SWEDISH FOUNDATION FOR STRATEGIC RESEARCH

FUTURE RESEARCH LEADERS

INDIVIDUAL GRANTS FOR THE ADVANCEMENT OF RESEARCH LEADERS

2005

Lisa Chytræus
Ninna Richnau
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The interviews in this publication were conducted by Lisa Chytræus (LC), Ninna Richnau (NR) and Louise Wandel (LW) – in part within the framework of their respective projects for the course in science communications at Uppsala University. The purpose of the course is to give persons with a scientific or technical undergraduate education the knowledge and skills they need to present scientific information to a non-expert readership in a clearly structured, factual and ethically satisfactory manner.

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Future Research Leaders

Individual Grants for the Advancement of Research Leaders

– INGVAR II

A RESEARCH GROUP – consisting of five to ten postgraduate students and postdocs under the leadership of a skilled and driving research leader with time to devote himself or herself to research – is still a central engine for scientific and technical development. In order to obtain grants, young researchers have often previously had to ally themselves with more senior researchers, with the risk that new research areas could not become sufficiently established within the country.

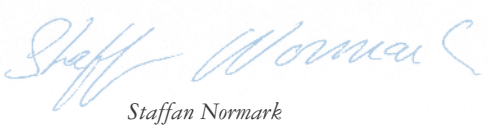
This led us to establish the INGVAR programme – Individual Grants for the Advancement of Research Leaders – for the purpose of placing a number of particularly promising young researchers in the driver's seat and giving them an opportunity to form their own independent and internationally competitive research teams.

The first announcement of grants took place in 2000, and in April 2001, 21 applicants were selected to receive Individual Grants for the Advancement of Research Leaders – INGVAR I. One important component of the programme is leadership training; another is the network which these young researchers build.

The programme was very well received and has been copied in other countries. What then could be more natural than to make a new grant announcement? This was done in 2003, and we can now present the second set of recipients of Individual Grants for the Advancement of Research Leaders – INGVAR II.

We expect our 18 new grantees to become internationally recognised researchers, but also leaders and mentors for their younger co-workers.

We also expect them to form research groups that can collaborate effectively with other groups in both academia and industry, and would be pleased if new companies were started up as a result of the discoveries that are made.



Staffan Normark

Name: William Agace

Nationality: British

Born: 1967

Awarded Ph.D.: 1996

Works at: Lund University

Title of project: Tissue-specific lymphocyte accumulation

IMMERSED IN THE IMMUNE SYSTEM

William Agace's research group is studying a type of white blood cells called T-lymphocytes (or T-cells) and their homing pathways in the body. Among other things, they are investigating a group of signalling proteins that help the T-lymphocytes home in on inflamed tissue. The research may eventually lead to new improved drugs for the treatment of cancer and autoimmune and chronic inflammatory diseases.

The role of the T-lymphocytes in the immune system is to quickly locate bacteria, virus and other foreign substances in the body. Certain types also kill dead tumour cells and virus-infected cells. In order for the immune system to function normally, the trafficking of T-lymphocytes and other white blood cells in the body must be carefully controlled. Different subgroups of T-cells are programmed to migrate to different tissues to perform their tasks. This is called "tropism". The tropism of the lymphocyte depends on what molecules are present on its surface and what molecular signals it receives.

For unknown reasons, an abnormal accumulation of T-lymphocytes sometimes occurs in certain tissues. The accumulated lymphocytes react to the body's own proteins and cells as if they were foreign, which can damage the tissue and lead to chronic inflammation. This is called autoimmunity, and is the root of autoimmune diseases.

William Agace is studying the homing of the T-lymphocytes to the tissues and trying to understand the molecular mechanisms behind tropism.

"We are studying how different subgroups of T-lymphocytes are generated and find their way to the right tissue. We want to find the molecules that are involved in lymphocyte homing and determine what the functions of these molecules might be. This knowledge can be used to develop drugs that prevent T-lymphocytes from accumulating in persons with autoimmune disease," he explains.

Love brought him to Lund

William was born and grew up in Walton-on-Thames, a small town on the River Thames southwest of London. Just before he began studying microbiology at the University of Bristol, he interrailed around Europe together with some friends. In Greece he met Marie, a Swedish girl. Marie then took a break from her social work studies to visit William in Bristol, and after William got his degree he moved to Lund to be with Marie.

William spent his first year in Sweden learning Swedish and looking for work. He was hired as a lab assistant at the Department of Clinical Immunology at Lund University, where he eventually obtained a postgraduate studentship.

"I liked the job right away. As an undergraduate immunology was my favourite subject, so I was glad to be able to devote myself to it," he says.

William and Marie are now married with three children: Adam, Hanna and Ella. William plays tennis with the family one day a week, and he also finds time to play on a local inter-company soccer team.

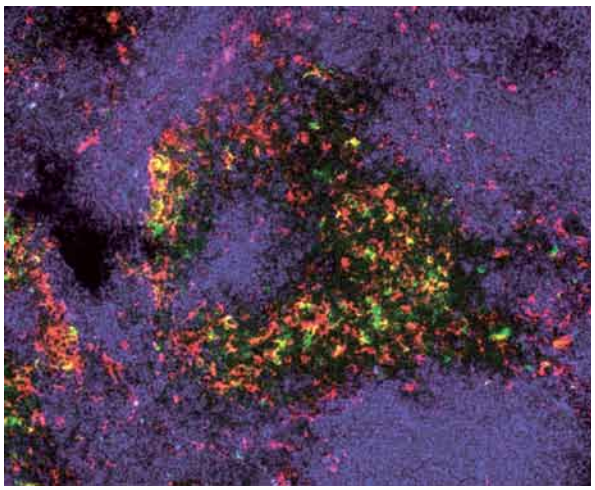
The gut – a good model

William's research group is studying the intestine or gut as a model system for the tropism of the T-lymphocytes. The intestine plays just as important a role in the digestive system as it does in the immune system. The intestinal tract contains a large portion of the body's lymphatic tissue, and most foreign bacteria that enter the body pass through the intestinal wall. Furthermore, the intestine is associated with a number of diseases that are in part due to an abnormal accumulation of T-lymphocytes. *Crohn's Disease* and *ulcerous colitis* are examples of autoimmune diseases that cause chronic inflammation of the intestine.

Chemokines are a large family of signalling proteins that play an important role in trafficking and recruiting T-lymphocytes and other white blood cells. They are emitted by the inflamed tissue and tell the blood cells to migrate there.

"One of the goals of our research is to identify which chemokines are involved in the trafficking of T-lymphocytes. If we can find a way to block the chemokines, we can find new ways to treat for example *Crohn's Disease* and *ulcerous colitis*," he says.

William is also studying "adhesion molecules". In order for a T-lymphocyte circulating in the blood to reach an infected tissue, it must bind to the



Specimen from the lymph node in the gut of a mouse, imaged in an immunofluorescence microscope. Dendritic cells (red) equipped with a certain adhesion molecule (green) are white blood cells whose function is to signal T lymphocytes to home to the tissue. B lymphocytes (blue) are another type of white blood cell that manufactures antibodies. The yellow is overlap of dendritic cells and adhesion molecules.

walls of the blood vessels and pass through them. This takes place via these adhesion molecules, which are present both on the lymphocyte and on the endothelial cell in the blood vessel wall. Subgroups of T-lymphocytes and different tissues express different types of adhesion molecules, which contributes to tropism. These molecules are also possible targets for drugs.

"There are already drugs that prevent T-lymphocytes from accumulating. The problem is that they are more or less broad spectrum drugs, i.e. they can act in several tissues. One purpose of our research is to be able to target specific molecules in specific tissues. In this way we can develop drugs that prevent T-lymphocytes from accumulating in, for example, the intestine of Crohn's patients, the skin of psoriasis patients or the joints of arthritis patients," he explains.

Increase trafficking as well

Certain T-lymphocytes are known for their ability to kill tumour cells.

"If you can understand which molecules are involved in lymphocyte homing to tumours, it may be possible to increase the trafficking of T-lymphocytes there. The lymphocytes could be 'programmed' for tumour tropism in test tubes and then be given to cancer patients."

In the long run there are also other clinical applications for William's research. The T-lymphocytes are involved in what is referred to as "immunological memory". This means that they can remember that they have already encountered a certain bacteria, for example. If the same bacteria turns up in the body again later on, the T-lymphocytes will respond more rapidly and more forcefully. This property is the basis of vaccination.

"Increasing the migration of T-lymphocytes to certain tissues could also make it possible to improve the effectiveness of certain vaccines," William says. • LC

Name:
Tomas Akenine-Möller

Nationality:
Swedish

Born:
1971

Awarded Ph.D.:
1998

Works at:
Lund University,
Faculty of Engineering

Title of project:
Use of culling and coherence algorithms by mobile devices

3D GRAPHICS FOR MOBILE TELEPHONES

Three-dimensional graphics may be the next big breakthrough in mobile telephony. A third dimension enhances the display graphics, makes them more interesting, and may even get us to work more efficiently. Tomas Akenine-Möller is conducting research to improve mobile telephone graphics and to make the graphics hardware as energy-efficient as possible.

In the early 1980s, Tomas Akenine-Möller's parents borrowed a computer. Young Tomas was fascinated by the possibility of creating pictures on the computer – especially moving pictures.

"Pictures convey a lot more than text. They say a picture conveys more than a thousand words, so moving pictures must tell even more," says Tomas.

The interest in computers led to a degree in computer science from Lund University's Faculty of Engineering. After a period spent first as an industry doctoral student and then as a consultant in Göteborg, Tomas was a postdoc fellow at the University of California in Berkeley in the USA. During the autumn of 2004 and the spring of 2005 he conducted research at the University of California in San Diego together with the Danish professor Henrik Wann Jensen and his research group. Now Tomas is an associate professor at the Department of Computer Science at Lund University.

Increased user-friendliness

Tomas and his research group are working on the development of three-dimensional graphics for mobile units such as mobile phones and handheld computers.

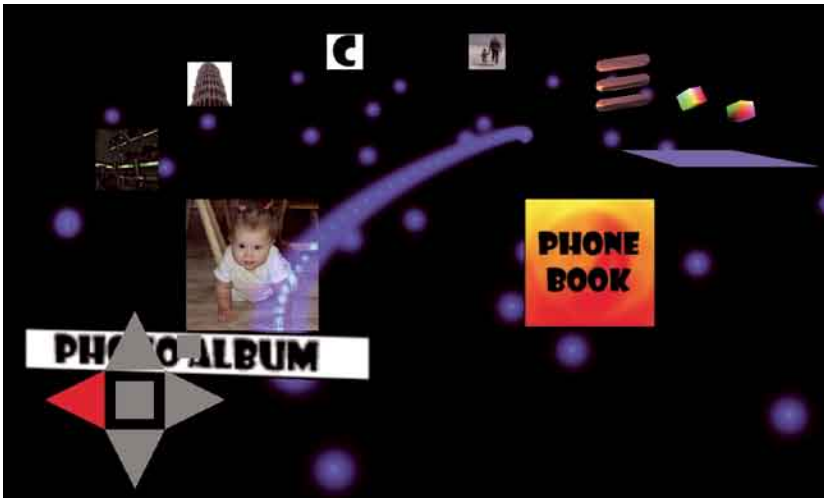
"This is an area with great expansion potential," says Tomas. "So far development has been slow in Sweden, but now mobile phone displays are so good that it's time to give them 3D graphics," he says.

Tomas is determined to build up a leading research group in the area of mobile graphics.

One area of application for three-dimensional computer graphics is user interfaces for mobile units, in other words the user's personal settings. For example, a mobile telephone display could be utilised better with three-dimensional graphics. The third dimension, depth, makes it possible to position icons and images in a more user-friendly way. The icon you want to use is enlarged in relation to the other icons in the menu.

"The user interface is what we use the most on our mobile phones, so it has to be both good and attractive. A better user interface could make us more efficient, both on and off the job," says Tomas.

Besides user interfaces, three-dimensional graphics can also be used for maps. The mobile telephone can then be useful when you need to find your way in a new city, for example. The city streets and buildings can be seen in three dimensions, which makes it easier to orient yourself.



Three-dimensional graphics can improve the user interface on mobile phones. The icon in the menu you want to use is enlarged in relation to the other icons.

Tomas Akenine-Möller

Games will undoubtedly be a big application, but also simpler things such as screen savers and animated messages.

Shading lends a realistic touch

Three-dimensional graphics draw a lot of power, which is a problem for the battery-powered units. Another problem that Tomas and his research group are tackling has to do with the screen's picture elements, called pixels. The screens on mobile units are held closer to the eyes than, for example, computer screens are. This means that each individual pixel must be of better quality on mobile units, but good quality costs energy.

"It's a conflict between high image quality and energy-efficiency," says Tomas. "We want to find a balance between long battery life and decent image quality by means of better algorithms," he explains.

There are two areas which computer graphics researchers are striving to improve. One is realism, i.e. that the image should be as realistic as possible. Here, shading and lighting are important. Often phenomena in nature are studied, and the lighting is simulated to imitate reality. The other area has to do with real time. The images in computer games, for example, have to be created in a very short time, preferably just 10 milliseconds.

"In the research group in San Diego we strove for both faster graphics and greater realism. It was very inspiring to work with Henrik Wann Jensen, who is one of the best in the world in computer graphics," says Tomas.

Jensen got an Technical Achievement Award for a technique that was used in "The Lord of the Rings". The technique, subsurface scattering, simulates light that passes through thin material such as skin. In the film the technique can be seen in Gollum's ears.

Seeks inspiration in spare time

Tomas usually encourages his Ph.D. students to make the most of their free time and not work late too often.

"I get 95% of my ideas when I'm not working," says Tomas. "Without being aware of it I think about my research a lot during my spare time, and that's when the best ideas and solutions pop up."

Tomas is the father of Felix and Elina, and together they like to watch animated film.

"I can watch a computer-animated film and just focus on the computer graphics," Tomas laughs. "If my research can lead to better algorithms and quality in animated films as well, I will be happy. Sure it's fun to do research and get good results, but it's even more fun to see the technique being used," he continues.

The family has recently moved to a house in Lund, which Tomas and his wife Eva are in the process of renovating. They spend most of their spare time with their children and fixing the house. Tomas considers the opportunity to do research a privilege. His greatest motivation is that it's fun, but he is also driven by a competitive instinct.

"We want to prove that we can do great research, even though Sweden is a small country. Research in mobile telephony carries a lot of weight, and I'm convinced that 3D graphics for mobile devices will have a huge impact," says Tomas. • LW

Name:
Lioubov Belova

Nationality:
Russian

Born:
1974

Awarded Ph.D.:
2000

Works at:
Royal Institute of Technology

Title of project:
Nanostructured novel magnetic materials for spin electronics and bio-medical applications

PROTEINS AS MOULDS FOR MAGNETS

Lioubov Belova's research concerns nanomagnets and how these particles can be utilised in different ways. For example, the tiny magnets can be used in computer memories with extremely high capacity. Another possible application is in nanorobots that deliver medicines to the right place in the body.

At the age of five, Lioubov Belova started playing classical piano in her home town of Moscow. She attended an ordinary school in the mornings and a musical academy in the afternoons. Lioubov was told she had a future as a concert pianist, but soon realised she wanted a career in research. Eventually she completed her undergraduate education and got a Ph.D. in physics, in Moscow. In 1999 Lioubov visited Stockholm to speak about her doctoral project – novel magnetic materials – and was offered a postdoctoral fellowship at the Division of Engineering Material Physics at the Royal Institute of Technology (KTH). She has been working there ever since, with magnetic materials for spintronic and biomedical applications. She has little time to play the piano nowadays.

