to have side effects. At the same time as they reduce the risk of osteoporosis, cardiovascular diseases and perhaps, according to the latest reports, Alzheimer's, the risk of developing breast cancer and thrombosis increases.

"The best solution would be to develop an oestrogen-like preparation that increases the positive effects of oestrogen at the same time as it avoids its negative effects. The existing medicines bind unspecifically and only partly to the oestrogen receptors, which sometimes results in the hormone affecting the wrong tissue, with side effects as a result."

There are at least two variants of the oestrogen receptor, called alpha and beta, and they are found to different extents in different organs. If it was possible to discover where the different receptors are and how the function, the chances of preventing and treating osteoporosis would increase considerably.

"It should be possible to produce some oestrogen-like preparations that only bind to alpha receptors and others that only bind to beta receptors. That would mean that the oestrogen receptor could be stimulated in certain organs, like the skeleton, and inhibited in others, like the breast

Interaction of oestrogen

To produce optimal oestrogen-like medicines it is necessary to understand how oestrogen interacts with somatotropin and thyroxin. That is why Claes Ohlsson and his colleagues have bred unique gene-modified mice. These mice have lost their oestrogen, somatotropin or thyroxin receptors. The hormones affected cannot therefore bind to their receptors and do not function, which has various effects on the bone tissue.

"By carrying out the same experiment in several different tissues for the respective hormones we hope to be able to draw even better conclusions about how the hormones interact with their receptors and thereby affect the bone tissue in various ways. Then we can obtain the positive effect on bone at the same time as the risk of side effects in other organs is reduced."

Youthful nature lover

Claes grew up in Göteborg and has lived all is life close to water. He likes to relax at sea as well.

"I don't have a boat of my own, but the past seven years me and a few friends have hired a boat for a week and sailed along the west coast. It's a very enjoyable and effective way of keeping in touch with friends – we have time to chat about everything under the sun. And it's so unbelievably beautiful out among the islands with their bare, open landscape."

"Do you see yourself as an adult?"

"Not really, if you want to be a good researcher you have to keep your childlike curiosity alive. And I think my colleagues would agree with me, because when I started as a professor at the department here I got a radio-controlled car as a present. That says quite a lot, doesn't it!" he says with a laugh.

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Project title:
Biomimetic and biological cells and cell networks for complex biosensors and bio-computer systems

INTELLIGENT NETWORKS OF ARTIFICIAL NERVE CELLS

Owe Orwar's research group at Chalmers in Göteborg is developing methods for creating "intelligent" networks of artificial cells and nerve cells. These networks should be able to receive chemical and physical signals, process them and store the information in a kind of chemical circuit. This project brings together subjects like nanotechnology, bioelectronics, biophysical chemistry, cell biology and biomimetic materials science. The goals range from understanding how chemical reactions take place in small-scale space to complex sensor systems for robotics and biological and chemical computers.

An artistic chemist

As a 17-year-old at high school in Helsingborg Owe was fascinated by the nerve system and how the brain functions. This fascination drove him to browse in all the second-hand bookshops in Helsingborg to find books that could still his thirst for knowledge.

"I can't say that I understood much of what was in the books I found. But I realised that a lot of the research in this field took place in Göteborg."

Laser-based measuring methods for identifying peptides in the central nervous system was the subject he later chose for his doctoral thesis at Göteborg University. After two years at Stanford University in the United States he is now back in Göteborg and has now for the past year been professor of biophysical chemistry at Chalmers. But for a long time he could not think of being a chemical researcher.

"I got involved in film and music when I was a boy and I thought that my future would be in one of the artistic professions. The nerve system and chemistry was just a hobby, but now it's the other way round."

The old neurological books left their mark and a central part of his research today deals with the way in which nerve cells in our body function and how knowledge of this can be used to build biological and chemical computers.

Artificial cells

The research program he is going to work on now has two lines. The first aims at creating small intelligent networks of artificial cells by means of micro- and nano-manufacturing technology. These networks consist of small spherical containers called lipsomes that are connected together with nanotubes. Methods have already been developed for introducing one or more chemical reaction systems into individual cells. Thus each individual cell in a network can carry out a unique chemical operation on an incoming chemical or physical signal that is transported via a nanotube from another cell, or is introduced to the cell via a membrane-bound protein. Orwar sees the fact that proteins can be integrated into the walls and into cavities in the artificial cells as a key factor.

He describes proteins as ingenious molecules that combine advanced functions with small scale. The networks that are built of artificial cells are like LEGO, where the parts consist of spherical cells and nanotubes of various sizes and crossings between nanotubes . The functions of the networks are largely determined by the proteins that are introduced into the various cells.

"It is fascinating that different proteins can do so many different things. They catalyse specific reactions, function as light and current detectors, identify scents, flavours and a lot more. The fact that we can introduce proteins into networks means that can use this broad repertoire of properties to create networks with complex functions."

Now Orwar believes it is possible to design networks for a wide range of applications. Since it is possible to transport chemicals in the networks and initiate chemical reactions in the cells in a controlled way, there is a good model for studying chemical reactions in spaces so small that they resemble the environ-


PHOTO: JAN-OLOF YXELL

ment in a biological cell.

"I also see great possibilities for designing networks that function as chemical sensors and computers. You can even imagine building logical circuits based on chemical kinetics and optimal structures for DNA-based computing algorithms.

It is particularly interesting that these networks can function together with various membrane proteins and so receive information in the form of various kinds of chemical and physical signals."

