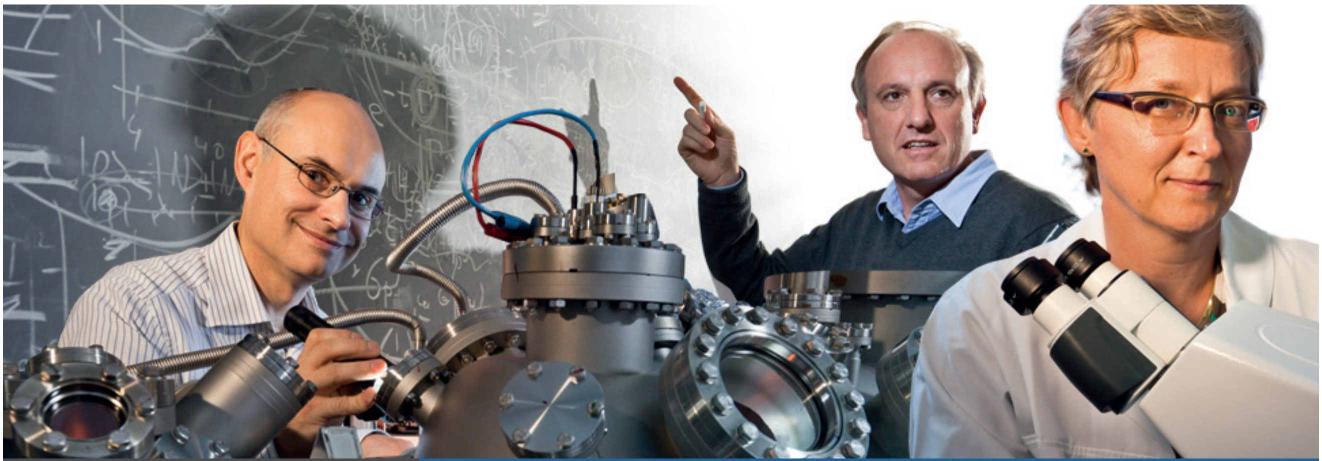


SNI SWISS NANOSCIENCE INSTITUTE
EINE INITIATIVE DER UNIVERSITÄT BASEL UND DES KANTONS AARGAU

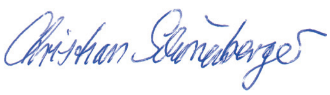
SNI update March 2013

Words from the Editor

The SNI management team had a busy start in 2013, as the preparations for the Swiss Nanoconvention were getting serious with the beginning of the year. Numerous discussions with sponsors and the Messe Basel were required to talk about the details. Now, all the essential topics are defined, and thanks to the generous support of our platinum sponsor Basel Area and the various gold, silver and bronze sponsors the financing of the event is secured. We can return to the scientific aspects and look forward to the excellent keynote speakers who have committed themselves to SNC 2013. For the satellite symposia, we were able to compose an interesting mixture of talks from industry representatives and academia. Have a look at the program and do not forget to register.

With the SNC 2013 in May, the NCCR Nanoscale Science will be finalized. We have known this date since the beginning of the NCCR in 2002. Nevertheless, it feels a bit strange to write the final report that we will send to the NFS in April. However, the positive aspect is that the SNI will continue with exciting activities, as you will read in this issue of *SNI update*. With the beginning of 2013, we started five new Argovia projects. The short introductions to these projects in this issue of *SNI update* demonstrate that again we were able to choose exciting and innovative approaches that reflect the potential of nanoscale sciences. Our PhD program as well is an investment in the future. The first PhD students are already selected, for other projects interviews are scheduled and on 1st April, the first PhD students will start their theses in the different laboratories. We will continue to publish our electronic newsletter *SNI update* in order to keep you informed about SNI activities. If you have suggestions and recommendations to improve *SNI update*, please let us know.