Small magnets – big applications

Spintronics is a new kind of electronics which makes use of both the charge and the spin of electrons. Spin stems from the fact that besides revolving around the atomic nucleus, electrons also rotate around their own axis, which causes magnetism. The direction of spin is either "up" or "down", and can be controlled by means of magnetic fields. The electrons are said to be "polarised". Spintronics could in many cases replace ordinary electronics, since it has many advantages. For example, the energy losses caused by the motion of electrons in electronics are avoided.

"When the direction of spin of an electron is reversed, no matter is moved. The polarised electron passes on the polarisation to the adjacent electron, which polarises the next one, and so on," explains Lioubov.

Among other things, spintronics can lead to cheaper data storage media with extremely high capacity. Achieving this requires very tiny magnets. Conventional methods for synthesising these nanomagnets are unfortunately not good enough. The problem lies in making magnets of exactly the same size, since it is vital that their properties don't vary. Lioubov therefore fabricates nanomagnets using a spherical protein – ferritin – as a mould. Ferritin is also present naturally in the body and is used to store iron. In simplified terms, the iron inside the protein is removed and the shell is instead filled with, for example, platinum and cobalt. The method is complicated, but the result is magnetic particles with extremely small size variations.

The nanometer-sized magnets have applications beyond spintronics, such as in biomedicine.

"People always want to improve their lives. The consumer market is driven by the desire for new devices and gadgets. Not because we couldn't live without them, but because we yearn for convenience and luxury. But in the western world we have reached a level where we no longer desire consumption as much. The average consumer is fairly content with his playstation, his mobile phone with video camera, etc. Then we start to look for products that can improve our health. Medical devices, such as nanorobots, are a product whose time has come," Lioubov believes.

The picture shows the protein ferritin, which is the form in which the body stores iron. Emptying the protein of iron leaves a mould that can be used to fabricate nanomagnets.

A nanorobot is a nanometer-scale robot that can locate and treat different diseases.

Nanomagnets could be used in these devices to deliver the medicine to the right tissue. By putting the drug on the surface of the magnets and positioning a magnetic collar at the diseased area, the medicine could be steered to the right location. This would permit more

Lioubov Belova

effective tumour treatment without undesirable side-effects.

Another application is in biochips, which deliver medicine, for example insulin, at certain predetermined times.

Lioubov's field of research is large and unexplored.

"I really have an opportunity to feel like an explorer. Naturally it's exciting and fascinating to study things that no one has studied before – but it's also a great challenge," she says.

Curiosity and creativity

Curiosity and creativity are what drive Lioubov in her research.

"Even as a child I was extremely curious and asked lots of questions. I wanted to know how things work, why the sky is blue or white and so on. Furthermore, there is a thrill in being able to change things for the better. It may sound trite, but it's true. It's satisfying to sow a seed and see it grow into a tree, even if I'm not the one who tends the tree later on."

It's all too easy to lose your creativity and become one-sided in your thinking, she says, adding that it's important to do other things than research. Lioubov has many hobbies that keep her from becoming one-sided. Singing and music is one hobby, others are karate, tennis, swimming, drawing and tending her orchid collection.

"Doing other things besides research gives me a perspective on life," she says, pointing at the potted plants vying for space on the windowsills in her office.

"I'm fascinated by nature and how it works. If you study the microstructure of flowers, you find a fantastic design. The complexity of nature's designs are far beyond anything man could come up with. We have a lot to learn there."

• LC

Facts about nanotechnology

Nanotechnology, which is based on extremely small (nanometer-sized) structures, is a very hot research area. "Nano" means billionth and comes from the Greek word nanos, meaning dwarf. A nanometer is a millionth of a millimetre. The technology involves manipulating materials on the atomic and molecular level and is sometimes called "molecular manufacturing". Nanotechnology makes it possible to synthesise new materials and miniaturise electronics.

Name:
Anna Blom

Nationality:
Swedish and Polish

Born:
1969

Awarded Ph.D.:
1997

Works at:
Lund University

Title of project:
Inhibitors of the complement system

COMPLEMENT INHIBITORS PAVE THE WAY FOR NEW THERAPIES

The immune system can be divided into two parts: innate immunity and acquired immunity. Anna Blom and her group are studying innate immunity, where the proteins of the complement system, called complement factors, play a crucial role. A lack of, but also uncontrolled activity among, these proteins can cause serious diseases. We therefore have natural complement inhibitors that regulate the activity of the complement factors.

Anna Blom and her group work at the Wallenberg Laboratory in Malmö. The building is situated in the middle of the Malmö University Hospital campus.

"Naturally occurring complement inhibitors are present in the blood as well as on the surface of cells," says Anna. "These are the molecules we are investigating. We are trying to understand their structure and function as well as how they inhibit complement factors. With this knowledge we can then synthesise drugs to treat diseases involving the complement system."

Dying cells and treacherous bacteria

"At first it was thought that the complement system was only involved in the body's defence against infections, but it has been found to have many more functions. The complement system appears, for example, to be very important in the removal of dying cells," says Anna.

Patients who lack complement inhibitors get infections and autoimmune diseases due to the fact that dying cells are not removed, but rot in the tissue. The cells open up and their DNA is then exposed to the immune system, which perceives them as foreign. This leads to an autoimmune response.

"The removal of dying cells thus appears to be a carefully regulated process, and we are trying to understand how important both complement factors and complement inhibitors are in this process," says Anna.

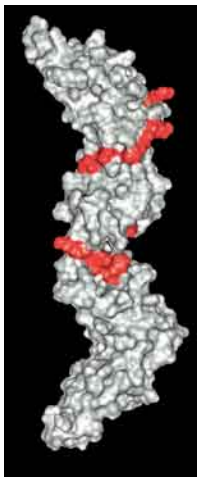
Anna and her group are also studying infections and the mechanism that causes them.

"Many bacteria that cause treacherous infections do this by capturing complement inhibitors from the blood."

In this way they avoid being attacked by complement factors and can establish an infection. Examples of such bacteria are *Neisseria gonorrhoeae* and *Streptococcus pyogenes*, which cause gonorrhoea and strep throat, respectively.

"We know exactly how the bacteria bind to the complement inhibitors, and by understanding this we can attempt to develop new vaccines," explains Anna.

Really advanced viruses, for example certain herpes viruses that can cause cancer, avoid complement attack in a slightly trickier way: they sponge on the host cell's DNA so that they can eventually produce their own complement inhibitors. It usually takes a long time from the actual virus infection until symptoms, i.e. cancer, appear. The complement inhibitor KCP (see picture) is expressed when the virus is on its way from one cell to attack the next one. The quantity of antibodies against KCP in a patient can perhaps be detected by a clinical test and this can be used as an indicator that the patient is infected and is developing cancer.



This molecular structure represents a complement inhibitor, KCP, which Anna's group has identified. It is expressed by a herpes virus associated with Kaposi's sarcoma. The amino acids that are important for the function of the complement inhibitor are shown in red.

Can blocked activation of complement factors cure rheumatoid arthritis?

Why do we suddenly turn on our own joints and try to eat them up? This is what happens in patients with the autoimmune disease rheumatoid arthritis. One of the prevailing theories is that antibodies are formed against the protein collagen 2. These antibodies in turn activate the complement system, which begins to regard the joints as an enemy.

Anna Blom

"We have found molecules in cartilage that directly activate complement factors," says Anna. "By understanding exactly which molecule activates complement factors, a peptide or antibody can be synthesised that can prevent the interaction between the activating molecule and the complement factor. In this way it may be possible to prevent or cure arthritis."

Tekla and Octan – Irish Wolfhounds

Anna originally comes from Krakow in Poland. She studied biomedicine at the Jagiellonian University in Krakow and came to Sweden at the age of 23 to do her degree project at the Biomedical Centre in Uppsala. During her first week in Sweden she met her future husband, Thomas, also a researcher.

"We actually met at a pub, not at the lab," she points out and laughs. Anna says it makes it easier that both are researchers. They have more understanding for the long working hours, and they can help each other by, for example, proofreading each other's manuscripts. Because Anna's husband's research also concerns arthritis – he is looking for genes that cause the disease – they also collaborate a bit.

"I like Sweden a lot," says Anna. "There's no big difference between Sweden and Poland, particularly within the academic world. It's the same kind of people and the same way of thinking."

Anna and her husband have two five-year-old Irish Wolfhounds called Tekla and Octan. She speaks affectionately about her dogs and says that the original idea was to have them as pets, but her interest in her dogs has grown into an all-consuming hobby.

"We show them and we compete with them in simulated hunting. Both dogs have qualified for the European Championships in Germany," says Anna proudly.

She has also become involved in compiling the health status of Irish Wolfhounds in Sweden. Unfortunately, dogs of this breed are not particularly healthy. They get cancer and heart disease and have an average lifespan of only seven years.

Pathologically curious

Anna says that she is pathologically curious, which is what drives her in her research.

"Plus it's so aesthetically satisfying when you see things fall into place," she says.

"I deliberately avoid setting goals for my research, because then I won't reach them. Research should be free. On the other hand, you have to think pragmatically too. Otherwise your curiosity might take you anywhere."

She says it requires a great deal of planning to put a group together, and she devotes a lot of time and effort to this.

"Half of the success is creating a good group with a composition that works," she says.

Anna tries to devote two days a week to laboratory work. She has done most of the experiments herself, which makes it easier when she has to help one of the group members with a problem. She also realises that she will have to stop working in the lab some day. Her group will expand, and other duties will take all her time. But for now she still finds time for lab work.

"A little experimenting so I can see my cells thrive," says Anna. • NR

Name: Johan Ericson

Nationality: Swedish

Born: 1965

Awarded Ph.D.: 1995

Works at: Karolinska Institutet

Title of project: Specification of neuronal cell identity

NERVOUS CURIOSITY

Stem cell research holds out the hope of new sources of tissue for transplants to replace damaged and diseased tissue. Johan Ericson's research is aimed at identifying signals and genes that control the development of stem cells into different types of nerve cells during the development of the central nervous system. He recently succeeded in generating dopamine-producing neurons that could be used in the treatment of e.g. Parkinson's Disease, and the results look very promising.

Approximately 20,000 Swedes suffer from the incurable neurological disease Parkinson's. The disease destroys the dopaminergic neurons in the brain that produce the important neurotransmitter dopamine. This substance is of great importance for motor function, and without dopamine the muscles become rigid. The patient suffers from tremors and gait disturbances.

Neurons, or nerve cells, are formed from stem cells during embryonic development. Stem cells can be transformed into virtually any kind of cell in the body, depending on the molecular signals they receive. Johan Ericson is studying what mechanisms control the development of stem cells into different types of neurons.

Applicable basic research

Johan calls himself a developmental biologist, and his research has largely been of a purely basic scientific nature. The research centres around how the spinal cord forms during embryonic development.

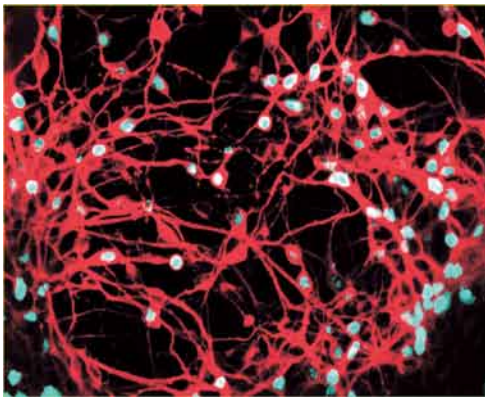
"The spinal cord is the simplest and therefore also the 'most boring' part of the nervous system. Most people want to work with the more complex part of the CNS – the brain. It is basically constructed in the same way as the spinal cord, but is more complex and therefore more difficult to understand. By studying the spinal cord we have arrived at general models for maturation of the cells during embryonic development, and these models can also be applied to more complex parts of the brain," he explains.

Johan has a project together with Professor Thomas Perlmann in which they are trying to identify genes that control the development of clinically relevant cell types, i.e. cells with practical medical uses. These include the dopaminergic cells that are formed in the midbrain. In the spinal cord, they have previously studied how so-called transcription factors, which turn genes on and off in the cell nucleus, can control the development of stem cells into different types of neurons. Based on knowledge of what these transcription factors look like, they have then looked for similar factors that control the formation of dopaminergic cells in the midbrain. They have found a couple such genes, one of which plays a crucial role.

"The gene activates the whole program for development of dopamine-producing cells. We have found it specifically in those stem cells that become dopaminergic cells. If we take the gene and insert it in the 'wrong' place in the brain, stem cells that would not normally have become dopaminergic cells are reprogrammed to do so," he says.

The research group has also managed to get it to work *in vitro*, i.e. in test tubes. They use embryonic stem cells from mouse, in which they insert the "dopamine gene", forcing the stem cells to transform into dopaminergic cells.

"It looks very promising. We can make dopaminergic cells from stem cells much more efficiently than anyone has done before. The hope is eventually to be able to treat Parkinson's Disease by implanting human dopaminergic cells made from stem cells with the



Dopaminergic neurons created from embryonic stem cells, photographed in a confocal microscope.

aid of the genes we have found," he explains enthusiastically.

Johan likes the idea that basic research pays.

"It's important to understand the fundamental principles that govern the development of the brain. It's no use trying to cut corners. Our project is a good example of the fact that even basic scientific and curiosity-based research can lead to clinical applications," he says.

And Johan's greatest motivation for research is in fact curiosity. He also has a strong desire to succeed, but perhaps an even greater fear of failing.

"My fear of losing has had a good influence on my getting things done. Otherwise I'm basically a pretty lazy person. But I'm extremely competitive. As a researcher you live with the worry that someone else will publish the same results before you do, and the whole point is to be first," he says.

Relaxing to renovate

Johan grew up in Boden in the far north of Sweden. He got his bachelor's degree in chemistry and molecular biology in Umeå, and his doctorate in developmental biology at the Department of Clinical Microbiology at Umeå University. After that he was a postdoctoral research fellow at Columbia University in New York, where he stayed for three and a half years. Johan moved back to Sweden in early 1999 to start his own laboratory at the Department of Cell and Molecular Biology at Karolinska Institutet, where he has been ever since.

Johan is married to Annika, a physical therapist who works with child rehabilitation. They have been married for 10 years and have two children, Alicia and Albin. Home and family have taken up most of their free time in recent years.

"A few years ago we bought an old house in Hässelby just outside of Stockholm. It's a big house that needed a lot of interior renovation, so it's still not completely finished. When I have time I love doing carpentry and renovation work at home. It's my biggest hobby and is very relaxing. Otherwise I play a little acoustic and electric guitar and sing. But I did more of that before. When I was a student I was in a band, as lead singer and rhythm guitarist. I have a couple of really nice electric guitars for which I recently bought a new amplifier, so I've started to play a little again."

Johan's future research plans include continuing with his basic research on the development of the spinal cord. "The more I learn the more I realise how little I know." He also plans to continue studying the dopaminergic stem cells, which he hopes can lead to clinical trials in patients within the course of a few years.

"We have already begun implanting them in various rat models of Parkinson's, and the preliminary results look very promising. At the same time we are trying to transfer the technology, which we have so far only used for mouse stem cells, to human stem cells. When it's time for more advanced animal experiments we won't be able to do everything ourselves, but I want to be actively involved in the process as far as possible." • LC

Name: Per Hammarström

Nationality: Swedish

Born: 1972

Awarded Ph.D.: 2000

Works at: Linköping University

Title of project: Misfolded proteins and related diseases

STRAIGHTENING OUT MISFOLDED PROTEINS

Per Hammarström's research group at Linköping University is investigating incorrectly folded proteins. Alzheimer's Disease and a number of other serious diseases are probably caused by proteins with the wrong structure. Per hopes that his research will eventually lead to new ways to diagnose and treat these diseases. "The methods that exist today treat the symptoms, not the underlying cause: the misfolded proteins," he says.