Orwar hopes that these artificial cell systems could be connected to microelectronic circuits and get them to communicate with each other.

"Chips like these, for example, could be used to equip a humanoid robot with advanced sensor systems that could register many of the stimuli that activate a mammal´s brain. A more distant goal is to build integrated sensor and computer systems based on artificial cell networks for robotics that, besides receiving information, could also remember and draw conclusions.

The simplest systems of artificial networks are no bigger than a few micrometres. Even now the group is working on nanorobotics, small cell-like robots that can move to a target area and carry out a specific operation there.

"The applications for such minute robots are countless," says Owe. If we let our imagination run wild, we can think of everything from robots that go in and heal gastric ulcers or remove tumours to robots that clean a computer screen of dust particles."

Designed nerve-cell networks

The other part of the research program aims at constructing complex nerve-cell-based biosensors. By integrating a nerve-cell network with a detector in the form of a silicon chip it would be possible to measure and register activities in each individual cell with very great sensitivity. More specifically the aim is to create techniques that can in parallel measure activities in individual receptor proteins. The group has already developed methods for genetically or chemically manipulating individual cells in a network. They now think that a combination of these two techniques will create new possibilities for investigating how nerve cell circuits function, for example in the human brain. The group has already proved that individual nerve cells can be used as detectors for drugs and the body's own substances that function as signal substances in the brain. They now believe that it is possible to design nerve-cell circuits on, for example, silicon chips that are optimated for complex sensor functions, for example for drug identification and for robotics.

A wide range

The work in Orwar´s group spans many of the traditional scientific boundaries. It is the meetimg place for chemistry, biology, physics, nanotechnology and electronics.

"We don't all have special competence ourselves but we have built up a good network both in Sweden and abroad. The students who come here to work with us have a very wide range of backgrounds as doctors, engineers, biologists, physicists and chemists."

Apart from the scientific breadth of their work, Owe points out something else that is important for his research – to be on the alert for the unexpected. Exciting results often pop up when one least expects them and often when one is actually looking for something else. And then it's vital not to ignore them.

Outside his work, too he has a wide range of interests in music, pre-Colombian textiles, Formula 1 racing, medieval, renaissance and modern painting and the history of furniture.

"The most important driving force in science and in life is curiosity."

Name:
Stephanie Margret Reimann-Wacker
Born:
1968

Nationality:
German
Doctor's degree:
1995
Works at:
Lund Institute of Technology

Project title:
Nanostructured quantum systems

ARTIFICIAL ATOMS FOR REAL ELECTRONICS

Stephanie Margret Reimann-Wacker is devoting her research to physics at the smallest level. Devoting oneself to artificial atoms in semiconductors might seem like hocus-pocus, but for Stephanie it is everyday reality when she tries to find out how they can arise.

From Germany to Scandinavia

Stephanie came to Malmö in the summer of 2000 to pursue studies in her field: physics at the smallest level. After reading physics at university in Germany she went on to take her doctor's degree. Soon after her thesis was presented in 1995 she went to Copenhagen and worked there for three years. During those years she met her future husband, Andreas, who she married this summer, and they are expecting their first baby in November. Andreas lives in Germany at present because it is difficult for him to find a job where Stephanie is.

"We do research in the same field – and unfortunately that's a rather limited one."

When Stephanie left Denmark, it was time to go to Finland for two years. Now, when she is living in Lund and working as a research assistant, you can say that she has tested life in Scandinavia. But Stephanie's first visit was something extra special. As an eighteen-year-old interested in physics she won a prize in a scientific competition, which led to an adventure.

"The prize was a trip to Stockholm, to take part in the Nobel festivities. That's not bad as a first impression of Sweden"

Artificial atoms

Stephanie is trying to gain an understanding of small and fundamental processes in physics. One type of substance she has looked at closely is semiconductor material of extremely small dimensions. The size is so small that classical physics laws can no longer be applied but have to be replaced by those of quantum physics. Electrons and other constituents of the atom do not behave as we are used to on extremely small scales. A very exciting discovery that has been made is that it is possible to create artificial atoms. When several layers of semiconductor material are placed on top of each other, a thin coat of electrons is formed between the layers. If a metal contact is placed over all of it, and an outside source of electric current is introduced, the electrons are forced to keep within certain limited areas. These small areas are called quantum dots. If these dots are made sufficiently small so that the laws of quantum physics begin to apply, it turns out that the quantum dots start to form fixed structures. They begin to look like atoms, both in form and in properties, so much so that they can be considered to be artificial atoms. Just like atoms there seem to be certain structures among the dots that are more stable than others, comparable to the noble gases. These quantum dots are not found in nature but have only been observed in the laboratory. Much about their origin is still unclear, and that's what Stephanie wants to do something about.

"My research aims at gaining a theoretical understanding of how artificial atoms behave, how they interact and how the electrons in them react to different situations. If we learn how to master and control these atom-like structures, they might be of use in a number of areas, among which small electronic structures is one of the most interesting."

Stephanie goes on to talk about the possibilities she believes lie hidden behind artificial atoms. Perhaps magnetic effects that they give rise to can be used, or it might be possible to build arti-

PHOTO: JOACHIM REIMANN

ficial molecules from them for technical purposes. Right now Stephanie is most interested in the fundamental theory behind particle systems.

"Of course I have ideas for applications in the back of my head when I work, but just now it is basic research and fundamental understanding that are my greatest interests."