I hope to see many of you in Basel in May. Best regards



Director of the Swiss Nanoscience Institute, University of Basel

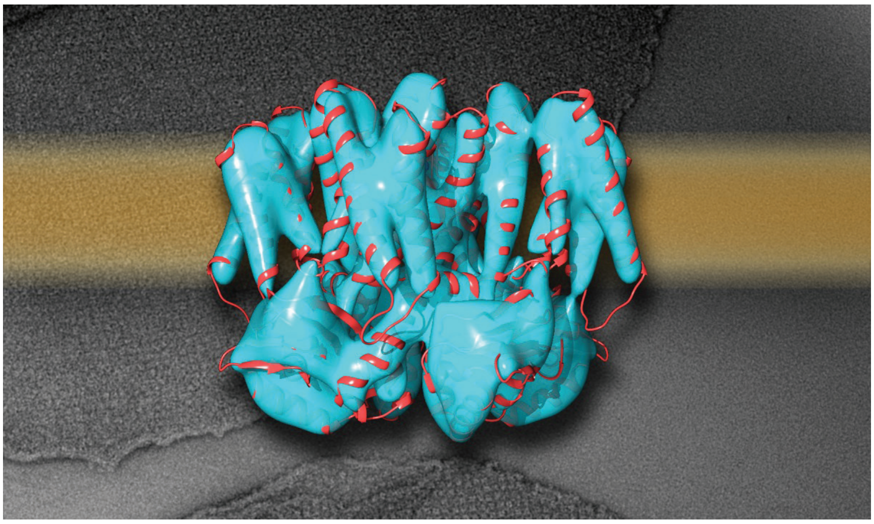
UNI BASEL

Cover Story

With electrons to new findings

The first insights into the nanoworld only became possible through the development of new microscopes. Even today, innovations in the area of microscopy provide new knowledge on atomic and molecular structures that control many processes of life and are possible targets for the treatment of diseases. Professor Henning Stahlberg of the Biozentrum at the University of Basel and his team investigate and optimize new methods in light- and electron microscopy to further advance this discovery process in the nanometer range.

In the 17th century, people began to study the world of small things using the first microscopes. Antoni van Leeuwenhoek, for example, managed in 1675 to enlarge the microworld using a single ground lens, so that he was able to see bacteria of only a couple of micrometers. In 1933, Ernst Ruska laid the foundation for the exploration of the nanoworld by developing the first working electron microscope (EM). During his PhD thesis in the group of Professor Max Knoll, the 24-year old scientist had discovered how an electron beam can be focused to a tiny spot. These findings were the prerequisite for the development of an electron microscope. To date, microscopy has been revolutionized and allows completely different applications than in its early days. However, even the most advanced devices are still based on the principles that were found by the inventors. In an optical microscope, light is focused by lenses and shines on or transmits an object. In the electron microscope, an electron beam is generated by a cathode. This beam is focused by magnetic fields and illuminates the object. The electrons pass the object either freely, are deflected by the atoms of the object, or they lose energy while striking the atoms. This can be measured and allows the calculation of a magnified image of the structures. The entire process requires a vacuum; otherwise the electrons would collide with air molecules and be stopped by these.



Electron microscopy examinations and image analysis in Henning Stahlberg´s lab allowed the structural analysis of a potassium channel. (Foto: Henning Stahlberg)