The human body is dependent on the proper functioning of more than 30,000 proteins, each with a specific biochemical role. Proteins are long chains of amino acids that are folded in a given manner, depending on the sequence of the amino acids. Fat-soluble amino acid groups are attracted to each other and hidden inside the protein, while water-soluble groups end up on the outside as a shell. Sometimes the folding fails so that the protein becomes "wrinkled" and gets stuck in a partially unfolded state. This means that the fat-soluble parts that are normally hidden are instead exposed. Since fat doesn't dissolve in water, the proteins clump together according to certain set patterns, so that the fat-soluble surfaces are hidden. The protein lumps are poisonous and harmful to human cells.

Form fibres

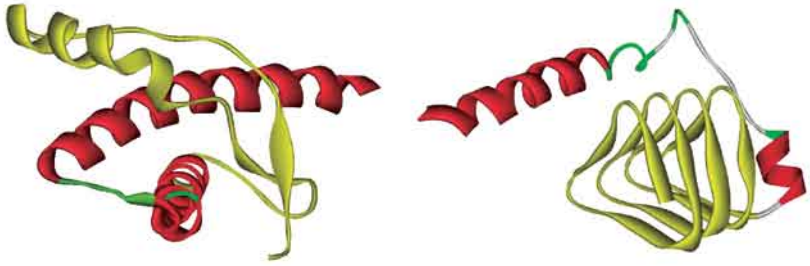
Per Hammarström's research is concerned with a group of misfolding diseases called the amyloid diseases. These include Alzheimer's and Skellefteå Disease. The clumped-together proteins form microscopic fibres called plaque when they aggregate. Plaque is found in various organs in deceased people with amyloid diseases. But the plaque isn't the only culprit here – the intermediate stages leading to the plaque also appear to be very harmful to the cells.

"We have seen that before the proteins form fibres, they pack together in spherical structures. These globs can probably cause damage by, for example, puncturing the cells. Exactly what the intermediate forms look like we don't know, however, and this is something we will take a closer look at. This research can eventually lead to new ways of making a diagnosis if we succeed in finding methods to detect them," says Per.

Infectious proteins in the new lab

Prions are proteins that occur naturally on the surface of the cells in the body and are normally quite harmless. But if they fold the wrong way, the prion proteins can cause, for example, Creutzfeldt-Jacob's Disease. The prion diseases resemble the amyloid diseases, except that they are infectious. In other words, the prions are infectious just like bacteria or virus despite the fact that they lack genetic material. The misfolded prions can convert correctly folded prion proteins to "sick", misfolded prions if they come into contact with them. We don't know how this happens yet, but there is much to suggest that the mechanism involves amyloid fibres.

"We have a lot to learn from basic research on misfolding of prions. That's why the prion research is extremely important, even though very few people are affected by these diseases. One urgent question is whether misfolding diseases in general are infectious. So far



A correctly folded prion protein (at left) next to a misfolded one. The yellowish-green part of the misfolded prion protein is folded to a beta helix, which fits like a building block in an amyloid fibre.

Per Hammarström

no one has succeeded in infecting mice with Alzheimer's. The prions don't differ molecularly from other proteins, however, so with the right experiment I think we can show that Alzheimer's and many other misfolding diseases are also infectious," says Per.

Per looks satisfied when he shows the newly built lab.

"The plan now, since I've received the SSF grant, is to start up the prion research here. Special safe laboratories are required to handle human prions with known genetic mutations. We are currently putting in instruments, and the work will get started in the autumn of 2005."

Hard-rocking father of two

Per has been married for six years to Åsa, who works as an accountant. They have two daughters: Maya and Tyra. He spends much of his leisure time with his family, and any time left over he devotes to running or ball sports, nowadays mainly as a spectator. Along with attending rock concerts (at least two a year), these are his favourite ways to relax.

"I like to listen to hard rock at the lab too, but the doctoral students aren't always so happy about that, so now we've set up a 'democratic list' where everyone gets to choose songs," he chuckles.

Per has always been interested in science since he grew up in Linköping.

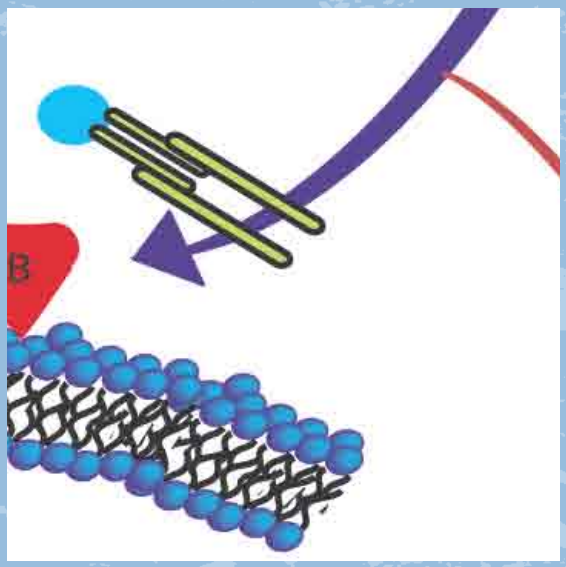
"I liked tinkering with things even as a kid, and especially liked making bombs. My father was interested in pyrotechnics, which I thought was fun and exciting. My big interest in upper secondary school was the origin of life. I borrowed lots of books from the library, which was how I got interested in biochemistry. Then when we took a class trip to the university to hear an excellent lecture on protein evolution, I was hooked. That became my interest during my biochemistry studies at the university," he explains.

After getting a bachelor's degree, Per got his Ph.D. in the field of protein folding at Linköping University. He then left home to continue his studies at the Scripps Research Institute in California, where he became interested in misfolding diseases.

Wants to find new molecules

An important goal of the research is understanding how misfolding can be prevented. There is no treatment for the fundamental cause of all amyloid and prion diseases: the misfolded proteins. The type of molecules needed for treatment are not available today. So far it is only possible to alleviate the symptoms, and for many of the diseases there is no treatment at all. Per hopes they will find molecules that can prevent misfolded proteins from developing in the first place, or clumping together if they do.

"I have always wanted to discover new things, and of course it will be very rewarding if what I discover can contribute towards curing sick people – then it will feel like I'm doing something meaningful." • LC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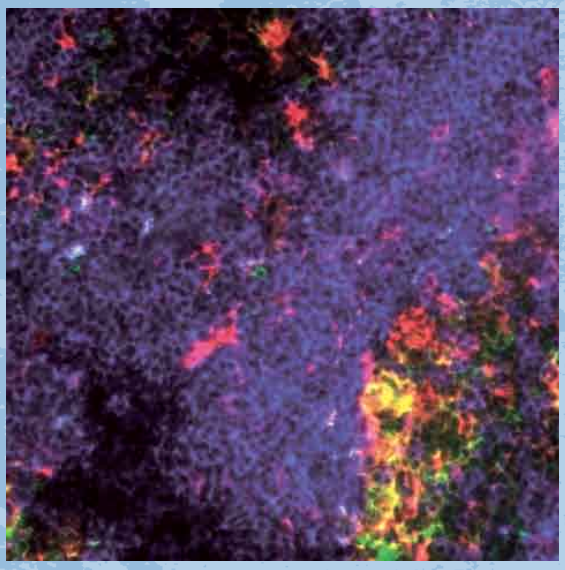

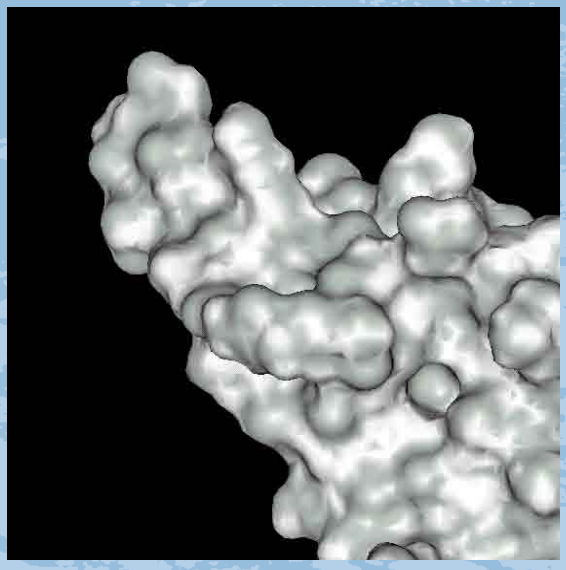

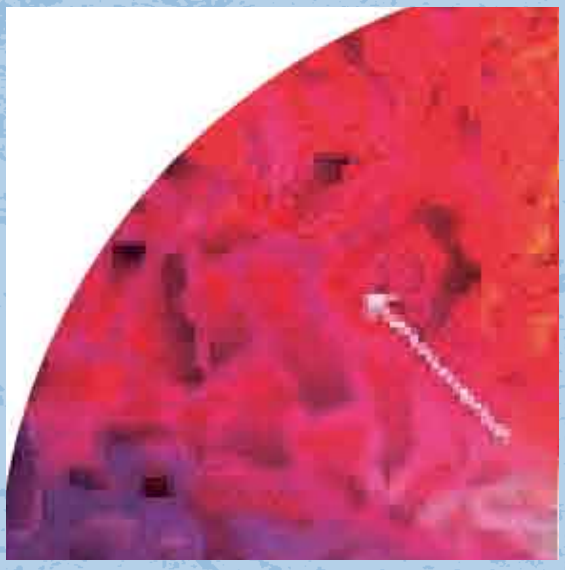

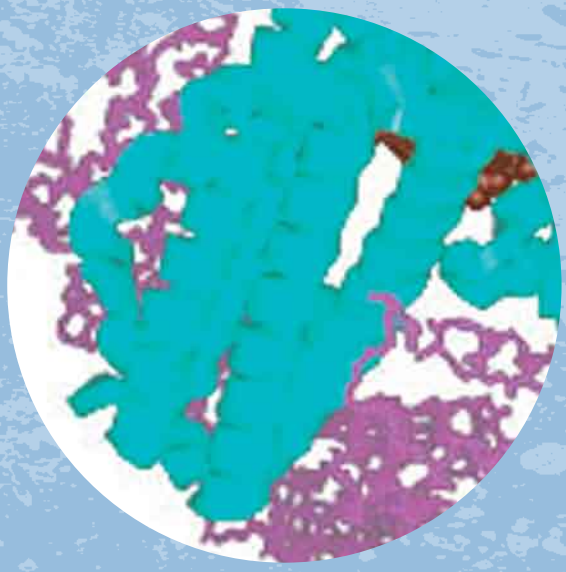

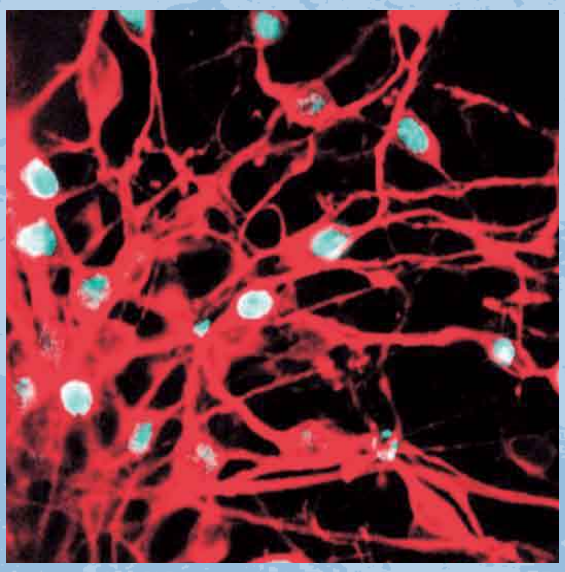

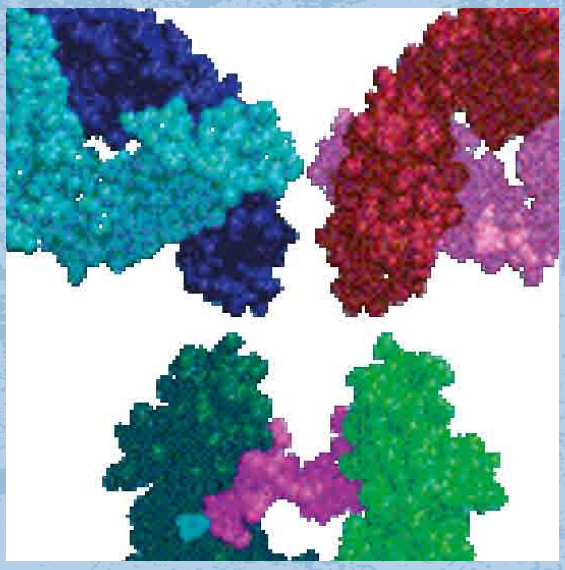

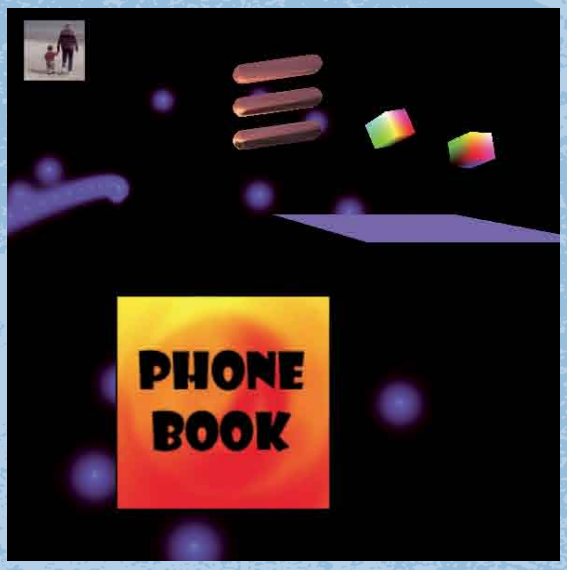
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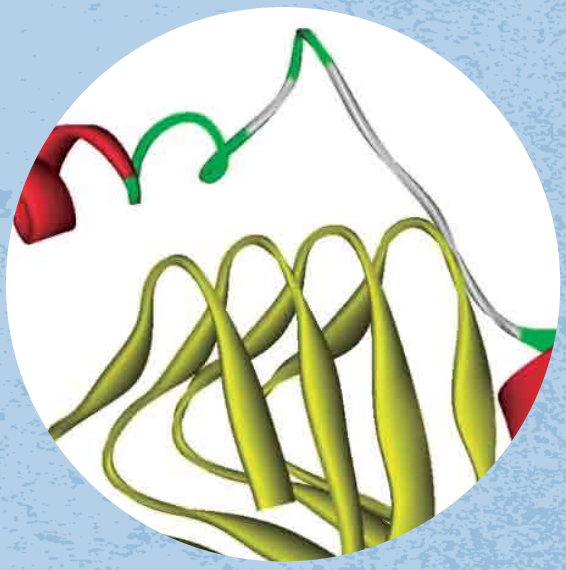
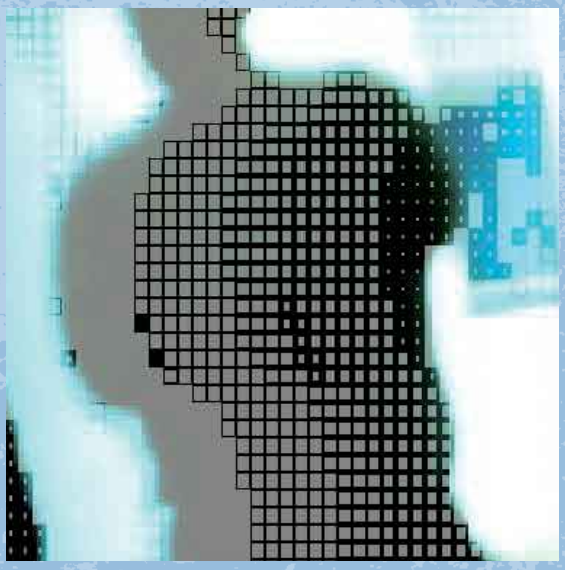
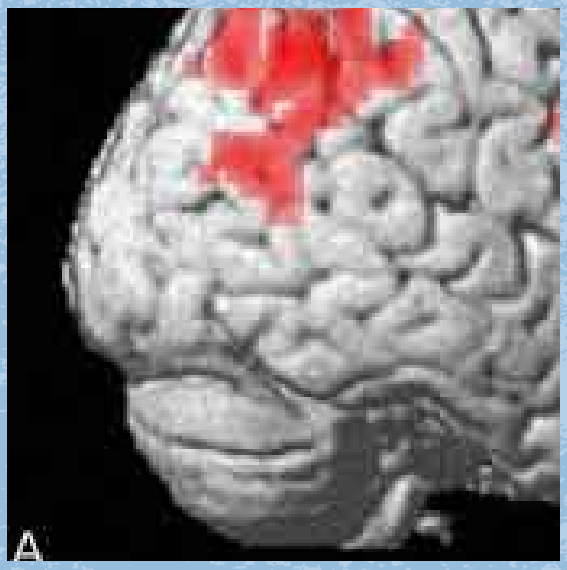