Stephanie believes that it is of the greatest importance for industry, if it wants to make use of these quantum physics systems, that it has really understood the mechanisms that lie behind all the processes.

"Certainly we need technical development, but it's not enough just to invest in directly applicable research if you want to get lasting results."

Fundamental theories

Stephanie says that it is extremely important to learn to understand the fundamental theories that lie behind processes. It is not always research focused on a specific goal that gives the most exciting results; it must be possible for researchers to be driven by pure curiosity. She mentions laser beams as an example.

"When the laser was being developed, no one really knew what practical uses it would have. It was something else that drove research forwards. But when the characteristics and function of laser had been learnt, the applications emerged."

Stephanie herself works mostly theoretically with computer modelling. She collaborates with various groups all round the world who are working both theoretically and practically with experiments. At present she is working mostly on her own and her goal is to start a research group consisting of both postdoctoral students and postgraduates. Her aim is a successful, efficient group, which is not something you produce at the drop of a hat. She looks forward to learning more about leadership and thinks that good communication within the group is one of the most important factors for successful cooperation.

Something that has accompanied Stephanie through all her years of moving house, studying and doing research is her cello. She has played the cello for a long time, preferably chamber music. When there's time for it. Much of her spare time is spent on another favourite hobby.

"I love sailing, so it's easy for me to enjoy life here. The west coast of Sweden has fantastic sailing waters, so I have no difficulty in making holiday plans."

Name:
Agneta Richter-Dahlfors
Born:
1961
Nationality:
Swedish

Doctor's degree:
1995
Works at:
Centre for Microbiology and Tumour Biology, Karolinska Institutet

Project title:
Bacterial induction of oscillations in the calcium concentration of cells as a new form of treatment

BACTERIAL POISON CONTROLS THE GENE ACTIVITY OF CELLS

Agneta Richter-Dahlfors wants to find out what it is that keeps us healthy. Now she and her colleagues have found a bacterial product that makes the body's innate immune defence more effective.

"Throughout our lives our bodies are exposed to bacteria. Although our air passages, our stomach and intestines and to some extent our urinary tract are exposed to many thousands of bacteria every hour, it is extremely seldom that they cause any illness or disease. That is because the body has an innate immune defence that can quickly be activated to keep the bacteria in check."

Along the air passages, the gastrointestinal tract and the urinary tract there is a protective mucous membrane. It is the cells in this mucous membrane, called epithelium cells that meet the bacteria first and start up a defence reaction. Agneta has now found an interesting bacterial product that affects the epithelium cells in a completely new way.

"By changing the calcium concentration inside the epithelium cells, the bacterial products can be made to increase the cells´ production of their defence substances. Thus the immune defence becomes more effective."

Memories from the other side of the Atlantic

After a while the smell of coffee begins to rise from our cups and spread round the room. Agneta looks happy and talks quickly but concisely.

"I've always thought that, if I went away somewhere, I would want to do something really good. After high school many of my classmates went off to be au pairs in various countries, but I refused. If I was going to move abroad, I wanted to have a job where I would have a chance to learn about the country's people and its culture."

Agneta´s dialect reveals that she comes from Karlstad. After taking her doctor's degree in microbiology at Uppsala Biomedical Centre she and her husband Christer wanted to realise their dream to live abroad for a year or two. They studied the map of the world together, with the result that they went to Vancouver in Canada. Christer took a year off from his job as an economist and studied computer programming while Agneta got a post-doctoral scholarship at the University of British Columbia.

"There was a chummy atmosphere at the lab. All my colleagues were incredibly friendly and relaxed and we quickly made friends. In our free time we would go down to the beach which was only a few minutes away and when you got tired of sun-bathing and swimming you just needed to put on your slalom skis. You see, Vancouver has mountains 1200 metres high that are covered in snow most of the year. As you might imagine, our friends in Sweden wondered whether we would ever come home again."

But they did and since 1997 they have been living in a house at Saltsjö-Boo. Christer has gone back to his old job as an economist and Agneta is working at the Microbiological and Tumour Biological Centre at the Karolinska Institute in Solna.

Calcium frequency is an important factor

Calcium ions function as messengers inside cells, regulating the cells´ activities. Paradoxically enough it is the calcium ions that give the signal of both life and death to the cell. Although an incre-

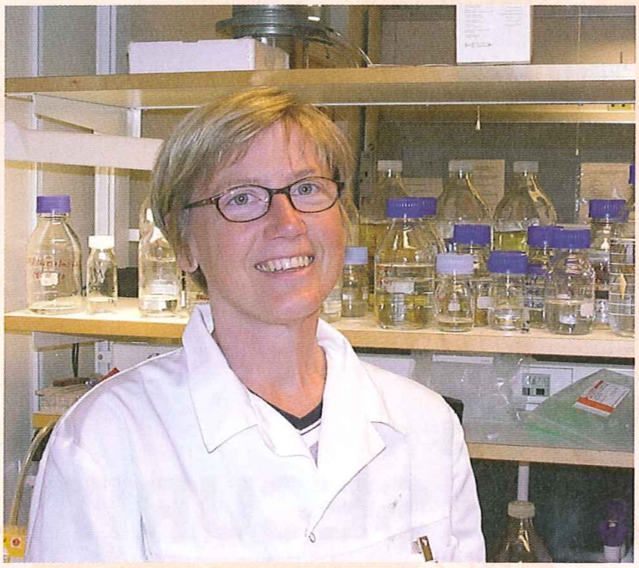


PHOTO: TOMAS SÖDERBLOM

ase in the calcium level is necessary for the calcium ions to be able to give a signal, the cell dies if the calcium content is too high for a long time. That is why cells often use repetitive signals called calcium oscillations.