A focus on membrane proteins

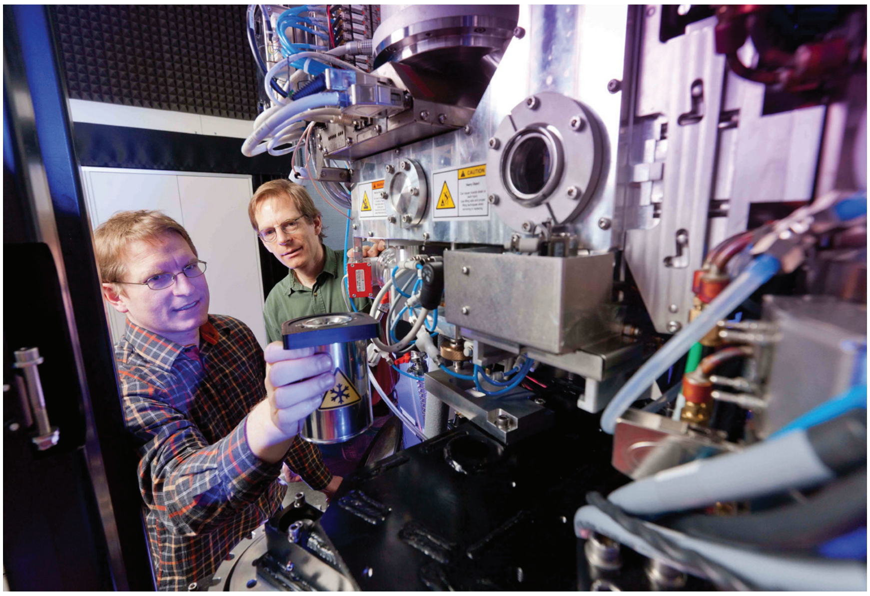
Today, numerous electron microscopy methods exist to study matter at various length and resolution scales. These different methods can be combined and further optimized. This is where Professor Henning Stahlberg and his team have found their niche. The scientists are aiming to optimize microscopic methods, so that cells, organelles and supramolecular complexes can be imaged in their natural environment. “Our research helps to get a better understanding of the complex processes in natural cells. We can use this knowledge to design new therapeutic strategies for the treatment of diseases,” Stahlberg comments his approach.

The investigations in the Stahlberg lab focus on the structure and function of biological membranes. These barriers in and around our cells are composed of lipid molecules and membrane proteins, which are special types of proteins in our body that fulfill a plethora of biological functions. Membrane proteins are the import and export specialists in our cells and they fulfill important functions for the cell-cell communication or the defense against bacteria and viruses. It is important to understand the function of membrane proteins, also because many medical drugs bind to these proteins to trigger a desired reaction.

Fast freezing – the road to success

In order to clarify how a drug binds to one of these membrane proteins and thereby alters its functions, it is important to understand the function of this protein in its natural environment. A solubilized membrane protein behaves differently than a membrane-embedded one. This is due to the fragile three-dimensional structure of many membrane protein complexes, which can be altered in the absence of their surrounding membrane. On the other hand, the function of the protein is determined by its structure. Therefore, the characterization of the three-dimensional structure is the basis for understanding the function of theses nanomachines. Stahlberg and his coworkers apply cryo-electron-tomography for their investigations. With this special electron microscopy method, they can image even large protein complexes in their natural environment without modifying them substantially.

Natural cells have a high water content, which complicates the electron microscopic examination, since this happens in a vacuum where water would evaporate. Cells can be best preserved for the electron microscopy investigations by a flash-freezing procedure without the formation of ice crystals. Treatment with chemicals is omitted here. However, the method



Using a new method, Thomas Braun from the Stahlberg group analyzes the proteom of a cell. (Foto: SystemsX)

requires that the samples are kept at -180°C during the microscopic examination. In the microscope, the sample rotates and images from many directions are taken. These different pictures are used to calculate a three-dimensional image of the analyzed structure on the computer.

A new method for the analysis

Not only the structure and function of specific proteins are of interest for the researchers. The entire set of proteins of a cell (proteome) is in their focus as well. Scientists are for example aiming to discover which proteins are expressed most frequently in diseased cells in order to find new treatment targets. The group of Dr. Thomas Braun in the Stahlberg lab has developed a new method to analyze the proteome of single cells. First, they cultivate the cells in a culture medium under reproducible conditions. Then they select one of these cells under the optical microscope, brake it up using an electrical needle and suck up the proteome. Afterwards, this "protein soup" is processed, analyzed and characterized using automated electron microscopy and digital image analysis. The microscopic results can be combined with other methods so that researchers receive information about the mass of the proteins in addition to the three-dimensional picture and are therefore able to identify the proteins. The scientists in the Stahlberg group currently apply this new method to study the distribution of Tau-protein filaments. These proteins are associated with Parkinson´s disease. However, it is not know whether they are the cause of the disease or if an aggregation of Tau protein is a defense reaction of the cells. In any case, the Tau-filament formation infects neighboring cells, and the aggregation process proliferates. Researchers are investigating this mechanism to be able to develop potential new drugs.