Name:
Lars Erik Holmquist

Nationality:
Swedish

Born:
1966

Awarded Ph.D.:
2000

Works at:
The Viktoria Institute and Göteborg University

Title of project:
The computers of tomorrow

INTERACTION BETWEEN COMPUTERS AND HUMANS

Computers are playing an increasingly large role in our lives. They are no longer viewed solely as work tools, but are now integrated in many things around us. Lars Erik Holmquist and his research group at the Viktoria Institute in Göteborg have many projects going. They all have to do with how to build on today's technology and find new uses for computers. "We are looking at existing technology and finding unexploited possibilities," says Lars Erik.

If things were different, Lars Erik might have been a music journalist today. He started out studying comparative literature and philosophy at the university and had envisioned a career in music or journalism. It was chance that he got into research in computer science.

"When I started studying computer science I had decided to become a game programmer," says Lars Erik. "But then I got into research instead, and I don't regret it," he continues.

Free thinker

Perhaps it is Lars Erik's background and life choices that have made his research on future uses of computers so successful. The field requires creative thinking and an ability to borrow ideas from various sources.

In one of the projects, Lars Erik and his research group have discovered a new function for mobile phones with integral cameras. Today's mobile phones have as much capacity as personal computers had a couple of years ago. But much of that capacity goes unutilised. The new function entails that the mobile phone picks up sounds and other information from its surroundings. Then when you take a picture with the phone, special images are created based on the background sound and the movements detected by the camera.

The microphone in the mobile phone can be used to take a new kind of picture with the phone's digital camera. The pictures are created from both the background sound and the movements detected by the camera.

Invisible computers

Many people associate the word "computer" with a monitor, a keyboard and a mouse. These components were developed in the 1970s for more efficient office work. At that time, computers were used to write and edit documents. Today the computer is used for much more, and only a small portion of its capacity is devoted to document editing.

"When today's user takes out his handheld computer, he doesn't need the same features and interfaces as a secretary needed in the 1970s," says Lars Erik. "But the appearance and function of a computer has changed little in 40 years," he continues.

The idea of ubiquitous computing, or ubicomp, is that computers can be embedded in everyday objects: mobile telephones, doors, dishwashers, etc. The computers perform different tasks depending on what they are embedded in. Much research today is aimed at improving the computers technically, making them smaller, and developing networks and programming languages.

Lars Erik Holmquist

Lars Erik wants instead to find new areas of application and interactive possibilities for computers. The research group looks at the potential of already existing technology when they develop the new features.

In one project the group has developed a new kind of "mobile music". They conducted a survey where they asked a group of people how they listen to music. The results showed people particularly enjoyed recommending music to others. The group has therefore developed a music player that allows you to send music to others. The song sent from one user to another is inserted directly as the next song in the playlist.

Research and development on ubicomp will grow strongly in the coming years. Lars Erik would like to remain in the area and work with the new possibilities for IT products and IT interaction.

"Ubicomp is the most important field of IT research," Lars Erik believes. "The traditional computer has to undergo development. In the future we may not even know there's a computer in the device we are using. Today we don't say we're going out to buy an electric hair dryer, since it goes without saying that it's electric. In the same way, the concept 'computer' may become superfluous in the future," says Lars Erik. • LW

Facts about ubiquitous computing

Ubiquitous means omnipresent, universal. Ubiquitous computing, or ubicomp for short, means that computers are integrated in objects instead of being standalone machines. One of the goals of ubicomp is that the computers should be able to adapt to the environment and the user. The father of ubicomp, Mark Weiser, has said:

"Ubiquitous computing is the name of the third wave in computing. The first was mainframes, each shared by lots of people. Now we are in the personal computing era, man and machine staring uneasily at each other across the desktop. Next comes ubiquitous computing, when technology recedes into the background of our lives."

Name:
Fredrik Höök

Nationality:
Swedish

Born:
1966

Awarded Ph.D.:
1997

Works at:
Lund University

Title of project:
Miniaturised sensors for biological recognition reactions

FINGERPRINTS FOR DISEASES

By combining nanotechnology with surface chemistry and molecular biology, physicist Fredrik Höök wants to develop new biological analysis tools and effective methods for diagnosis of diseases. He is conducting research on special sensors that can, for example, sense molecules in the blood that are markers for a given disease. The molecules must be able to be detected without first being labelled chemically.

Fredrik Höök is an artist in researcher's clothing. He gives a calm and relaxed impression, and I'm not surprised when he tells about his artistic side.

"I knew that I was going to be either an artist or a scientist. The choice fell on physics, but I still continued painting for a long time. In my work as a researcher a creative atmosphere is very important, for both me and my co-workers."

Fredrik has put a couch in the doctoral students' room, and almost every morning he comes in to chat over coffee. He was recently made professor of Nanoscience for Biophysics at Lund University's Faculty of Engineering after having worked at Chalmers in Göteborg. Fredrik got engaged to Malin last spring, and they have two daughters: Elsa, aged 7, and Tora, almost one. The girls take up a lot of Fredrik's leisure time, which he otherwise likes to devote to nature. He is an adventure-loving outdoorsman, and has bicycled across Iceland.

During his undergraduate studies in engineering physics, Fredrik spent six months in Glasgow. He had decided to focus on laser physics, but changed his mind during a lecture. The British lecturer talked proudly about how his laser was going to be installed in a missile headed for the Kuwait war. Fredrik wanted to use his knowledge for other purposes and decided instead to specialise in biophysics.

Biosensors – diagnostic tools of the future

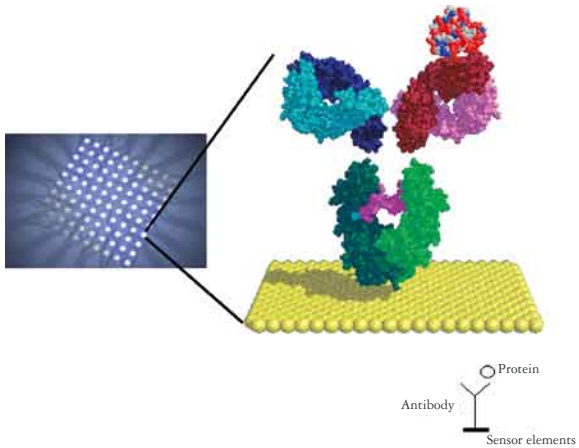
After obtaining his Ph.D. with a doctoral dissertation on the interaction of proteins with surfaces, Fredrik started the company Q-sense AB in 1996. Q-sense develops analytical tools based on a patent which is partly his: a quartz crystal that serves as a very sensitive scale. When something binds to the quartz crystal, it detects the change in mass. The analytical tools detects when a reaction takes place on a surface and can be used in diagnostic medicine.

Fredrik and his research group are now working to develop the sensors so that they not only sense when something has bound to the surface, but also what it is.

"The surfaces can be made selective with the aid of e.g. antibodies on sensor elements. When a protein has bound to an antibody, the sensor element sends a signal. It may be an optical, electrical or mechanical signal. Since an antibody only binds to a specific protein, we can conclude that this particular protein has bound to the surface. This is called a biosensor and is used to test blood to diagnose diseases. The technology makes it possible to discover proteins without first labelling them chemically," explains Fredrik.

The research group is trying to develop a sensor with several different antibodies on the surface. In this way, changes in the concentrations of several different proteins can be detected in the same sample.

"This makes it possible to obtain a 'fingerprint' for a disease consisting of a certain combination of proteins in the



When the protein binds to the y-shaped antibody, the sensor element (the yellow plate) sends a signal. Since the protein is specific for the antibody, the signal reveals which protein has bound to the sensor.

Fredrik Höök

blood. This would permit faster and more reliable diagnosis," says Fredrik.

Miniaturising the sensors from today's macroscopic level (10^{-3} metre) to nanometer level (10^{-9} metre) increases their sensitivity to reactions on the surface. Miniaturisation increases the ratio between surface and volume, which means that the material properties are determined more by the nature of the surface.

"For once we don't have to compromise in one area when we're trying to improve performance in another. Now we can both increase the sensitivity of the sensors and make them smaller."

One difficulty is getting the antibodies to bind to the right place on the surface. The sensor elements on which the antibodies are supposed to sit are located very close together. A possible solution is to study how nature solves this problem.

"A cell organises itself in order to perform a function, and we should be able to imitate this."

Fredrik hopes that his research will contribute to a development of medical analysis tools that permit earlier diagnosis of many serious diseases.

Borderless cooperation

"Doing research is the greatest job there is! Sometimes it's a bit time-consuming, but that's a choice you make. I get to work with fantastic people all over the world and borders don't exist," Fredrik relates enthusiastically. "I hope that as a Research Leader of the future I will have an opportunity to influence tomorrow's research environments. It's important to invest in good undergraduate education and provide attractive research settings for new graduates."

The combination of nanotechnology, surface chemistry and molecular biology makes Fredrik's research unique. The research group is a felicitous mix of people with different backgrounds.

"Research is innovative. New ideas and concepts emerge when we broaden our views concerning what we understand about biology and physics. It's important to take inspiration from other research fields and from nature in order to see the interdisciplinary connections," concludes Fredrik. • LW

Name:
Kristina Höök

Nationality:
Swedish

Born:
1964

Awarded Ph.D.:
1996

Works at:
Stockholm University, Royal Institute of Technology and SICS

Title of project:
Design of emotional interaction for body and mind

FOCUS ON FEELINGS

Interpersonal interaction has changed in recent years. It is easy to just send off a text message from a mobile phone or write an e-mail on the computer. The disadvantage of these forms of communication is that it is more difficult to convey emotions. The means of expression are more limited in modern interaction tools. Kristina Höök wants to change this and allow more room for feelings in the interface between human and technology.

The word "ubiquitous" means omnipresent, and "ubiquitous computing" (ubicomp) means that computers are embedded in many of the devices around us. The concept can be described as the opposite of virtual reality. In the virtual world, human is in a world created by computers, while ubicomp can be described as a world where the computers are adapted to human. Today, computers are embedded in mobile phones, doors and dishwashers, even in clothes. But are their functions adapted to our needs? Kristina Höök's research explores what functions we humans want around us and how we interact with them.

Initial feeling is crucial

When faced with a question, we often base the decision we make on our initial gut feeling. Then after having pondered the problem we usually arrive at the same decision as indicated by our initial feeling. In other words, feelings are of great importance for our rational thinking. It is therefore important that the tools used today for communication, such as computers and mobile phones, take human emotions into account. Kristina develops methods and software that focus on our senses in the interaction between human and machine. She particularly examines how humans can convey feelings to each other via mobile and computerised interaction tools.

"The technical gadgets around us are a part of our culture. We must integrate human's fundamental values – our social and emotional sides – in the technology we develop," says Kristina.

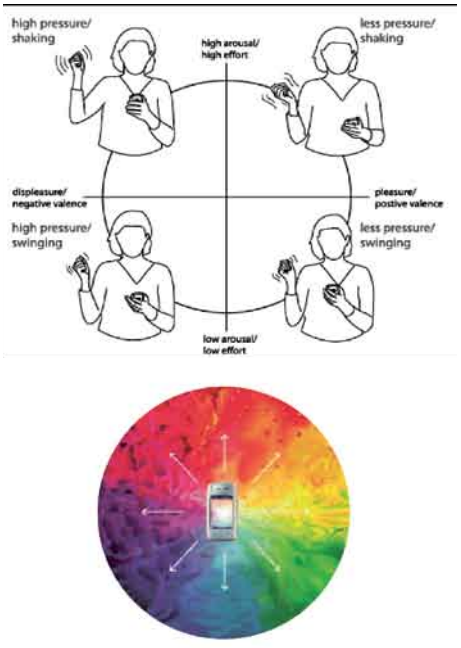
Kristina Höök is a professor at the Department of Computer and Systems Sciences associated with both Stockholm University and the Royal Institute of Technology (KTH), but she is also active at SICS, the Swedish Institute of Computer Science. Kristina's favourite leisure-time activity is riding Icelandic horses.

"When you have a job like mine, where I spend a lot of time in front of the computer, it's wonderful to be outdoors. We ride no matter what the weather," says Kristina.

She is married to Sverker, and they have two sons: Adam, aged 16, and Axel, aged 11. The whole family also likes to ski.

Body language determines background colour

Kristina and her research group have developed a function that makes it possible to reinforce the emotions in a mobile phone text message (SMS = Short Message Service) by choosing a suitable background. After having written the message, the user can translate his movements into colours, shapes and animations in the background by holding a sensor in his hand. If, for example, you want to show that you are angry, you can make an angry motion with the sensor. The background will then be an angry red with edgy animations.

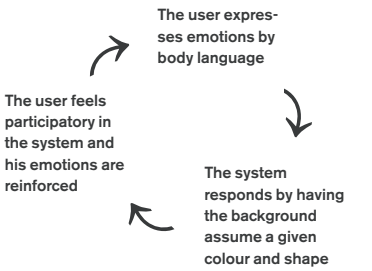


The upper figure shows different gestures, which are perceived by the handheld sensor. The body language is then translated to the colours and shapes illustrated in the lower figure.

Kristina Höök

Today a text message (SMS) is just a line of text that can easily be misunderstood. The new function permits body language to be conveyed, which clarifies the communication. The purpose of the text message function is that both the sender and the receiver should be affected. When the sender has made a gesture that describes the feeling he or she wants to convey, this reinforces that feeling even more. Kristina calls this an "affective loop".

In another project, Kristina has, together with her research group, developed an interactive doll for a computer game. If you angrily shake the 15 cm tall doll, the sensors in the doll perceive that you are angry. The sensors signal this to a computer, which in turn controls a figure in the game, which then makes angry body movements. Altogether there are six different movements which the sensors in the doll can translate to the computer figure's body language. Just like the text messaging function, this is a physical interaction that reinforces the sender's perceived emotion.