"Now we want to find out how the bacteria affect the calcium oscillations. Quite recently we showed that the frequency of the oscillations that our bacterial product causes leads to certain genes in the immune defence being activated. If we can find out which genes are activated at what frequencies, we can customise production of the substances that produce the specific calcium oscillations. Thus we can get the cells themselves to produce the desired defence molecules. Then we wouldn't need to use antibiotics as often, which would reduce the risk of side effects such as disturbances of the intestinal flora and the emergence of antibiotic-resistant bacteria."

A popular partner

Agneta collaborates with Anita Aperita, who is a professor at the Department for Women's and Children's Health at the Astrid Lindgren Children's Hospital. Together

They produced results about the frequency-dependent activation of genes that attracted a great deal of attention, including requests from other researchers. One of them was Professor Katsuhiko Mikoshiba from the RIKEN Institute in Tokyo who has done pioneering work on the role calcium oscillations play in the transmission of information in the nervous system.

"By bringing together his and our know-how we hope to get even more knowledge of how bacteria can affect signals in various types of cells. And in doing so we may be able to understand how certain nervous diseases arise and how they could be cured."

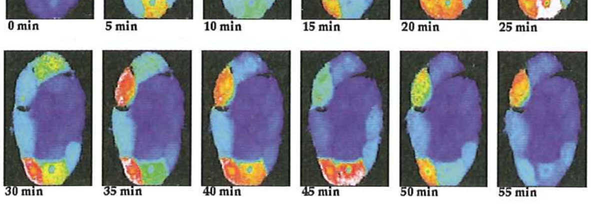
Quality of life

Agneta puts the quality of live before the quantity of life. This priority has been self-evident since she moved to Stockholm and has to travel two hours a day. She tries not to be sucked into the fast pace of life in society but treasures the time she has with her family and friends. And the quality of life for her can be anything from being out at sea on a sunny summer's day or just living in the present.

"This morning when we were having breakfast together, it struck me how lovely it is to be able laugh and have fun instead of rushing off to work, slightly irritated, as so many people do. You don't lose any time by being cheerful- rather the opposite."

She also sees positive thinking as one of the most important qualities a good leader should have. If you can't get your colleagues to enjoy life and their work, it's more difficult to get interesting results. And live gets boring.

"I hope that the positive attitude to life that my husband and I have will be passed on to our daughter, so that she continues to be the happy little songbird she is today."



Approximately 15 cells. The basic level of calcium in the cells is shown at time zero (blue). When the bacteria product is added, the cells change colour after only five minutes, indicating an increased quantity of calcium. The red-white colour indicates a maximum quantity of calcium. The process is tracked for one hour and an oscillating movement is observed in which the calcium levels of the cells increases and decreases alternately.

Name:
David Sands
Born:
1965
Nationality:
English

Doctor's degree:
1990
Works at:
Chalmers University of Technology and Göteborg University

Project title:
Programming language methods for computer security

IMPROVING COMPUTER SECURITY

Many people today have a computer at home to which they download programs, music and games from various companies' home pages. If the files contain viruses, they can lead to computer errors because of inadequate security measures. David Sands is creating methods for investigating more easily whether a program is safe to use or not.

"Imagine you have downloaded a program called "Your Doctor 2002" from a company that you know but don't completely trust. "Your Doctor 2002" promises to give you good medical advice via the Internet directly to your home. Their employees are sworn to professional secrecy, the program is free and financed by medical trademarks advertised at the top of the program's front page. Is a program like this safe to use? At the same time as it has to have access to your personal medical information, it also has to be connected to the Internet in order to get the latest information about influenza epidemics and the latest commercial offers. How can you be sure that the company or its sponsors do not use your medical information for some other purpose?"

It has become even more difficult today to decide which programs you can rely on. The security that protects programs includes passwords and standard systems like fire doors. These systems prevent unauthorised persons from entering and reading protected information as long as no one downloads a document to the computer from the Internet or receives an e-mail from outside. If the document or the mail contains an attachment with a virus, this is not stopped by the system and protected information may be lost. Nor is it impossible for existing passwords to be broken by an experienced and eager hacker.

"Now we want to make more flexible and more reliable security programs. Many of the ones that exist today only recognise viruses they have met previously and are therefore defenceless against any new destructive viruses that come out. If instead we could find methods that decided whether a program or a document was safe to open or nor, whether it had been met before or not, a great deal of program damage and illegal misuse of data could be avoided."

Scandinavia beckoned

David comes from the North Kent coast in southeast England. The maths studies he did at York University developed at Imperial College in London more and more into computer and programming languages. During his doctoral and postdoctoral work he was involved in a European project concerning the Scandinavian countries. This resulted in his working for three years at the Datalogical Institute, DIKU, in Copenhagen.

"My wife Anita and I very much enjoyed living in Copenhagen with its rich cultural life, many restaurants, cosy pubs and theatres, but when I got an offer of a post at Chalmers in Göteborg, I took the chance. We wanted to discover another Scandinavian country, and my new work meant very good opportunities for research."