Hurdles to overcome

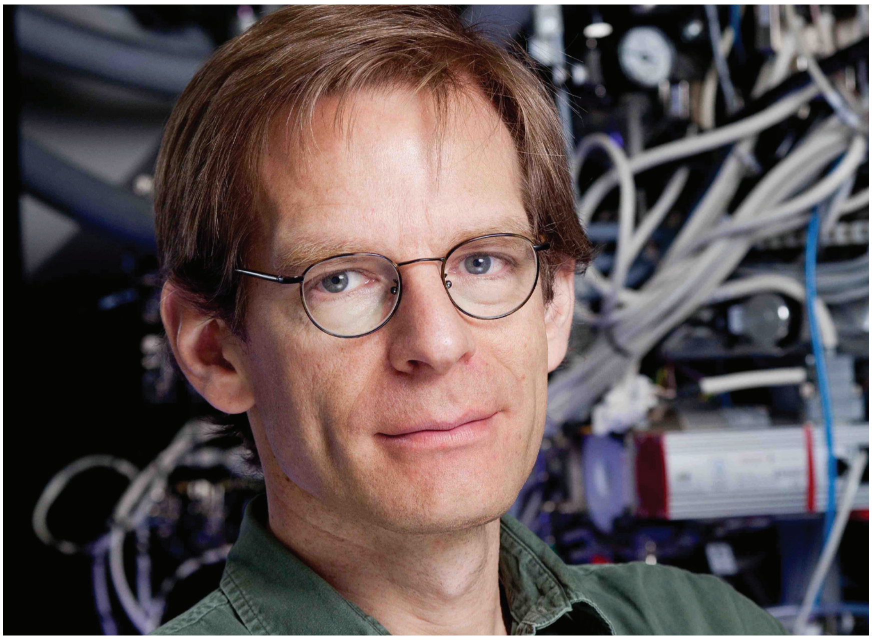
These analyses sound easier than they actually are. During the work with natural samples, several hurdles need to be overcome. Biological samples can only be imaged using a relatively low intensity of the electron beam - otherwise they would be quickly destroyed. This increases the noise-signal ratio of the readout. Additionally, most biological objects are comparably poor in contrast.

Currently, 35 physicists, biologists and mathematicians work closely together in the Stahlberg lab in order to find creative solutions to overcome these problems. However, such research does not only require expensive electron microscopes, but also microscope operators that have gathered rare expertise through many years of training. To provide this knowledge and these techniques to research groups outside their labs, the University of Basel has founded the technology platform C-CINA (Center for Cellular Imaging and NanoAnalytics) with the support of Hoffmannn-La Roche. C-CINA is a partner for projects of the Swiss Nanoscience Institute and works closely together with labs of the ETH Department for Biosystems Science and Engineering (D-BSSE), the Biozentrum, and other labs of the University of Basel. In interdisciplinary teams, for example in several projects sponsored by SystemsX.ch, researchers improve the microscopy and sample preparation methods. New and optimized, easy to use computer software is developed in the group of Henning Stahlberg, and is distributed as open source program to scientist worldwide. These efforts contribute to the ongoing discovery process of the complex interactions between the vital components in our cells. Stahlberg´s research provides some pieces of the complex molecular network puzzle of life and allows deeper insights into the nanoworld.

We introduce ...

Henning Stahlberg, Professor of Structural Biology at the Biozentrum, University of Basel

Professor Henning Stahlberg appreciates the flexibility and diversity of his profession and lives both of these values. He studied physics, but now teaches biology. He built up a successful research group in Davis (CA), but now leads a team of scientists at the Biozentrum in Basel. Preferably, he hires researchers who have some knowledge or expertise he can learn from and he appreciates the cultural diversity of his research group. Diversity with respect to the scientific background is essential in his field, as he and his colleagues are trying to decipher the secrets of membrane proteins in our cells. To achieve this, new methods need to be developed by scientists coming from different disciplines.