The user is integrated in the system and perceives an "affective loop" via the new text messaging function.

Kristina hopes that her research will lead to increased awareness and interaction between humans and machines, and thereby interaction in society as a whole.

"The new technology is changing us and the way we think. But since it is we who are building the new technology, we must also build in our values. 'Ubiquitous computing' is often called the second IT revolution, and we now have a great opportunity to influence it," concludes Kristina. • LW

Name:
Karl Henrik Johansson

Nationality:
Swedish

Born:
1967

Awarded Ph.D.:
1997

Works at:
Royal Institute of Technology

Title of project:
Embedded control systems in a network environment

A SOCCER REFEREE IN THE RESEARCH WORLD

The need to measure, monitor and control systems exists everywhere in society. When technical systems are connected together into networks, new methods and computer tools must be developed in order to ensure that all parts work. Functions must often take place in real time, i.e. without any time delays. When an airbag has to deploy in an accident it mustn't be delayed by other systems in the car.

Karl Henrik never really planned his education or his choice of career, he has always just done what he thought was most interesting. Gradually he has increasingly felt that he has found his way to the right field. Karl Henrik got his master's degree in Electrical Engineering at Lund University's Faculty of Engineering and had only taken the undergraduate course in control engineering before starting work on his Ph.D. in the field.

"I met Karl Johan Åström at the Department of Automatic Control in Lund, and he was very inspiring. There was such a positive atmosphere at the department, and I was convinced it was the right place to take my Ph.D.," says Karl Henrik.

What is control engineering?

Control engineering has to do with measuring and regulating a system so that it behaves in the way you want it to. A simple example of this is temperature control in a room. A thermometer measures the temperature in the room and a regulator adjusts the radiator so that the desired temperature is achieved. But the whole room doesn't reach the same temperature at once. First the area nearest the radiator is heated, and then the heat spreads. This means there is a delay in the system. When it comes to controlling the temperature in a room, some time lag may not matter so much. But imagine if it takes too long for the airbag in a car to deploy when the car crashes. The consequences then are much more dramatic.

The theories surrounding control engineering can be applied in a variety of areas: engineering, biology, economics, medicine, etc. Karl Henrik is working to develop general methods for network-based control engineering. The fact that it is network-based means that the system is connected to a network, e.g. the Internet, where information can be transferred. Interconnecting different information systems enables more functions to be utilised, but the complexity of the system leads to many difficulties. One example of a network is the Internet, another is a mobile phone network. They work relatively well by themselves, but when you connect the networks together, for example by connecting to a website via a mobile phone, problems sometimes arise. The networks are not designed to work well together. Karl Henrik is working to develop tools and methods to improve the technology of such interconnected systems.

After receiving his doctorate, Karl Henrik worked for two years at the University of California in Berkeley in the USA. He likes to compare Berkeley to Lund.

"Berkeley is a small university town located on the eastern side of San Francisco Bay. South of Berkeley is the industrial city of Oakland, just as Malmö is located south of Lund. And on weekends you cross the bay into San Francisco, just like you cross the Sound to Copenhagen if you live in Lund," says Karl Henrik.

Since 2000 he has had a position as an associate professor at the Department

With digital maps and a GPS navigator, the truck engine is prepared to climb a hill. This can reduce fuel consumption. (Photo: Scania)

Karl Henrik Johansson

of Signals, Sensors and Systems at the Royal Institute of Technology. Karl Henrik and his wife Liselott love to travel and visit friends all over the world together with their two sons, Kasper and Felix.

Predicting hills

Vehicles equipped with networks have been manufactured for the past 15 years or so. They have, for example, a sensor on the wheel to measure speed, radar to see if something is approaching, temperature sensors, and of course lock and alarm systems. These are examples of automotive functions that are connected to a network. Today, safety considerations preclude certain functions, such as the airbag, from being connected to the network. The reason is that if anything in the network breaks down, other functions can be disabled. Karl Henrik's research is aimed at improving these systems. If the functions could be prevented from being disabled, the vehicle would be safer. The information obtained from the vehicle's network of sensors and measurement transducers could be used to avoid a collision if, for example, a deer should run out onto the road.

"My research is a little like a good soccer referee. It should do its job but not be noticed," says Karl Henrik. "It can be described as a hidden technology. You build technology that no one notices as long as it works," he continues.

Karl Henrik and his research group are collaborating with the automotive industry to reduce fuel consumption in trucks. By using digital maps and GPS, the topography of the route can be predicted. When the truck approaches a steep hill, the engine can be prepared automatically so that the climb is managed with less fuel consumption. The truck can also be connected to a traffic information network. If the intensity of traffic on a section is known in advance, the truck can be prepared for this. The driver can even get alternative route suggestions.

International cooperation

Karl Henrik and his research group are running the project in cooperation with several companies. In this way they know they are working on problems of relevance to Swedish industry. A project is particularly successful when the group not only solves a company's particular problems, but the theories can be applied to other systems as well. The solutions lead to tools that make it possible for researchers and engineers to develop functions and applications within other areas as well.

"There are fundamental issues within control engineering and network design that are independent of the application. These are the issues I want to address in my research," says Karl Henrik.

There is extensive international cooperation within network-based systems. Karl Henrik is particularly involved in two EU projects, RUNES and HYCON. These projects engage both industry and academic researchers all over Europe to collaborate on problems in networks and infrastructure. Network-based systems are found everywhere: in industrial production, transportation systems, energy distribution and communication systems. Karl Henrik's goal is to establish a research laboratory to strengthen Sweden's role in this rapidly growing field. • LW

Name:
Torkel Klingberg

Nationality:
Swedish

Born:
1967

Awarded Ph.D.:
1997

Works at:
Astrid Lindgren children's hospital at Karolinska Institutet

Title of project:
Development and plasticity of cognitive functions

WORKING MEMORY CAN BE IMPROVED BY TRAINING

Children with ADHD and stroke sufferers have a common handicap. They have an impaired working memory. Working memory is the ability to retain information for a few seconds. It may be a question of solving a math problem or remembering recently given instructions or directions. Torkel Klingberg and his co-workers at Karolinska Institutet have shown that working memory can be improved by training.

Concentration difficulties or ADHD (Attention Deficit/Hyperactivity Disorder) is something many children and adults suffer from. These difficulties are in part due to impaired functioning of the patient's working memory. Torkel Klingberg and his research group at Astrid Lindgren Children's Hospital have developed a training programme where patients can improve their working memory through training.

We need to know more about working memory

Working memory is situated in a network between the frontal lobe and the parietal lobe. In everyday life it is used for various types of problem solving. Working memory also makes it possible to remember instructions, numbers and positions. Reading each individual word in this article doesn't make demands on working memory, but reading and comprehending the whole text does.

"If the frontal portions of the brain are damaged, this causes problems with working memory," explains Torkel. "In order to develop a training program for our patients, we need more knowledge of how working memory works. In our research we are therefore studying how working memory develops and what happens in the brain when it develops. We are also looking at what can go wrong during this development and why someone's working memory may be better or worse," he continues

Music, diving and research

As a young man, Torkel's musical talent brought him to a conservatory in Toronto. There he played the violin and studied mathematics for a year. Torkel ultimately decided against a career in music in favour of studies at Uppsala University, but he still takes out his violin and plays once in awhile. Another favourite pastime is scuba diving, either on the west coast of Sweden or in Thailand.

After earning a bachelor's degree in biology and psychology, Torkel started medical studies at Karolinska Institutet. Since he has always been fascinated by the connection between human behaviour and brain structure, Torkel immediately became interested in brain research.

During his postdoc period at Stanford in California, he studied the activity of the brain and the connections between its different parts. Among other things he showed that dyslexia is associated with disruptions in connections in the brain.

Computer game for memory

Back in Sweden, Torkel started research at Astrid Lindgren Children's Hospital on brain structure and working memory. This field is called cognitive neuroscience and involves investigating the relationship between brain activity and cognitive functions. Examples of cognitive functions are memory and attention.

The training program developed by the research group is tailored to the abilities of each individual patient. The idea is that the patient should remember and reproduce what is presented on the computer screen. The patient trains for 45 minutes a day, five days a week for five weeks. The training program for children with ADHD looks like a computer game. The children must have fun with the program in order to be able to concentrate. More than 200 children have undergone the training, and the results show a significant improvement in working memory. The research group has also conducted a smaller stroke study where twenty patients underwent the program, also resulting in an improvement in working memory.

"There are of course many differences between children with ADHD and stroke patients, but one similarity seems to be that they can improve their working memory by about 15% through training," says Torkel. "Clinically, the training program produces such strong effects that it could be considered a treatment method," he continues.

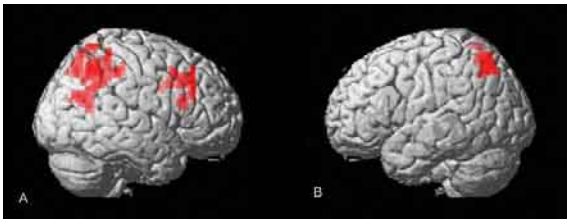
Torkel Klingberg

Medicinal treatment of ADHD is given in the form of stimulant drugs such as amphetamine. Paradoxically, the drug has a calming effect in small doses.

"The medication prescribed differs from case to case depending on what the symptoms are, but many patients with ADHD could reduce their medication by instead carrying out the training program," says Torkel. "An improved working memory also leads to better results in school," he continues.

The research group has initiated a joint project with the Stockholm Institute of Education where they are looking at how the training improves maths results for pupils with ADHD, and so far the results are positive. Stroke patients only get occupational therapy today, so working method training could help the patients to return to their everyday activities. Encouraged by the research findings, Karolinska Development has helped start a company, Cogmed, to further develop the method for practical use.

Magnetic resonance imaging (MRI) can be used to measure working memory in children and adults. The MRI scanner detects the increase in the flow of blood to the part of the brain that is activated. Before the start of the training program, the scanner measures brain activity in the area where working memory is located. After the five weeks of working memory training, new scans are made of the blood flow in the brain.



Pictures from an MRI scanner. A is the right brain half and B the left brain half. The red spots show the improvement in working memory after five weeks of training in a group of young healthy adults.

The difference between the images before and after show the increase in blood flow to the area and thereby also the improvement in working memory.

From nerve cells to programming

Torkel's research spans a broad field. The research group is studying both what happens at the cellular level and how changes in human behaviour are related to changes in the brain. The group is working together with computer programmers, who develop the training programs. The training results provide new knowledge about how the brain can be stimulated.

"Today we know very little about the brain and how it works," says Torkel. "The brain's cognitive functions can almost only be studied in man, or at best in certain types of monkeys. We can't stick needles into people's brains, which makes it difficult to study the details."

"Our research project on working memory training will lead to greater knowledge of how plastic, or formable, the brain is. This may in turn result in better rehabilitation methods for stroke patients and children with ADHD," concludes Torkel. • LW

Name: Mikael Käll

Nationality: Swedish

Born: 1963

Awarded Ph.D.: 1995

Works at: Chalmers University of Technology

Title of project: Biophysical imaging

IN THE BORDERLAND BETWEEN PHYSICS AND BIOLOGY

At an interdisciplinary scientific research centre in Göteborg, Mikael Käll works with so-called biophysical imaging. This means that he is trying to develop advanced optical microscopy and spectropscopy to study cells and biological molecules. Among other things, he studies how gold and silver particles can be used in biosensors.

Before the invention of light microscopy, people didn't even know cells existed. The microscope has enabled us to learn about the structure of cells and some of the processes that occur inside them. But demands on resolution and contrast are constantly increasing. The resolution of the light microscope is limited by the wavelength of visible light, which is between 400 and 700 nanometers. It is impossible to see objects smaller than about one wavelength. In cellular and molecular biology research, it is necessary to be able to quantify and locate proteins and other biomolecules, which are often only a few nanometers, inside living organisms. This is a prerequisite for the development of "systems biology models" – mathematical models of the molecular processes that occur in cells.

During the first half of 2005, Mikael Käll has been a visiting professor at Rice University in Houston, Texas. Back home in Sweden, he has been the director of the Centre for Biophysical Imaging CBPI at Chalmers University of Technology since 2002. The interdisciplinary research centre aims to build bridges between cellular and molecular biology and applied physics.

Mikael is first and foremost a physicist, but after his postdoctoral training he studied biology for one year.

"I have always been interested in both physics and biology. Physics was not an easy choice. My research field – biophysical imaging – reflects the conflict within me. It enables me to combine my interests, and I am learning a lot of biology all the time," he says.

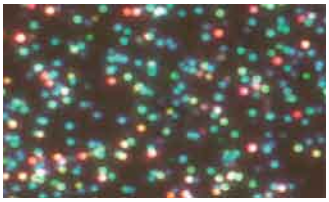
Gold and silver valuable in nanooptics

One of Mikael's projects lies within the field of plasmonics. Nanoparticles of gold and silver have special optical properties that enable them to be used in sensors for biomolecules.

All metals have free electrons, known as electron gas, that enable them to conduct current. The electron gas in gold and silver nanoparticles can be made to oscillate at a resonance frequency if visible light is shone on the particles. The phenomenon is called surface plasmon resonance, and the exact resonance frequency is determined by the shape and size of the metal particle. The particle then emits light at the same frequency as the resonance, which gives it a certain colour.

"It's similar to the resonances, i.e. the tones, of musical instruments. In an organ pipe, the tone is determined by the size of the resonance box. In the same way, the particle size determines the resonance, and the electron gas can be compared to the air," explains Mikael.

If a biomolecule adheres to the metal particle, this changes the resonance frequency and thereby the colour. The change in colour can be detected by various types of optical spectroscopy, which is the principle employed by biosensors based on surface plasmon resonance. Being able to detect and measure small quantities of biomolecules simply is of great importance in biological research.



Silver nanoparticles that exhibit different colours due to the phenomenon of surface plasmon resonance. The silver particles can be used in sensors for biological molecules.

"Sensors for detecting e.g. DNA and proteins already exist. But with surface plasmon sensors based on nanostructures, it is possible to study even smaller volumes and fewer molecules," says Mikael.

Automated microscopy method for stressed yeast

In another project Mikael wants to develop and use an established microscopy method – fluorescence microscopy – together with researchers in cellular and molecular biology. In fluorescence microscopy, various dyes are added to

Mikael Käll

a sample in order to image selectively stained structures and molecules inside the cell that would have been impossible to see in an ordinary light microscope.

"There is a great heterogeneity in biological systems. The cells look very different when examined in the microscope. We want to develop techniques for automated fluorescence microscopy and image analysis where the information obtained is independent of a given person's assessment. We want to be able to take many pictures of many cells and then subject the results to quantitative statistical processing to obtain large quantities of relevant information. Such quantitative information can be used as input for designing systems biology models for how the cells work," explains Mikael.

Mikael wants to use the method to develop such models for "stress proteins" in yeast cells. "Stress" in these contexts refers to a number of suboptimal conditions for a cell. Examples are changes in temperature or in the concentration of free radicals. Different types of cell stress appear to be involved in many human diseases, and yeast cells can be used as model systems for research on these diseases.