Now they live with their sons Oscar (7) and Daniel (5) in a house with a view across the sea at Hovås, Göteborg. David works as Professor and Director of Studies at the Department of Computer Science at Chalmers and Göteborg University – and is very involved in educational matters. As well as developing new training courses of various kinds with other researchers, he is on a large number of international research committees that arrange conferences on computer security.

"Computer security is a fairly new

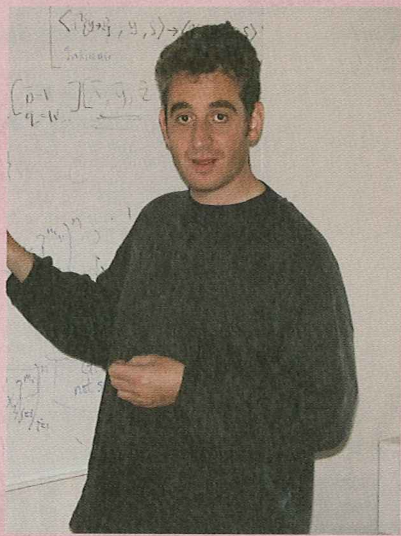


PHOTO: CATHARINA JERKBRANT

research field. It's only recently that people have realised that systems are not secure enough and that more and more dubious companies and dishonest persons are trying to profit from this. If we want to be able to use the programs that exist today in a secure way, there will have to be changes."

Analysis of mathematical combinations

It is not just weaknesses in the technology that have caused security problems, cultural factors also play a part.

"The most important thing for most people today is to have easily-managed programs. To meet consumer demand the computer companies make simple programs, which unfortunately creates problems. Today's complex programming languages have to be translated into a much simpler level that computers can understand, and that loses a lot of security."

To reduce the negative consequences of translation, David and his colleagues will use a special method of analysis. By making an abstract form of data processing they can automatically analyse the properties of a program without needing to start the program.

"An everyday example of an abstract interpretation is when you're going to bake a cake. If you look through the recipe, you can work out how long it will take before the cake is ready, and then decide whether or not you have time to bake it. In the same way you can decide if you want to start a program, which corresponds to the recipe, depending on whether it appears safe or not."

"A more mathematical example is if you ask "Will $((-23 \times -423) + 99)/7$ be a positive number? Without using a pocket calculator most people can quickly see that the answer is Yes. That's because there is a rule in mathematics that tells you that a negative number multiplied by a negative number always results in a positive number. In this example the pocket calculator represents the program."

As in mathematics, computer security comprises a set of rules that determine a program's reliability. These are much simpler than the actual programming rules but good enough to detect certain mathematical sequences that might, for example, be a virus. If you find dangerous mathematical combinations in a program, you decide not to start it.

However, we have no clear definition today of what makes a secure program. One of the main problems that David is working on is how information can be provided in confidence. What do you do to make sure that only certain people in a company, for example the managers, are allowed to read the employees´ personal details while others are prevented from getting hold of the information?

"It is mathematically impossible to create a method of analysis that is 100% secure all the time. But by letting the computer answer Yes only if the system is totally convinced that the person trying to open a document is the right person, and No if it does not know, you can get a comparatively reliable method. A future goal is also to try to develop a programming language with a higher security level than those existing today. That will raise the security level of computers even more."

Journeys in all directions

If you live on the coast in England, some kind of water sport is a common leisure activity. For David it was windsurfing, but more recently he has embarked on a relatively new sport called kite surfing. You get an extra push on your board by being harnessed to a parachute. The idea is that you can jump up in the air from the water and do various acrobatic tricks.

"It's a really crazy sport, but great fun. Maybe I'm getting a bit old to fly around in the air, but you are what you do, and I don't want to be old yet," he says with a grin.

David's wife Anita is also from England, but she has a brother in Canada, a sister in Australia and her parents in Germany. David's parents still live in England.

"It's marvellous to be able to enjoy so many places by going to visit all your relatives. And when I'm in England, I eat the food I miss in Sweden – really strong Indian curry with lots of cumin in it. That gets your taste buds tingling!"

Name:
Maria Strømme
Born:
1970

Nationality:
Norwegian
Doctor's degree:
1997
Works at:
Uppsala University

Project title:
Pharmaceutical materials science

PHYSICS AND PHARMACEUTICS IN AN EXCITING COMBINATION

Combining research with leisure-time activities is what gives Maria her energy. By starting a research group in the field of pharmaceutical materials science she will also be able to combine her favourite subjects – physics and medicine.

From the fjords of Norway to the river Fyrisån in Uppsala

Maria was born and grew up in Lofoten in Norway and moved to Sweden in 1989. First she lived in Falun but a year later she moved to Uppsala to start studying at the university there.

"My student days have given me a feeling of being a real Uppsalian. I moved around a lot from digs to digs, so now I feel that I know all the nooks and crannies of the town – and I still like it just as much."

Space and the stars aroused her interest in science when she was still at middle school and when she got to secondary school she knew what she wanted to be – a physicist. The choice was not entirely without influence from her father, who is a nuclear physicist and high-school teacher. Her passion for astrophysics waned, however, and when she started at university she chose to study technical physics to get the educational breadth she wanted. During this period Maria studied for six months in Ohio, USA as well as spending some time in Poland.

"It's extremely educational to study and live in a different environment than you're used to. Travelling has made me a more extrovert person, more alive to people and attitudes."