Henning Stahlberg is Professor for Structural Biology at the Biozentrum since 2009. (Foto: SystemsX)

Diversity during his studies

At school, Henning Stahlberg did not develop a special interest for biological questions. His biology lessons had been cancelled quiet often and when he got the opportunity to drop the subject, biology was not a topic for him anymore. After graduating from high school in Bremen 1985, Stahlberg decided to return to Berlin, the city where he was born. He began to study physics, maybe because he had experienced a certain admiration for physics as a child. His godfather, a theoretical physicist, had impressed him a lot as he was able to work while sitting in the sun and smoking his pipe. Besides physics, Stahlberg also studied mathematics, worked as a programmer and earned some extra money with chemical smoke analysis in a power plant. During the years in Berlin between 1987 and 1992, he tested many things – but nothing related to biology. Only for his doctoral thesis, he again came into contact with the subject that he researches and teaches today.

Learning French

After his physics diploma thesis, in which he had examined magnetic metal layers using electron microscopy, he moved to Lausanne to start his PhD thesis in 1992. The main reason for a French-speaking city was his desire to learn French properly. At this time, no PhD position was available in the physics department. However, in biology they were looking for a physicist. This was the start of Stahlberg's career as a biologist. For two years, he drove daily from Lausanne to Geneva to purify and isolate proteins and to immerse himself in the world of biochemistry under the guidance of Professor Ghosh. One of his supervisors in Lausanne was Professor Dubochet, an expert in electron microscopy and the inventor of cryo-electron microscopy. Stahlberg learned this innovative new method, which allows the examination of proteins in their natural environment. Professor Andreas Engel from the Maurice Müller Institute at the Biozentrum in Basel also became interested in the technique and in 1997 he hired Henning Stahlberg as a post-doc. By this time, Stahlberg had already been an expert and established cry-electron microscopy in the Biozentrum. In 2002, Stahlberg finished his work in the group of Andreas Engel with a Habilitation.

Long nights spent with preparations

Stahlberg had to dig deeper into biology in 2003 for his next career step as Professor of Molecular and Cell Biology at the University of California in Davis. Suddenly, he had to give basic lectures for more than 200 students on a subject he had given up in high school. So, he bought a pile of biology text books and prepared himself for the lectures evening after evening. "That was a hard time - however, that's how I gained my biological knowledge. And by now, my colleagues respect me as a biologist", he says. He not only learned for the lectures, in addition he asked his lab members to lecture him and even give him homework, when he wanted to learn a new technique or method. "Preferably, I hired post-docs that could teach me in a particular area," he recalls. Stahlberg likes to remember these intensive six years in Davis. Over time, he had established optimal research conditions and his family felt comfortable in California. However in 2009, Stahlberg received an offer for the professorship of microscopy in structural biology and biophysics at the Biozentrum. The family decided to return to Switzerland, so his wife was able to practice as a medical doctor again and the grandparents in the Ticino could see their grandchildren regularly.

Swiss NanoConvention 2013

The program for the Swiss NanoConvention 2013 is final and the registration is open. The Swiss NanoConvention covers all aspects of nanoscale sciences and nanotechnology – from basic research to applications and regulation.

Program and registration under
swissnanoconvention.ch/2013/swissnanoconvention.ch/2013/

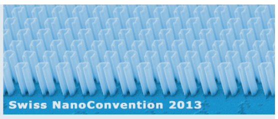
Fresh start in known environment

Although Stahlberg had lived in Basel for six years during his time as postdoc, it was a new beginning for him. He was not able to continue his most favorite project from Davis, the development of phase contrast scanning transmission electron microscope, for which he had received tremendous support from industry. Instead, he dwelled deeper into the structural and functional investigations of membrane proteins. He strives to improve methods to study membrane proteins in their natural environment. In Basel, new opportunities for collaborations with the pharmaceutical industry opened up. For pharmaceutical companies, his basic research is important as membrane proteins play an essential role in the development and treatment of various diseases. In addition, contacts with colleagues from the Biozentrum, the Department of Biosystems Science and Engineering, and the Friedrich Mischer Institute stimulate the work of his group, which has grown to 35 co-workers by now.