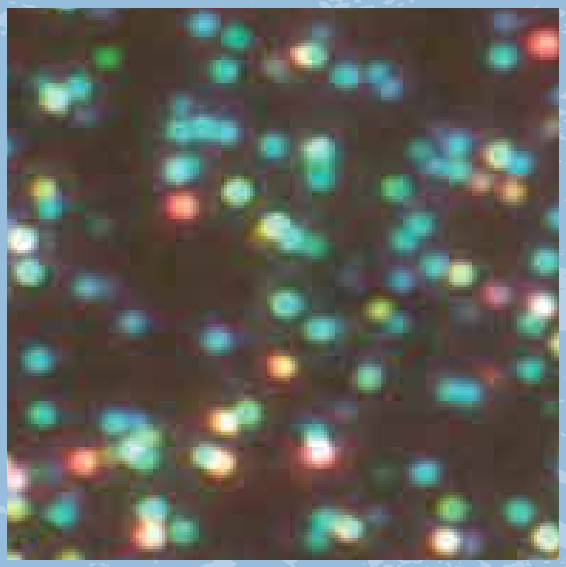
Bird watcher and tour guide

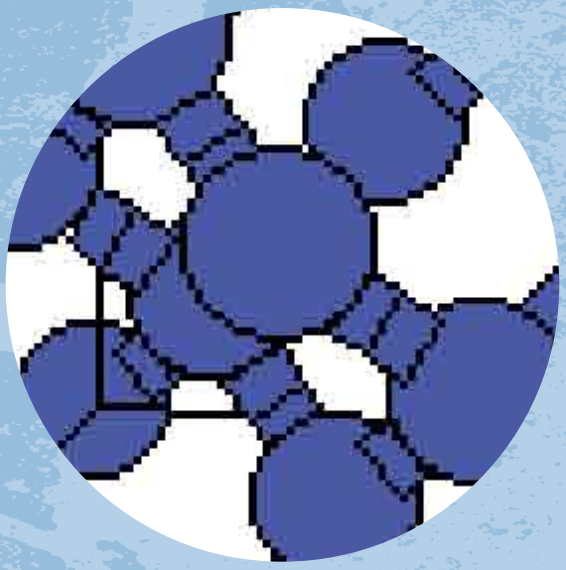
Mikael Käll was born and raised in Göteborg (Gothenburg), and the family currently lives in northern Halland. His great interest besides research is bird watching.

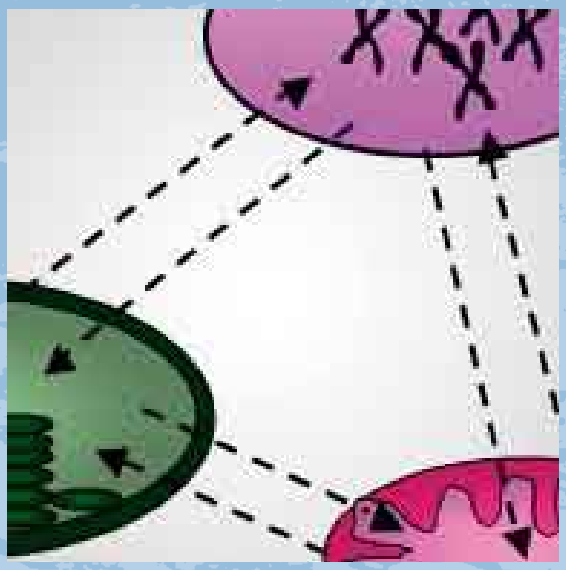
"I've been an ornithologist since I was 12 or 13 years old. It's a great hobby not only because of the birds themselves, but also because you meet all kinds of people. Many of the other ornithologists conduct various kinds of research on birds. When I was younger I found a lot of inspiration, as far as discovering and trying to understand things, in this diverse group of people," he says.

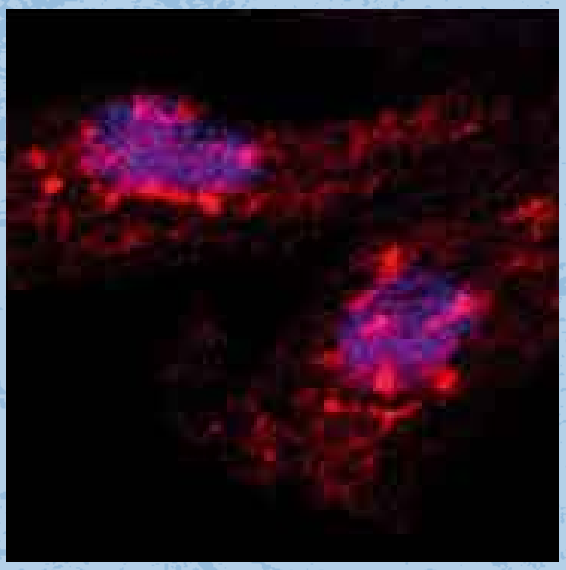
Mikael is also a tour guide on arranged birding trips. This winter he travelled to Gambia, and in the autumn he's off to South Africa.

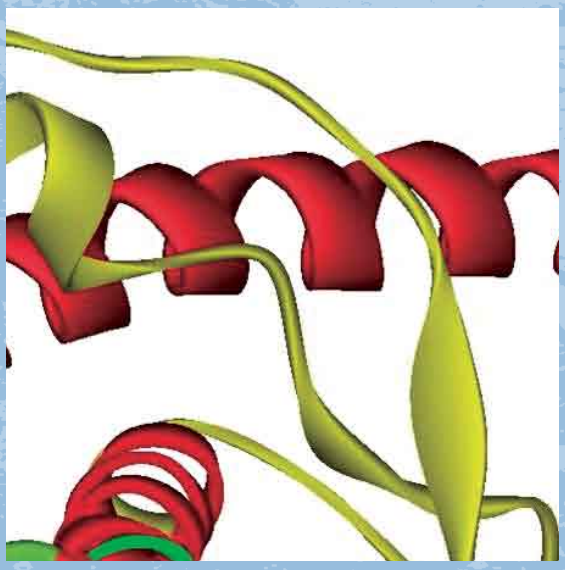
"It was through birding that I met my wife, Paula. Before our son Styrbjörn was born we travelled a great deal. Now we can't travel as often, but travelling and birding are a very important part of me," he concludes. • LC

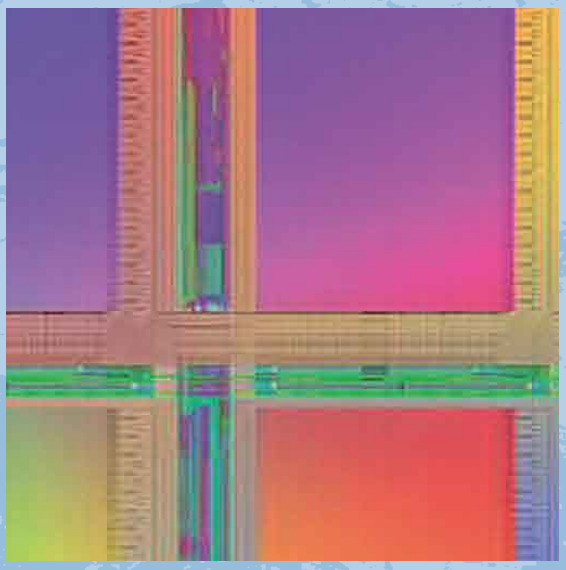


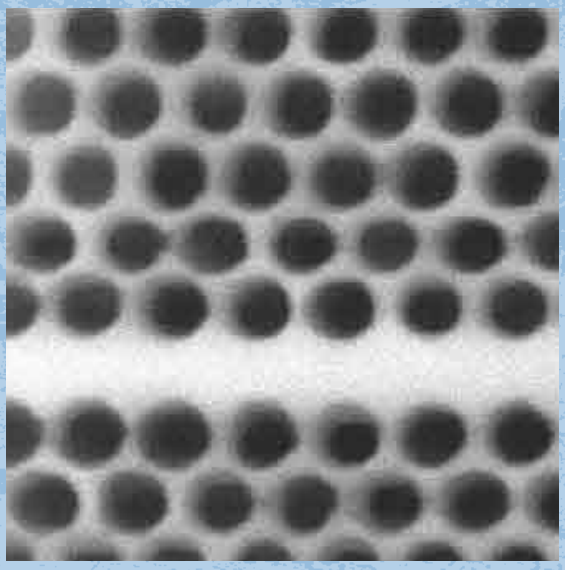


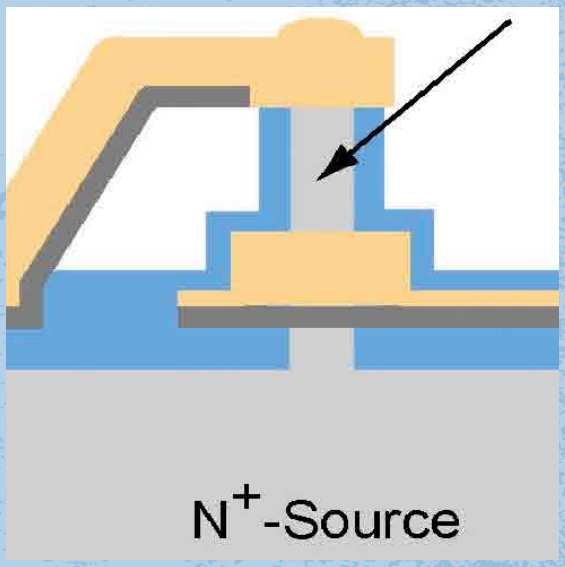











N+-Source

Name: Min Qiu

Nationality: Chinese

Born: 1975

Awarded Ph.D.: 1998 and 2001

Works at: Royal Institute of Technology

Title of project: Photonic crystals: Light magic at work

BUTTERFLIES CAN TEACH US ABOUT THE FUTURE OF OPTICS

When light falls on a butterfly wing, light of certain wavelengths will pass through while other wavelengths will be reflected. This explains the shimmering, iridescent colours. It is the special tiny pattern in the butterfly wings that affects the path of the light. Now researchers are trying to imitate nature so they can put this phenomenon to use in technical applications.

Photonic crystals are artificial materials that makes it possible to control the flow of photons, i.e. light particles. The crystals can be used in technical applications at all kinds of wavelengths, but Min Qiu is concentrating his research on how they can improve optical communications. By introducing photonic crystals into the optical circuits, the flow of photons can be focused and controlled. This technique makes it possible to increase the speed at which information is transmitted and processed.

From China to Kista

A large map of China hangs on the wall of Min Qiu's room in the Electrum building in Kista. Min came to Sweden in 1999 with a Ph.D. in semiconductor physics to conduct research in the borderland between solid-state physics and electromagnetism. His research focused on a new area: photonic crystals. After two years of research and another Ph.D., Min ended up at KTH's Department of Microelectronics.

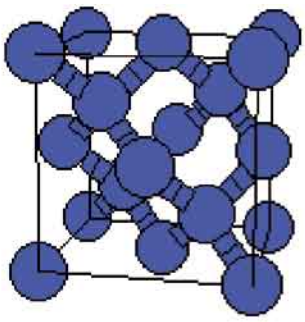
While growing up in China, Min and his classmates thought being a researcher was the best job they could get. Research scientists were considered to be smart, highly regarded and hard workers. At that time earning money wasn't so important, since everyone had low wages.

"Now all Chinese children want to be pop stars," laughs Min.

Min found inspiration in the books he read about prominent Chinese scientists. He had always been fascinated by physics, and had long been driven by a desire to understand how everything works.

Learning from nature

Photonic crystals could have a periodic structure reminiscent of the crystal structure such as diamond. The difference is that the carbon atoms have been replaced by metals or dielectric materials in the artificial photonic crystals.

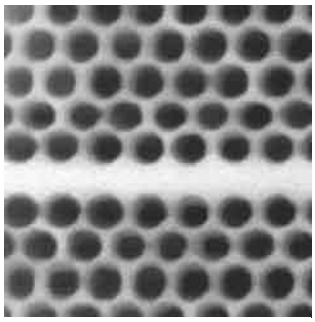


The blue spheres represent the carbon atoms that build up the structure of diamond. In diamond-like photonic crystals the carbon atoms are replaced, but the structure is retained.

In ordinary crystals, electrons flow between the atoms, while in photonic crystals photons do.

In analogy with electronic bandgaps in ordinary crystals (e.g. Silicon), photonic crystals may posses a forbidden band for light with certain frequencies, i.e. a photonic bandgap, where light cannot propagate but is reflected or diffracted.

In order to be able to control how the light is transported, the crystal must be processed. For example, the fact that the crystal behaves like a perfect mirror at a given wavelength can be utilised. This means that all incident light of that specific wavelength is reflected. The processing then introduces a defect (e.g. a waveguide) in the crystal, which forces the light to travel there instead of being reflected. The rest of the crystal is intact and does not allow the incident light to pass through.



A line defect in the photonic crystal structure where the light is forced to travel.

Not so long ago it was discovered that these special crystal structures also existed in nature. The lovely iridescence

Min Qiu

of butterflies and opals is attributable to photonic crystals.

If you look at the feathers or skin of colourful animals in a microscope, it is very likely you will see the photonic crystal structure. The structure is colourless in itself, but at a distance it emits a wealth of colours. The reason is that light of certain wavelengths passes through, while other wavelengths are reflected and perceived by the eye as colours.

Photonic crystals exist in nature. They are, for example, responsible for the lovely colours of this butterfly.

"It is very difficult to fabricate photonic crystals, but nature manages quite well. We should learn from nature," says Min.

"The 21st century might be the century of photons"

The desired wavelength of light to be emitted is taken into consideration when photonic crystals are fabricated. The distance between the "atoms" in the structure determines which wavelength is allowed to pass through. Since photonic crystals can be adapted to all wavelengths, they can be used for everything that is related to photons. Besides having applications in optical circuits, the crystals can, for example, be used in microwave technology and for radio waves. Today there are photonic crystals adapted to radio waves used for mobile communications in the antennas of mobile telephones and base stations. Another area of application is the delivery of drugs to specific targets in the body. The drug is embedded in a crystal and forced out by a laser beam. This technique makes it possible to treat very small parts of the body, for example a cell.

Min and his research group are currently working to design small filters for optical signals. The filters make it possible to distinguish an individual signal at a given wavelength from all other signals. This results in a higher capacity of information transfer. The research group currently consists of four people, but two more will soon be added. Min considers the opportunity to do research a great privilege and would like to compliment Sweden on its openness to foreign researchers. The grant from SSF has made it possible for Min to stay in Sweden, for which he is grateful. His family likes Stockholm and Min's wife Sophia Li will soon graduate with a degree in computer engineering from the Royal Institute of Technology. Their two children, Katarina (aged 2) and Henrik (aged 1), were born in Stockholm and currently attend nursery school.

More functions of photonic crystals will be discovered in the future, and Min hopes that the field will grow in the years to come. Photonic crystals have been described as a material with a potential for manipulating photons in the same way as semiconductors manipulate electrons. The difference is that this takes place at the speed of light.

"While the 20th century was the century of electrons, the 21st century might be the century of photons," predicts Min. • LW

Name:
Åsa Strand

Nationality:
Swedish

Born:
1970

Awarded Ph.D.:
2000

Works at:
Umeå Plant Science Centre, Umeå University

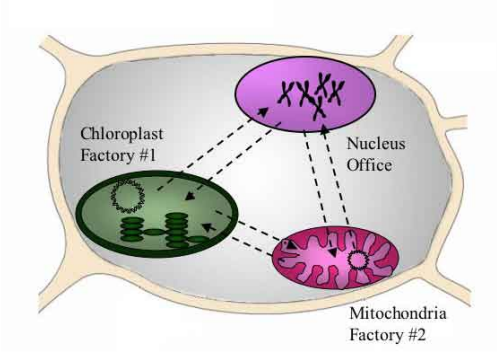
Title of project:
Intracellular communication between chloroplast and nucleus in the plant cell

RESISTANCE RESULTS IN REDUCED HARVEST LOSSES

Much of Sweden's potential harvest is lost each year due to unfavourable weather conditions. Frost and drought damage occurs when the crops fail to sustain photosynthesis and are thereby unable to get enough energy. Åsa Strand is studying how photosynthesis is affected by various stress conditions, such as cold, and how crops can be made more resistant by means of genetic engineering. The improvements could lead to better profitability in agriculture and forestry.