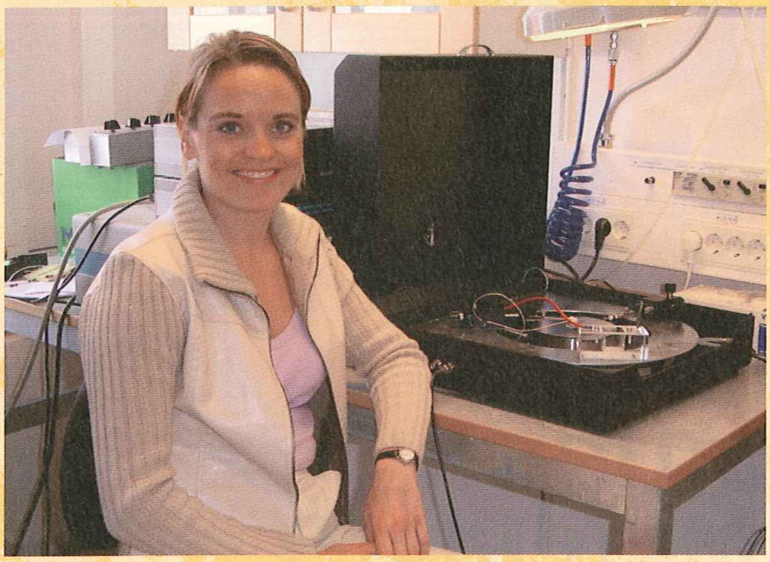
Physics and nasal spray

During her time as a doctoral student Maria worked on developing measurement methods for solid-state physics. After taking her doctor's degree she was contacted by one of the researchers in pharmaceutics who needed help in studying a problem related to the way in which pharmaceuticals, primarily nasal sprays, are absorbed in the nose. There was no good method for simulating the environment in the nose and the mucus membrane, or for studying how substances in a nasal spray absorb liquid from the mucus membrane. They carried out a project together and it became clear to Maria that there was a great deal waiting to be discovered in this field. There is no established research at present in which the classical laws of physics are used to study how pharmaceuticals are released and absorbed. With the aid of a research grant Maria is going to start an interdisciplinary project group with a core of seven to eight people, which she hopes will grow. By combining knowledge of pharmaceutics, physics and materials science they will set up a system that can measure the release of pharmaceuticals in a very small volume of liquid while carrying out measurements during a very short period of time.

"There isn't much more than sporadic cooperation between the fields of pharmaceutics, physics and materials science. This will be the first established group in the world, and I'm working on creating contacts with other groups all round the world that are also waiting for the starting signal. It feels very exciting to be part of a completely new type of project."

It feels natural to Maria to be working with a combination of physics and pharmaceutics since she has always been interested in the human body.

"My favourite present for my doctor's was the ten-volume Doctor's Encyclopaedia!"



A long process

On average it takes ten years from the discovery of a drug to the time when it is put on the market. When a new drug is first sold, it has been preceded by an exhausting process. The substances are tested first in the laboratory, then in tests on animals and finally in clinical tests on humans. This long process could be considerably shortened by refining the methods used at present. If a major part of the trial work could be carried out in a laboratory and the effects were more accurately investigated before they were tested on animals, both time and money would be saved. Medicines would be cheaper, which would benefit the consumers. There are many shortcomings at present in the tests systems that are in use, since they often do not simulate at all well the environments that prevail in the human body.

"One of the uncertain factors is that laboratory methods that are used to investigate the absorption of a pill demand a much greater volume of liquid than is found in the relevant part of the body. It is particularly vital to be able to simulate an environment with the right volume for fast-absorbed drugs like pills that dissolve in the mouth for certain kinds of heart problems. These pills should disintegrate rapidly, releasing the drug in the thin layer of liquid in the mouth before it is transported into the bloodstream. If it were possible to simulate not only the right amount of liquid but also the movements, structure and salt contents that exist in the body, the composition of the medicine could be adapted to optimise assimilation."

In the long term this research will aim at creating more effective drugs that can be absorbed by other parts of the body than the gastrointestinal system, which is the most usual type today. This will increase the patients´ possibility to choose the medicine that suits them best.

A pioneer

When asked if she has run into any sort of trouble in her career because she is young and a woman, Maria shakes her head so that her blond hair flies.

"I've got used to working in a male-dominated environment. In my first year at university there were just two girls and over a hundred men. But I never felt held back by that, or that it was a disadvantage. If anything it's been an advantage because people remember me just because I'm the exception. I think a mixture of men and women is good for the work climate, but when it comes to collaboration it's really the personal chemistry that counts."

The qualities she sets most value on in a good leader is that he or she can see things from other people's points of view, is straightforward and ethical and focused on getting results.

"If you can't see beyond the end of your nose how things should be organised. I think it's very difficult to lead people successfully. Different kinds of employees need different kinds of encouragement and guidance to be motivated and perform better."

An ideas woman

During her first year in Sweden Maria worked as a guide at the Falu Copper Mine and then as a media consultant for a while. She likes having contact with people, and that helps her in her connections with industry.

"The pharmaceutical companies I've spoken to are positive about collaboration. I like the thought of us, with our pioneering methods, being a source of ideas for them and for high-tech industries like manufacturers of analytical instruments."

When she herself wants to get inspiration and energy, Maria loves being out in the countryside, taking exercise and spending time with her partner, Tomas Lindström, and their two children, Adam (5) and Märta (2).