In his team, researchers from numerous disciplines such as biology, physics, engineering, materials science, and image processing meet. “Our research approaches are too complex for most individuals, so that only an interdisciplinary team is best prepared to tackle them. We have biological questions with medical applications. The analyses are carried out with high-tech equipment and require complex image processing programs. It needs a team to tackle these issues,“ comments Stahlberg the composition of his team. He himself is primarily motivated by his wish to improve quality of life. “Once, we were asked to do some investigation for military industry. But that is not appealing for me - even with the best payment,” he says.

Diverse dream job

Apart from the hope to contribute to the elucidation of diseases like Alzheimers or Parkinsons, Stahlberg also appreciates the diversity of his work. He likes teaching students or working with good PhD students and postdocs. Once a week, he tries to reserve an hour for each of his co-workers to discuss projects and other topics. Writing papers and giving lectures to interested young people, and being involved in politics from time to time, complements his work. When he leaves his lab in the evening, a busy family life is waiting for him. Since Stahlberg›s wife works as a medical doctor again, he tries to contribute to running the household as much as possible. Having dinner with the family, to listen to the kid›s stories from school, sports or music lessons, to put them to bed or to walk the dog - these are the jobs that keep the Stahlbergs busy most evenings. Henning Stahlberg enjoys this variety, but it leaves him little time for hobbies. So his cello, which he played in Lausanne in the Symphony Orchestra of the EPFL, probably has to wait a few more years until it is used more often again.



Don´t forget to register your poster

You can register your poster for the SNC 2013 poster session until 1st Aril 2013.

Please contact Tibor Gyalog for further information **(tibor.gyalog@unibas.ch).**

New Argovia projects

With the beginning of the new year we have started several new Argovia projects, which were approved in fall 2012. In this issue of *SNI update* we will introduce these five new research approaches.

Argovia projects are always run by teams of researchers from academia and industry. Two academic partners from the University of Basel, the University of Applied Sciences Northwestern Switzerland, the Paul Scherrer Institute, the CSEM Basel or the Department of Biosystems Science and Engineering of the ETH in Basel collaborate with a company in Northwestern Switzerland. Approvals are initially granted for one year; the teams can request a second year.

Bio-Duraclean

In the project Bio-Duraclean, an interdisciplinary team under the leadership of Dr. Olfa Glaied from the Institute of Chemistry and Bioanalytics of the University of Applied Science (FHNW) aims to develop a durable dirt repellent surface that can be used among other things for painting trains.

Researchers involved in the project will combine different promising approaches. First they use nature as a model and mimic the lotus effect. They accomplish this task by combining nano- and microparticles on a polyurethane matrix. A specific arrangement of the different particles will results in a roughness similar to that of the lotus plant leaves, so water drips off and takes dirt along. Different nanoparticle arrangements will be studied, for example silica. To optimize the water and dirt repellent effect, the scientists plan to cover the whole surface using a water repellent polymer. It will be a challenge for the project team to link the different components of the surface with each other and to attach them to the matrix and previous layers of paint. Researchers from Mäder AG, who are the industry partners of this project, will make a major contribution in this respect and will share Mäder´s adhesion technology.

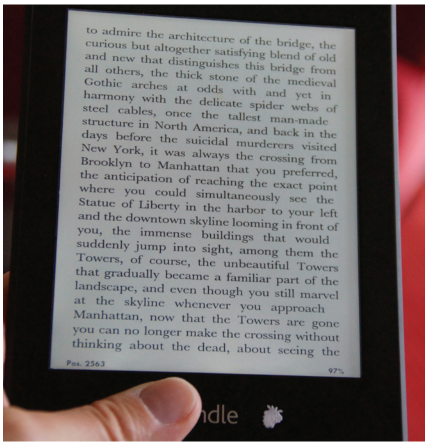
In the project Bio-Duraclean, scientists from the teams of Dr. Olfa Glaied, Professor Uwe Pieles (Institute for Chemistry and Bioanalytics, FHNW), Professor Wolfgang Meier (Department Chemistry, University of Basel) und Dr. Jörg Reiter (Walter Mäder AG, Killwangen) work closely together.