Man has been crossing agricultural crops to obtain the desired properties since time immemorial. Previously, when breeding efforts focused on qualities such as high yield or good baking properties, certain tolerance properties were lost. Today we can restore the crops' tolerance to environmental stress (for example cold, drought and changes in light conditions) by means of genetic engineering. Åsa Strand of the Umeå Plant Science Centre UPSC at Umeå University is studying the cellular processes of plants, i.e. what happens in the smallest parts of the plants. The goal is to understand how plants know that they are exposed to stress and how they adapt to it.

The plant's genetic material is divided between the nucleus, the chloroplast and the mitochondrion. Most of the plant's roughly 25,000 genes are located in the cell nucleus. The chloroplast contains a hundred or so genes, which code for components of importance for photosynthesis. The mitochondrion's fifty or so genes are responsible for basic tasks in energy production.



The genetic material in the plant cell is divided between the cell nucleus, the chloroplast and the mitochondrion. Plastid-nucleus communication plays an important role in the stress acclimation of plants.

Signals in the plant cell warn of stress

In order for photosynthesis to work there has to be communication between the nucleus and chloroplast. This is because certain of the reaction's components are coded in the nucleus. The chloroplast has to signal the nucleus how much of these components it needs. It is this signalling system that Åsa and her research group are trying to understand. Photosynthesis is very sensitive to stress. When it is cold, for example, the chloroplast's membranes get stiff and the photosynthesis reactions slow down. As a result, the plant cannot utilize all of the absorbed light, resulting in damage to the plant.

To reduce the damage, the chloroplast must adapt to the lower temperature. The chloroplast therefore communicates its needs to the cell nucleus, which synthesises protective proteins. These proteins can absorb the excess light or prevent the cell's membranes from becoming too rigid. When the research group has defined how this chloroplast-nucleus communication works under stress conditions, the plants can be modified to become more tolerant. By means of genetic engineering, the signals between the chloroplast and the nucleus can be influenced so that protective proteins are formed in larger quantities. The chloroplast can then retain its photosynthetic activity under stress, and the plant survives. Large sums of money could be saved in agriculture and forestry if damage to crops and trees caused by environmental stress could be prevented.

Increased knowledge of human diseases

Åsa's research on intracellular communication is also important as basic research since it leads to a greater knowledge of fundamental biological processes. Results based on plant cells can also add to knowledge of human cells. Animal cells have no chloroplast, but nucleus-mitochondrion commu-

Åsa Strand

nication is similar to that in the plant cell. We know that the mitochondria play an important role in human ageing. Defects in the mitochondria can lead to diseases such as Parkinson's and diabetes. The cause has not yet been established, but it may be related to impaired communication with the nucleus.

The test plant used most in the research is thale cress, Arabidopsis thaliana. It is a small plant with white flowers that grows on sandy soil.

"Arabidopsis is the leading model organism. It is easy to work with, self-pollinating and has a short generation time. It is easy to cross and transform Arabidopsis, and it's genome has been determined," says Åsa.

The idea is that the results from Arabidopsis should be able to be transferred to other agricultural plants. We have good tools today to develop agriculture and forestry. Genetic engineering makes it possible to improve the properties of plants with great precision. It is also much faster than traditional plant breeding. It recently became possible to genetically engineer trees as well. Previously it has taken nearly a human lifetime to cross two tree varieties. Spruce, for example, takes 15 years to flower. Now the genes that control flowering can be activated so that the trees flower after only a few months. It is thereby possible to tailor trees to specific purposes, for example to improve their fibre quality. If permission is given for the technique to be used, it could be very important for the Swedish forestry industry. Åsa is happy to be a part of this "revolution".

"All the tools exist, now it's only a question of allocating the necessary resources," she says.

Likes living in Umeå

Åsa comes from Värmland in central Sweden but likes living in Umeå. It's close to the mountains, where she likes to ski in the winter and hike in the summer. In recent years her leisure-time interests have come to include fly fishing as well. Åsa and her husband, Vaughan Hurry, also a researcher at UPSC, recently purchased a house just outside of Umeå.

"Now I have my own garden! I never thought I would be interested in gardening," laughs Åsa.

Plants and plant breeding have always fascinated Åsa, and she regards having an opportunity to do research in this field as a privilege. The work is exciting and requires creativity. The drive to make new discoveries is strong in Åsa, who is happy with her career choice. • LW

Facts about photosynthesis

Photosynthesis is the process by which plants make use of the energy in photons, i.e. light particles. The light energy is converted in the plant cell's chloroplast to chemical compounds, which become the plant's energy carriers. Photosynthesis consists of a series of reactions. The first steps are called the light reactions, where the light is absorbed by chlorophyll molecules. Carbohydrates are then formed in the carbon reactions. The carbohydrates can then be used as fuel by the plant. A simplified formula for photosynthesis is:

$6\,H_2O + 6\,CO_2 + \text{solar energy} \rightarrow C_6H_{12}O_6 + 6\,O_2$

Name: Marie Wahren-Herlenius

Nationality: Swedish

Born: 1967

Awarded Ph.D.: 1994

Works at: Karolinska Institutet

Title of project: Molecular pathogens in autoimmune disease

DIAGNOSIS AND TREATMENT OF AUTOIMMUNE DISEASES

Marie Wahren-Herlenius and her group are investigating the inflammatory process in patients with the autoimmune rheumatic disease Sjögren's syndrome. The disease is caused by autoreactive antibodies that attack the body's own tissue. In pregnant women, these antibodies are transferred to the foetus and can cause severe cardiac arrhythmia, or heart block, in the child. Marie's group is trying to understand the pathogenic process in both Sjögren's disease and cardiac arrhythmia in order to be able to develop methods for preventing, diagnosing and treating these diseases.

In autoimmune diseases such as diabetes, multiple sclerosis and rheumatic diseases, which affect around 5% of the population, the body's immune system attacks and destroys the body's own tissue. Very little is known about the molecular mechanisms behind autoimmune diseases. At the same time there is a great need to develop methods to diagnose and treat them.

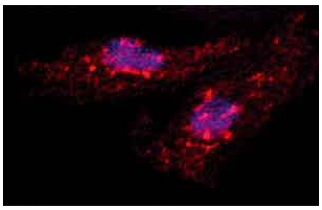
"We want to understand why people get autoimmune rheumatic diseases, what happens in the body, and how these diseases can be prevented, alleviated and cured," says Marie.

Focus on Sjögren's syndrome

She is focusing her research on Sjögren's syndrome, a common but relatively unknown rheumatic diseases. Sjögren's syndrome mainly affects the salivary and lacrymal glands, but also other secretory glands in the body. A certain type of cell, B lymphocytes or B cells, which are a part of the body's immune system, drive the inflammatory process. B cells also produce antibodies that target the body's own tissue.

Marie's group is collaborating within a large network of specialists in a project to investigate the pathogenic processes in Sjögren's syndrome. Proteins that are involved in the progress of the disease have been identified. Now the structure and function of these proteins are being studied, as well as how they are expressed during the course of the disease and what role they play in its development. They are also studying how heart block is caused in foetuses by transport of the mother's autoantibodies across the placenta to the child. Heart block is a cardiac arrhythmia caused by the fact that the electrical signal controlling the heartbeat is blocked on its way between the atria and the ventricles.

"We know that 2% of women with Sjögren's syndrome will have children with heart block," says Marie. "One of the goals has been to identify the risk pregnancies," she continues.



Cultured heart cells to which antibodies that induce heart block have bound. The specific antibody, p200-Ro/SSA, has been stained for viewing in the microscope with a red fluorescent dye. The blue dye shows where the cell nucleus is.

The block develops gradually during pregnancy, and this process can be arrested or reversed by steroid treatment before the block is fully developed. This can save the child's life or prevent it from needing a pacemaker for the rest of its life. Without treatment, the foetus dies in 20–30% of the cases.

Antibody can be detected by blood test

By studying the immune system in women with Sjögren's syndrome as well as in healthy and affected children, Marie's group was able to find the specific autoantibody, p200-Ro/SSA, that causes the heart block.

"We have shown that this antibody binds to certain heart cells in the foetus and causes a misregulation of the quantity of calcium in these cells," says Marie. "As a consequence the cells become overfilled with calcium and die. This leads to a local inflammation which results in calcification of the tissue, causing disrupted conduction and heart block."

Now that Marie's group has found the specific antibody that causes the block, mothers can be given a blood test to determine whether their foetus is at risk. If the blood test shows a high-risk mother, the foetus's heart is examined during weeks 18–24 of pregnancy. If there are signs that a

Marie Wahren-Herlenius

block is developing, treatment is given.

The next step is to identify the molecule to which the antibody binds on the surface of the heart cell. Marie's group wants to know the mechanism for how the antibody affects the child's heart. This is being done in collaboration with a group at Harvard University in the USA.

Skiing the bumps

Both of Marie's parents are researchers, and Marie conducted many chemistry and electronics experiments with her father in the kitchen as a child. One summer when Marie had completed her second year of medical school she tried working in a lab.

"I really loved working at the lab. I, who usually love staying up late, went to bed early every night so I could get up early in the morning and get to the lab as soon as possible," she says with a laugh.

Marie's husband is also a doctor and a researcher working on neuronal development at Astrid Lindgren Children's Hospital. They have done postdoc research together in Norway, Japan and the United States. They have two daughters, aged four and eight, and Marie likes to spend as much of her free time as possible with her family. She enjoys being on the west coast, where the family has a country place. In the wintertime her big interest is alpine skiing, preferably "skiing the bumps" on mogul hills.

Marie speculates on what may happen in her field in the next twenty years or so:

"I think we will come to understand a lot of the immunological mechanisms behind rheumatic disease, and that many of the immune-regulating therapies that are under development today will be in clinical use. Perhaps we will see the same revolution for other autoimmune and rheumatic diseases as that which anticytokine treatment aimed at TNF- alfa has entailed for rheumatoid arthritis. One area in which I think we will do a lot of research then is the importance of environmental factors for the development of autoimmune disease." • NR

Name:	Born:	Works at:	Title of project:
Lars-Erik Wernersson	1968	Lund University	High-speed, low-power nanoelectronics
Nationality: Swedish	**Awarded Ph.D.:** 1998		

NANOTECHNOLOGY PAVES WAY FOR FASTER ELECTRONICS

"In the world of electronics we want everything to get faster and smaller. Computers are being developed to handle larger and larger quantities of data at increasingly high speeds. But physical limitations will ultimately set the limit for the miniaturisation of components. We have to switch from classical mechanics to quantum mechanics in order to scale size down further," says Lars-Erik Wernersson.

Lars-Erik has been professor of nanoelectronics at the Department of Solid State Physics at Lund University since June of 2005. His research group is conducting both basic research on materials science and electronics and applied research. The applied research has to do with improving transistors – semiconductor devices that serve as switches and signal amplifiers in electronics. With today's technology, one transistor is needed to turn the current on and off, and another to determine the frequency (number of oscillations per second). By integrating metals in tunnel diodes, transistors can be made to work as both switches and frequency controllers. In this way, two functions are integrated in one component, saving space.

"Another advantage of tunnel diodes compared to ordinary transistors is that the frequency can be adjusted. This makes it possible to increase the speed of data transmission," explains Lars-Erik.

Today's computers work with frequencies of around 3 GHz, but with the technology being developed by Lars-Erik they may achieve frequencies of over 200 GHz. The tunnel diode also minimises the resistance in the circuit, resulting in lower energy losses. The device also makes it possible to transmit signals at many different frequencies. The signals are then addressed at the recipient. This is called "silent signalling" since each individual signal has so little power that the noise takes over, preventing eavesdropping.

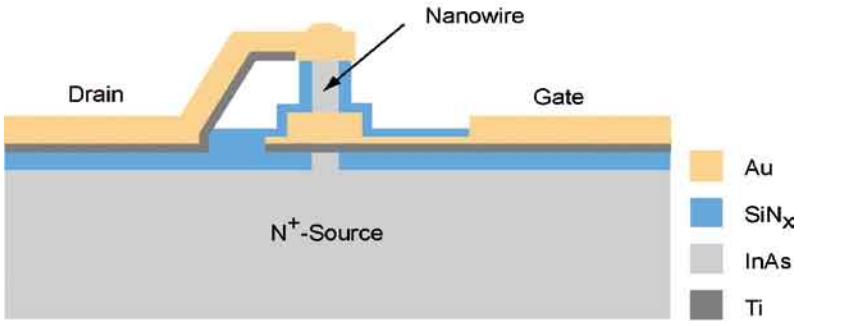
Nanowires made using gold particles

In a joint project with Professor Lars Samuelson, also at the Department of Solid State Physics in Lund, Lars-Erik is working to introduce transistor technology on nanowires. Nano means "a billionth" and nanowires are strings no longer than a billionth of a metre (10^{-9} m). The nanowires are made by using a gold particle as a catalyst on the surface of a semiconductor crystal. A nanowire of the semiconductor material "grows" up from the surface, with the gold particle at its tip. A layer of insulating material is first deposited on the wire, and then a metal layer. This makes it possible to conduct current through the wire and use the metal jacket to determine how much current will be allowed to pass.

The research group is part of an interdisciplinary programme called the Nanometer Consortium in Lund. Experts from the fields of physics, biology, materials science and electronics are collaborating to lead the world in nanotechnology research.

The third part of Lars-Erik's research has to do with how the performance of the transistors can be increased by using materials in which the electrons can move more readily.

"Lowering the resistance of the material increases the mobility of the charge



Gold (Au) acts as a catalyst when the nanowire, made of the semiconductor material indium arsenide (InAs), "grows" up from the surface.

Lars-Erik Wernersson

carriers, primarily electrons. Today silicon is often used as a semiconductor material, but substances with much better properties exist, such as indium arsenide."

The research group is trying to find ways to fabricate and develop these materials. By introducing a metal around the semiconductor in the same manner as in the technique described above with tunnel diodes, the mobility of the electrons in the material can be controlled. The goal of the project is to build a Swedish research platform in the field and contribute basic techniques around these semiconductor materials.

Saxophone and clarinet

After taking his Ph.D. in physics, Lars-Erik worked with educational matters at Lund University for about two years. Among other things he was involved in the reform of the programme in engineering physics. This was followed by a period as a visiting professor at the University of Notre Dame in the USA before he returned to Lund to put together his research group.

"It's easy to be consumed by your research. It's important to have a hobby so you can get away from your work, and in my case it's playing the saxophone and the clarinet," says Lars-Erik.

At the time of the interview, Lars-Erik is particularly busy. Only a few days remain until Walpurgis Night (April 30th), when he and his fiancé Maria are getting married.

Lars-Erik considers the combination of basic and applied research to be very important.