Name:
Jan Swenson
Born:
1966

Nationality:
Swedish
Doctor's degree:
1996
Works at:
Chalmers University of Technology, Göteborg

Project title:
Structure and dynamics of soft matter

DYNAMIC STRUCTURE IN SOFT MATERIALS

Small distances and large molecules are a combination that fascinates Jan Swenson. By enclosing large molecules in small spaces of a thousandth of a micrometer, he investigates the way in which their ability to conduct electric current is affected. But in his free time it's the big distances that count.

You might say that Jan got his science in his blood. He grew up at his home in Mölndal near Göteborg with his mother, who was a chemical technician, and his father, who was a director of studies for physics. After graduating from high school he read physics and did his degree project at Ericsson. At that point he did not plan to take a PhD but wanted to find a job.

"It all happened by pure chance. When I had got my degree, Sweden was in the middle of a recession and it was difficult to find a job. One day when I picked up my dad, who was working at Chalmers, I saw a notice about a postgraduate studentship. This led to a thesis in the field of ion-conducting glasses. After that he went straight to University College, London, where he came into contact with what was to be a part of his field: clay.

Thin layers

The clays Jan uses are made into laminates and used to build model systems of thin layers. They are placed on top of each other with less than a nanometre between them. These thin layers can be used in several ways. For example, they can act as models of cell membranes or other commonly occurring structures in nature. By introducing molecules like water and polymers between these thin layers, interesting information can be obtained about the way molecules react in an environment of the same size as the gap between the clay layers.

"Water is the most common molecule, absolutely essential for all biological life. Usually you find it equally distributed in networks of small pores and membrane layers, which affects their structure and dynamics."

By studying this Jan wants to try to understand why precisely this mixture of oxygen and hydrogen is so decisive for life on earth. What happens to proteins and other molecules when they integrate with surrounding water molecules? Another purpose of the clay layers is to find out how structure and dynamics in other liquids and polymer materials are affected by restricted space.

The development of technological material has contributed greatly to the creation of new types of soft and malleable, non-crystalline materials. Such examples are polymer electrolytes and ion-conducting glasses used as solid electrolyte in microbatteries.

"This is very interesting for the future of microelectronics. Electronic components are getting smaller and smaller and these ion-conducting materials can be used as internal sources of current for components in, for example, computers. Each little unit has its own source of current, without any external source of electricity."

To optimise the properties of polymer microbatteries it is vital, says Jan, to find out how these soft materials change in very small spaces. He does this by introducing interesting material between hundreds of thousands of layers of clay. Jan shows a jar of packets of clay layers like this. The space between the layers is 15Å. The laminates are negatively charged and positive ions between the layers make them keep close together.

"We have discovered that it is possible to put all sorts of things in between the layers of these almost perfectly paral-

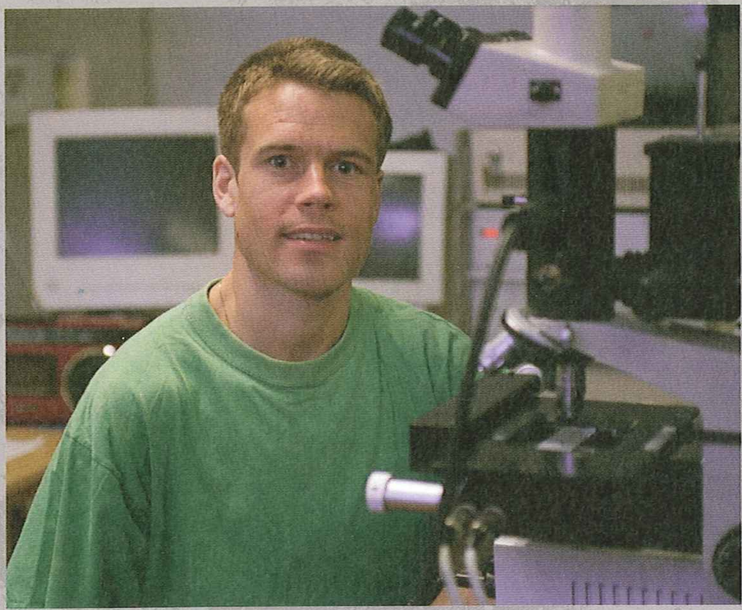


PHOTO: JAN-OLOF YXELL

lel laminates, for example a polymer. You can put the clay laminates in the polymer and it is sucked into the small layers and then you have the polymers in a restricted space."

From long-distance to micrometres

In his free time Jan moves over considerably longer distances than at work. He has gone in for long-distance running since he was a boy and has run marathons and represented Sweden in the 1994 European Championships. At the end of his doctoral studies he was running 200 kilometres a week, so he was forced to choose between running and physics.

"I realised I wouldn't be able to get to the very top and that I wouldn't manage both studies and running. I always want to do my utmost in everything I do and there was neither time nor energy for both. But I still run regularly to keep fit and gather energy."