Professor Uwe Pieles, Dr. Olfa Glaied, Virginie Vaché, Andrea Leisibach develop a dirt repellent surface.

ELE-NA

Professor Uwe Pieles from the Institute of Chemistry and Bioanalytics (FHNW) is the project leader of ELE-NA. Within this project, researchers study the use of specific nanoparticles as e-ink and for e-paper applications.

Electronic books are becoming more and more popular. They are light, handy and easy to use. Using an e-reader, a whole library is always at hand and nowadays they can be read in bright sun as well as in the dark without any problems. Whereas the latest models mimic the appearance of printed black and white text on paper, the first prototypes for colored displays are still plagued with insuf-



Black and white e-readers are already available in good quality. In the project ELE-NA researchers investigate special nanoparticles for the use of e-readers that have a colored display.

ficiencies. The researchers engaged in ELE-NA would like to chance this. Instead of using pigments, as in the current, energy consumptive e-readers, they plan to choose stable colored nanoparticles exhibiting electrophoretic mobility. Upon the application of a current, the particles migrate in the electrical field, accumulate in the visible area and therefore cause a color change. To achieve this goal, the scientists plan to produce functional hybrid nanoparticles. The core consists of silica, whereas the shell carries a latent charge and the dyes. Like for an inkjet printer, the dyes cyan, magenta and yellow are sufficient to create all other colors.

Before such a color e-reader is available, numerous studies are required. The size of the particles as well as the optimal proportion between core and shell are of great importance. Additionally, the color strength and the controlled charging of the particles are essential for optimal functioning. Co-workers of Professor Uwe Pieles and Professor Gerhard Grundler (both Institute for Chemistry and Bioanalytics, FHNW), Dr. Giovanni Nisato and Dr. Wolfgang Tschanun (both CSEM Basel) work closely together in this demanding project. They are suppported by the industry partner in this project Dr. Reinhold Öhrlein and Dr. Andreas Hafner (both BASF Research Center).

NANOX

Besides ELE-NA, Professor Uwe Pieles is leading another Argovia-project called NANOX. With this approach, scientists plan to develop a new catalyst that facilitates the decomposition of hydrogen peroxide.

Pharmaceutical products and food are produced under strictly controlled sterile conditions in order to prevent contamination with microorganisms. Nowadays, vaporized hydrogen peroxide is often used for surface decontamination in clean room facilities and isolators. After the decontamination, the systems are aerated with sterile air. To save energy and to reduce the effect on the environment, the air is recirculated. This requires an active decomposition of the hydrogen peroxide at the end of the sterilization process. The scientists in the project NANO are now planning to develop a ceramic composite catalyst, in which metal and metal oxide nanoparticles in an inert inorganic matrix are combined with immobilized catalase molecules. Catalase is an enzyme that can be commonly found in many organisms and that efficiently catalyses the decomposition of hydrogen peroxide into water and oxygen. In the proposed catalyst, the metallic nanoparticles work hand in hand with the natural enzyme.

In the project NANOX, scientists develop a new catalyst that facilitates the decomposition of hydrogren peroxide. SKAN is the industry partner in the project. (Foto: SKAN)

In NANOX, co-workers from the FHNW from the teams of Professor Uwe Pieles and Professor Patrick Shagaldian are collaborating with researchers from the University of Basel from the groups of Professor Catherine Housecroft and Professor Edwin Constable. The industry partner in the project is Olivera Scheuber from SKAN AG, Allschwil, a market leader for isolators and clean room facilities.