"Basic research on materials and electronics has to constitute the foundation on which applied research can later be based. The research fields will come closer together in the future, so that electronics can be applied to biological materials, for example. We will encounter new exciting challenges when electronics and engineering are integrated with yet another field," predicts Lars-Erik. • LW

Facts about diodes

A diode is an electrical device that conducts current when the voltage exceeds a given threshold value. The name comes from the fact that the device has two poles, an anode and a cathode, between which the current is conducted in one direction. A tunnel diode is a diode adapted to the microwave range (frequency range of 1 GHz–1000 GHz). Unlike an ordinary diode, the current decreases when the voltage increases in a tunnel diode, an effect called *negative differential resistance*. This makes it possible to change the frequency, which can increase the speed of data transmission.

Name:	Born:	Works at:	Title of project:
Juleen Zierath	1961	Karolinska Institutet	Identification of molecular mechanisms for treatment of type 2 diabetes
Nationality: American	**Awarded Ph.D.:** 1995		

IN SEARCH OF NEW DRUGS FOR TYPE 2 DIABETES

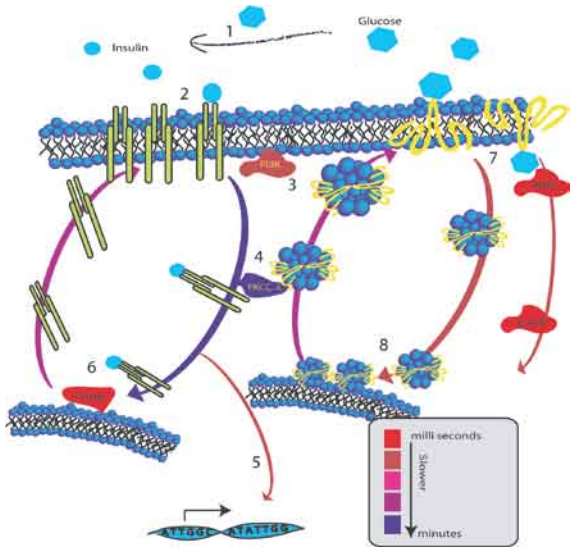
There are 120 million people with type 2 diabetes in the world today. The WHO predicts that this figure will have reached 300 million by 2025. The medicines that are used today to treat type 2 diabetes are inadequate, and there is a great need for new, better treatments. Juleen Zierath and her group are looking for target molecules that control the metabolism of glucose in the body and that could be used for treatment of type 2 diabetes.

The sun is shining on this fine spring day when I come to Karolinska Institutet's campus to meet Juleen Zierath. The first thing she does is show me around the lab and introduce me to her research group. Then we sit down in her office.

"Many drugs used to treat diabetes have been developed without an understanding of how they work," says Juleen. "Our research can contribute to a better understanding of this mechanism."

Disrupted signalling in type 2 diabetes

The name "diabetes" covers a group of diseases: diabetes insipidus, diabetes mellitus, bronze diabetes (hemochromatosis) and gestational diabetes. Diabetes mellitus arises when the body cannot absorb glucose from the bloodstream, and as a result the blood sugar level rises. Glucose uptake is controlled by the hormone insulin, which is produced by the beta cells in the islets of Langerhans in the pancreas. There are two types of diabetes mellitus: type 1 and type 2. Type 1 arises because the body produces autoantibodies which attack and destroy the beta cells, so no insulin is produced. In type 2 insulin is produced, but the transport of glucose into the cell is impaired. The insulin binds to insulin receptors on the cell surface, starting a signalling process inside the cell (see figure). This signalling takes place via a number of molecules and leads to transport of glucose from the blood into the cell. In type 2 this signalling is disrupted, and Juleen's group is trying to find the molecules responsible for this disruption.



The insulin signalling pathway leading to an increase in the uptake of glucose in skeletal muscle cells is a dynamic process (1–8). Insulin binds to insulin receptors on the cell surface. As a result, the receptors are internalized in the cell, and a number of proteins inside the cell are activated. The activated proteins set off a signalling cascade, which results in the translocation of glucose transporters to the cell surface, where they can bring about the uptake of glucose into the muscle cell.

Skeletal muscle most important organ

In type 2 diabetes, tissues such as skeletal muscles – muscles attached to the skeleton that move for example the legs and arms – adipose (fat) tissue and liver are less responsive to insulin. This is called insulin resistance. During her first year in Sweden, Juleen and a colleague developed a new technique for studying human skeletal muscle.

"We took out muscle and studied it in the absence of hormones and other factors and were then able to show that insulin resistance in patients with type 2 diabetes was specifically localised to the skeletal muscle," explains Juleen. "Since the skeletal muscle is the largest organ in the body in terms of weight, it is also the most important organ when it comes to maintaining a uniform blood glucose level. If the patient has a defect in his skeletal muscle, glucose cannot

be transported from the bloodstream into the muscle to be stored as glycogen, and as a result the blood glucose level becomes elevated."

Now Juleen's group is trying to understand why the skeletal muscle cells are so sensitive to insulin, what the defects are, and what can be done to correct or circumvent them.

"In the early '80s when I was doing research in St. Louis we discovered that exercise can increase glucose uptake in the cells and counteract some of the defects in animals and humans with type 2 diabetes. This is something we are currently studying."

Target molecules

Juleen's group is trying to systematically determine the target molecules that are involved in the insulin signalling pathway inside the cell. Using a method called gene array they have compared gene expression in the skeletal muscle of healthy individuals with that of patients with type 2 diabetes.

"We saw that the expression of a protein called DGK-delta was down-regulated in the muscle of patients with type 2 diabetes. Now we are investigating whether someone can be made insulin-resistant by down-regulating DGK-delta. Together with a group in Utah, we have an animal model where we have down-regulated the expression of DGK-delta. We have seen that these animals weigh more than the healthy animals. The difference in weight is due solely to the fact that they have more fat tissue, which is one of the distinguishing characteristics of insulin resistance."

Marathon woman

It is Juleen's interest in sports and exercise physiology that has brought her to where she is today. As a student she competed and trained to run marathons. She has a degree in physical education from the University of Wisconsin in the USA, the state where she was born and raised. Her goal was to become a better athlete, which led to an interest in how the body responds to exercise. This eventually led to a degree in exercise science from Ball State University in Indiana, plus two years of research at Washington University School of Medicine in St. Louis, where she studied how insulin and muscle contraction increase glucose uptake. Juleen came to Sweden to do her Ph.D. at Karolinska Institutet in 1989.

"There was really no other lab in the world besides Karolinska Institutet where research was being done on muscle glucose metabolism," says Juleen.

She then did her postdoctoral work in Denmark and at Harvard University in the USA, where she studied the genetics of type 2 diabetes and glucose transporters, respectively. But Juleen returned to Karolinska Institutet and is very happy working there:

"I appreciate the opportunity to work near the patient while at the same time doing experimental medicine. There are very few places in the world with that connection between clinical and experimental research."

When Juleen is not working she likes to work out at the gym.

"I work out every day and I'm pretty strong. I can bench press 170 kilos, so don't mess with me," she says with a laugh.

She also likes to run on Lidingö, where she lives in a little sports cottage from the 1920s; she has run three marathons. Juleen believes that as a leader you have to provide a good example.

"There's a saying in sports: 'An athlete is a reflection of the coach'," she says. She means that the leader of a group sets the tone for the group. It's not just a question of scientific and technical skills. A lot also has to do with motivation and helping the group members realise their own potential.

"I don't know whether my group will ever find a cure for diabetes, but I truly hope we can at least help to identify new strategies for treating and curing the disease." • NR

Name:
Johan Åkerman

Nationality:
Swedish

Born:
1970

Awarded Ph.D.:
1998

Works at:
Royal Institute of Technology

Title of project:
Spintronics: circuits, computers and biochips

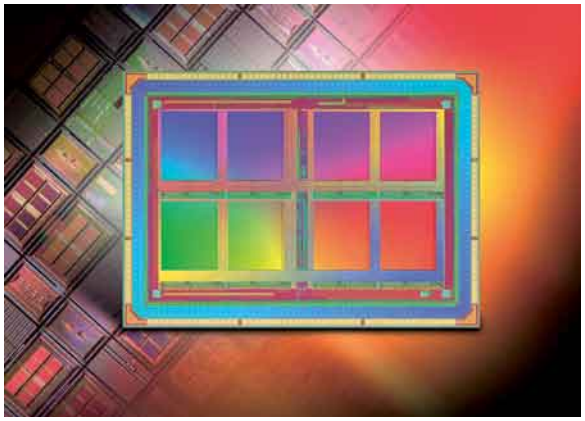
SPINTRONICS – TOMORROW'S ELECTRONICS?

Johan Åkerman's research concerns a new type of electronics – spintronics – which makes use of the electrons' "spin". The technology is already being used in the read heads of computer hard drives, but Johan envisions more possible applications, such as within artificial intelligence. He wants to develop analog neural networks, spintronic circuits modelled on the brain.

The kind of electronics we use today is based on making use of the electrons' charge. Spintronics uses their "spin" as well, a property related to how the electrons rotate around their own axis. This is the phenomenon that causes magnetism in iron and other magnetic materials. The spin of the electrons can be controlled so they can be used as information carriers – ones and zeroes – in computers, for example. A one or a zero is written in the memory by changing the direction of the spin by means of a magnetic field.

Simulates the brain

RAM, or random access memory, is the working memory in a computer. Magnetic RAM (MRAM) is a spintronic type of RAM where information is stored in microscopic magnets. Thanks to these magnets, the memory remains intact when the power is turned off. Nowadays, Flash memories have the same property but have slow write speeds and cannot be rewritten more than about 10,000 times. MRAM could improve electronic products by making it possible to store large quantities of data faster than Flash with no limit in the number of rewrites. Today, combinations of different memory types are used due to the limitations of the Flash memory. The complexity of many systems could be reduced by instead replacing them with a single universal MRAM.



Magnetic RAM (MRAM) – a variant of an ordinary RAM (random access memory). MRAM is based on spintronics and may replace several current types of memory.

Johan Åkerman currently works at the Department of Microelectronics and Information Technology at the Royal Institute of Technology (KTH) in Kista, but was previously employed by Motorola and Freescale Semiconductor, where he conducted research on MRAM. He got a Ph.D. in magnetism and superconductivity at KTH and was then given a postdoctoral fellowship at the University of California in San Diego, where he studied magnetic tunnelling elements – the core of MRAM.

At KTH, Johan plans to study new areas of application for magnetic tunnelling elements. One such area is analog spintronic devices that can be used in analog neural networks (ANN) , circuits that imitate neurons. One such ANN attempts to simulate the function of the brain. For example, the basic building block in a neural network corresponds to the brain's neuron. By simulating the function of the brain, better methods can be found for solving difficult mathematical and technical problems.

"Neural networks are particularly effective for such tasks as voice recognition, robot learning, image analysis, process control and data searching. There are digital neural networks that perform these tasks today, but not well enough," says Johan.

Like ordinary RAM, MRAM is digital. But the basic device, the tunnelling element, is actually an analog device. However, it is used in a digital manner, to store two different states: ones and zeroes. Johan says that it should be possible instead to make an analog memory with the tunnelling element and store any numbers between zero and one.

An analog computer would be faster and more information-dense, since a real number contains much more information than zeroes and ones.

Johan Åkerman

"Digital computers dominate today, but I believe this research can lead to more efficient analog computer components. I hope and believe that analog logic will eventually regain its rightful place," he says.

The way our brain works is essentially different from how a computer works, and superior in many ways. We can learn to generalise and make judgements with insufficient input data. These features can be simulated by ANNs.

"An ANN is not programmed. We instead say that we "train" the network, and it can accumulate experience that enables it to recognise similar situations. In this way it can gradually get better at a given task. I have great hopes when it comes to, for example, designing robots that can learn. In 20 years' time I believe that analog neural networks will be superior to digital ones in controlling the motor functions of robots as well," says Johan.

Another possible area of application for spintronics and MRAM is within biotechnology. Modified MRAMs can be used as biochips for medical diagnostics. The chip's magnetic sensors can detect magnetic nanoparticles that are attached to target-seeking molecules. When the target-seeking molecules bind to the substance being sought, the random movements of the nanoparticles change, which is registered and analysed by the chip. The method is fast, sensitive and cheap.

Curious and musical

Johan says that he has always been curious about how things work. He got a lot of inspiration from both his parents and learned that it's fun to learn things.

"When I was little I liked reading about Thomas Edison and other inventors. I soon became interested in mathematics and later chemistry as well. Chemistry was my best subject in upper secondary school, and I won a silver medal in the Chemistry Olympics in Finland," he says.

Another great interest is music, and when Johan was younger he considered a career as a pianist. He thought about applying to the music programme in upper secondary school, but instead chose the natural science programme in order to get more time to decide what he wanted to do. After graduating from upper secondary school he thought about studying music but eventually opted for engineering physics at Lund University's Faculty of Engineering. But he hasn't given up music entirely. When he has time he likes to play the piano and sing in choirs such as the Stockholm Academic Male Chorus and the Phoenix Symphony Chorus. Nowadays, however, much of his free time is devoted to his one-year-old twins, Hanna and Silas.

Important materials research

A central part of Johan's research is improving spintronic materials. The principle of spintronics is actually simple, but many challenges remain to be overcome before it can be commercially applicable. Materials research is a large and important part. The materials need to be developed in order to achieve good programming properties, larger memories and greater power efficiency.

Johan deems the commercial prospects of spintronics to be very good. He believes that magnetic RAM will in many cases be able to replace today's memories by combining their best features.

"I want my research to be practically applicable and lead to new devices and products," he concludes. • LC

Future Research Leaders

Individual Grants for the Advancement of Research Leaders – INGVAR

BACKGROUND

The INGVAR programme (Individual Grants for the Advancement of Research Leaders) covers the Foundation's full range of activities and is thus aimed at researchers in science, engineering and medicine. The research must be of the highest international standard and of importance for the development of Sweden's future competitiveness. The programme is aimed at Swedish or foreign researchers with particular potential for becoming leading researchers in Sweden and an ability to attract qualified co-workers. In other words, they should be individuals who conduct research at an internationally high level and also have leadership qualities such as initiative, enterprise, organisational skills and the ability to inspire their co-workers.

In 2001, the Foundation awarded 21 individual grants of SEK ten million each for six years of research in the programme – INGVAR I. A special leadership development programme was also linked to the programme. The programme attracted great interest and was very well received in the scientific community. In view of the positive experience from INGVAR I, the Governing Board decided to make a new announcement calling for proposals in February 2003 – INGVAR II.

INGVAR II

The second announcement in the INGVAR programme (Individual Grants for the Advancement of Research Leaders) included 17 individual grants of SEK 6 million each for four years of research with the possibility of continued funding for another two years following evaluation. Special funds were also allocated for leadership training.

At the time of the deadline in October 2003, 401 applications had been received. 37% of the applications came from female applicants and 33% of the applicants were foreign citizens. A Selection Committee handled the selection of grantees, which took place in several steps. In the first steps, four expert panels were utilised in the following areas: Life Sciences, Life Science Technologies, Information and Production Technologies and Materials and Electronics. After evaluation by these panels, the Selection Committee selected 92 applicants for international review by 40 foreign experts. Based on the international review, 42 applicants were invited to submit complete applications, and 41 such applications were received. They were examined by 42 foreign experts – essentially the same persons as in the preceding step – and each application was sent to at least three experts. Based on the findings of the international experts, 28 applicants were then invited to a hearing. A special hearing panel with representatives from the expert panels conducted the hearing, where each applicant gave a brief presentation with an opportunity for questions and discussion with the panel. The hearing resulted in the recommendation by the Selection Committee that 18 of the applicants should receive grants. In December 2004, the Governing Board decided in accordance with the recommendation of the Selection Committee. 33% of the grantees are women and 28% are foreign citizens.

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