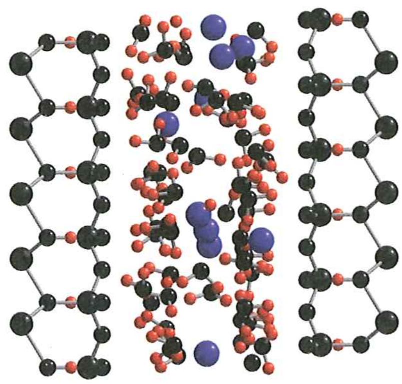
When asked what his research dreams are, Jan answers that he wants to be able to explain why water is of such decisive importance for biological processes and increase understanding of how ion-conduction in glass and polymer electrolytes functions. The project with clays as a model system is so far pure research. By introducing substances between the thin layers they are scaled down to a two-dimensional level, which simplifies studies of the dynamic processes. By limiting the geometry it is possible to investigate how the molecular movements are affected. Then you can go on and investigate how that in turn affects, for example, ion-conducting properties in a polymer electrolyte. The movement of a polymer molecule is also affected by its so-called free volume.

"Imagine a pile of spaghetti where some sticks of spaghetti have got stuck in a lump and are packed tightly together. Then none of the sticks of spaghetti can move about freely, the whole lump has to move together, the free volume is small. The spaghetti sticks that are free, on the other hand, can move in whatever direction they like, and have a larger free volume."

The methods used to investigate structures and movements in molecules are mainly neutron scattering, light scattering and dielectric measurements. Neutron diffraction provides information about the structure of molecules, that is, how the atoms are bound to each other. Computer simulations are also used to get a "picture" of the microscopic structure, where known facts about molecules and atoms are utilised.

Jan looks forward to playing a more supervising role as well as continuing with his research.

"That will be different and exciting and I hope to be able to combine my own research with giving my colleagues encouragement. A good leader, for me, has the ability to be a guide without controlling too much, to give his colleagues freedom and to encourage creativity. I hope I will succeed in that."



Probable structure of a "Na vermiculite" clay containing only two molecule layers of water between the ca. 1 mm thick, crystalline clay plates (consisting mainly of silicon, magnesium and oxygen). The millions of parallel and negatively-charged clay plates are held together by the intermediate positively-charged sodium ions (blue particles). The hydrogen atoms are symbolised by the small red particles and all the other types of atoms are black. Half the thickness of the clay plate is shown on each side of the intermediate water.

INDIVIDUAL GRANTS FOR THE ADVANCEMENT OF RESEARCH LEADERS 2002

THE SELECTION PROCESS

In January 2000 the Swedish Foundation for Strategic Research announced a new program whose aim is to identify and support young researchers who are expected to be the scientific leaders of the future. This program was named Individual Grants for the Advancement of Research Leaders.

A research leader is a researcher at the highest scientific level who also has leadership qualities such as initiative, drive, organisational skills and the ability to enthuse his or her colleagues. The Foundation set aside funds for twenty grants, each of SEK 10M, for six years of research in one of the Foundation's strategic fields. By the final application date in May 2000 as many as 504 applications had been received.

After they had been scrutinised and ranked in the Foundation's strategy group, 115 went on to an international level where each of the applications was assessed in writing by at least two internationally chosen scientific experts and one Swedish strategic assessor. After all the judgements have been weighed up, 43 of the applicants were invited to send in a comprehensive application. Forty such applications were received and assessed during December by foreign scientific experts.

During February 2001 these applicants were called in for interviews whose aim was to form an opinion about their leadership qualities, commitment and scientific and popular scientific communication skills. These interviews were carried out by a Swedish group led by Professor Ingvar Lindgren. The group consisted of three well-known researchers and three representatives from industry and the community with experience of leadership development. This group then drew up a ranking list based on both the written scientific assessments and on the impressions gained at the interviews.

On April 5 the Board decided to appoint the following as *Research Leaders of the Future:*

02 **Igor Abrikosov**
UU, Uppsala University

04 **Ernest Arenas**
KI, Karolinska Institutet

06 **Magnus Berggren**
LiU, Linköping University

08 **Mats Danielsson**
KTH, Royal Institute of Technology

10 **Claes Gustafsson**
KI, Karolinska Institutet

12 **Leif Hammarström**
UU, Uppsala University

14 **Anders Karlsson**
KTH, Royal Institute of Technology

16 **Maria Kempe**
LU, Lund University

18 **Anna Kidiyarova-Shevchenko**
Chalmers University of Technology

20 **Jörgen Larsson**
LU, Lund University

22 **Nils-Göran Larsson**
KI, Karolinska Institutet

24 **Andreas Molisch**
LU, Lund University

26 **Richard Neutze**
Chalmers University of Technology

28 **Ove Nilsson**
SLU, Swedish University for Agricultural Sciences

30 **Claes Ohlsson**
GU, Göteborg University

32 **Owe Orwar**
Chalmers University of Technology/ GU, Göteborg University

34 **Stephanie Margret Reimann-Wacker**
LU, Lund University

36 **Agneta Richter Dahlfors**
KI, Karolinska Institutet

38 **David Sands**
Chalmers University of Technology

40 **Maria Strømme**
UU, Uppsala University

42 **Jan Swenson**
Chalmers University of Technology

SANDLER MERGEL DESIGN

THE SWEDISH FOUNDATION FOR STRATEGIC RESEARCH

- supports research and graduate training in the natural sciences, engineering and medicine for the purpose of strengthening Sweden's future competitiveness
- finances at present over 90 large research programmes at Swedish universities – many of them in collaboration with industry
- awards individual grants to particularly prominent researchers
- supports important areas such as biotechnology, materials research and IT
- invests heavily in graduate training – almost 1 000 doctoral students are currently employed in the Foundation's various programmes
- has a total annual allocations volume of just over SEK 700 million (2002)
- has a capital of about SEK 8 500 million (October 2002) as the basis for its operations

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