NAPOHIC

Renewable energies such as wind and solar energy are only available locally and their power output fluctuates tremendously. This calls for a massive expansion and renovation of power grids. A large part of the networks has to be realized underground or underwater by insulated high voltage cables. Todays multi-layer insulation systems have proved to be successful. However, this technology reaches its limits when it comes to the requirements of the future networks. Among others, these need to have an increased transmission power and a high load changes stability.

Installation system for submarine high voltage cable (Foto: ABB).

The goal of the project NAPOHIC (Nano carbon based semi conductive polymers for high voltage cables) is the examination of new nano-additives based on carbon in the individual polymer layers of the isolation system of high voltage cables so that these fulfill future requirements.

Partners of the project NAPOHIC are: ABB Corporate Research, FHNW Technique and the Paul Scherrer Institute. Professor Jens Gobrecht is leading the team.

TIGHTSEAL

Under the leadership of Marcus Waser from the FHNW, scientists in the project TIGHTSEAL develop a thin gastight film for graphite sealing.

Gaskets for gases and liquids that are used in the chemical and petrochemical industry need to comply with certain requirements, which set a limit for emission. Even under the exposure of chemicals, they need to be tight and should be independent from temperatures in their sealing properties. Flexible graphite sealing fulfill many of these prerequisites. They are chemically resistant to almost all media and long-term stable in air from cryogenic up to temperatures as high as 500°C. Due to the nanoporous structure of several layered graphite nano sheets, the graphite sealing does not fully meet the requirements for emission. In the project TIGHTSEAL, the graphite foil will be coated with a thin airtight film in the nanometer range. This coating should improve the tightness so that safety standards are met without altering the excellent properties of graphite itself.

Teams of Marcus Waser, Professor Uwe Pieles (both FHNW), Professor Jens Gobrecht (PSI) as well as the industry partner Dr. U. Wegmann (Klinger AG, Egiswil) contribute to the project TIGHTSEAL.

Press releases and uninews

Basel, 20.02.2013. New nanotech method helps to recognize viruses

Scientists of the University of Basel and the University of Applied Sciences (FHNW) have developed a method to apply an innovative nanotechnological method in order to detect viruses. The technique could be used to produce viruses and for the diagnosis and treatment of various diseases. The results were published in the recent issue of “Nature Communications”.

Basel, 05.02.2013. Nanosensors support therapy of skin cancer

Malignant melanoma is the most aggressive form of skin cancer. In more than half of the cases a specific gene mutation plays an important role. As there are drugs available that significantly prolong the life of people carrying this mutant, it is important to identify them reliably. Researchers of the University of Basel and the Ludwig Institute for Cancer research in Lausanne have developed an innovative method for this mutant. The results of their studies were recently reported in the science journal “Nature Nanotechnology“.

Basel, 28.01.2013. University of Basel onboard of the flagship "graphene"

Today, the European Commission announced the start of two new research initiatives that will be supported in the next ten years with up to 100 million Euros per year. One of the programs aims at using new materials derived from two-dimensional carbon structures in information and communication technologies. Two groups of the Department of Physics are involved in the program.

Aarau, 11.02.2013. Dr Martin A. Bopp elected as Managing Director of the HighTechZentrum Aargau

The board of directors of the HighTechZentrum Aargau has appointed Dr. Marin A. Bopp as Managing Director. He will start on February, 11th 2013.

Martin Bopp worked as department head and member of the executive board of the Förderagentur für Innovation (KTI) in Bern and as member of the executive board of a biotech-start-up company. Martin Bopp was born in Lupfig, finished high-school in Baden and studied experimental physics at the ETH Zurich before he received his PhD from the University of Basel in nanotechnology. For three years, he was running research projects at the University of Pennsylvania, USA. Currently, he lives in Basel.

Please contribute

Please give feedback and submit ideas, success stories and news that might be of interest for the SNI community to the editorial team:

Dr. Christel Möller (c.moeller@unibas.ch) and
Dr. Tibor Gyalog (tibor.gyalog@unibas.ch).