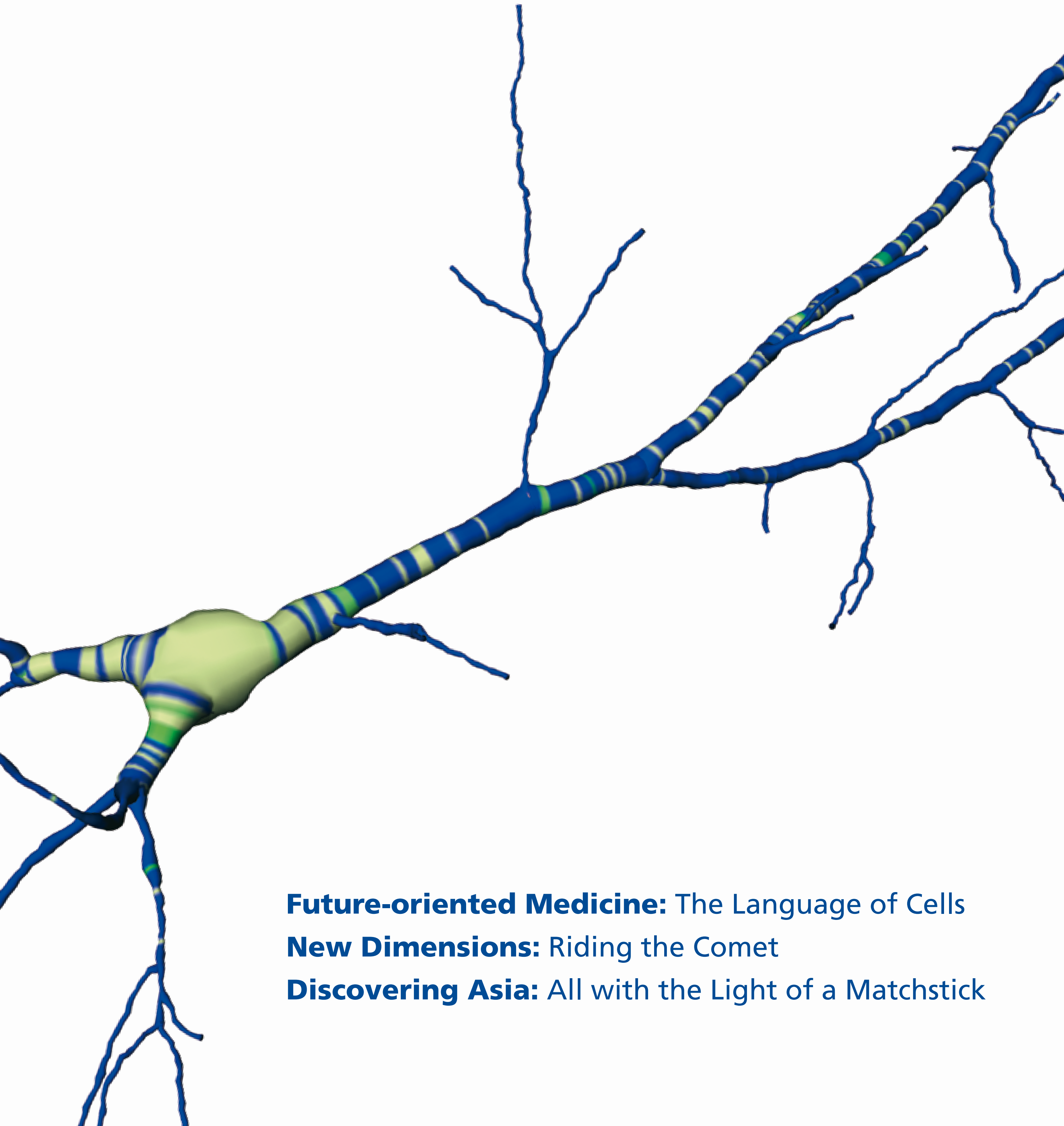
The Magazine from Carl Zeiss

Issue 19
3/2008

Innovation



Future-oriented Medicine: The Language of Cells

New Dimensions: Riding the Comet

Discovering Asia: All with the Light of a Matchstick

Neural representation of learning processes at the synapsis

The genetic expression of the cytoplasmatic protein (Arc) associated with learning is induced in a subpopulation of pyramidal neurons through research into a new environment. The specificity and necessity of this Arc expression for learning processes were verified in previous papers. Additional studies have shown that Arc RNAs specifically localize in activated, dendritic subregions after electrical stimulation.

All dendritic trees can be displayed using transgenic mice forming yellow fluorescent protein (YFP) in neuron subpopulations. An optimized method of fluorescence in situ hybridization (FISH) permits the simultaneous display of Arc and the endogenous YFP signal (e.g. activated neuron subpopulations in the hippocampus, see picture on page 16). Efforts will be made to identify synaptic connections and changes using the automated recognition of the dendrite structure and the localization of Arc RNA and the Arc protein depending on the behavioral process.

Dr. Michael Calhoun, Molecular Imaging Group, Hertie Institute, Tübingen (http://www.hih-tuebingen.de).
Daniel Eicke, Data Analysis and Visualization

Editorial

Dear Readers,

It does not even take a trend researcher like Matthias Horx to recognize that health is a subject that truly deserves the label "megatrend." We all know how miserable we feel even if we are only suffering from a common cold or the odd headache. However, what a diagnosis like cancer or Alzheimer means for the person affected and for their environment can only really be understood by someone who has experienced these diseases at close hand.

In the almost two-and-a-half millennia that have passed since the discoveries of Hippocrates of Kos, many pioneering advances have been made in the field of medicine. Some of these were inextricably linked to instruments from Carl Zeiss. Something which has not changed in all these years, however, is that a disease cannot be diagnosed until it has actually broken out.

With molecular imaging, medicine and medical technology will experience a real revolution: in several years, they will help us to reach a stage where we can find the causes of illness and therefore diagnose diseases long before their outbreak. This will increase the chances of effective therapy and cure.

Therefore, Carl Zeiss has joined the Molecular Imaging Technology Initiative launched by the German government and has become one of five founding partners. As a leading company in the field of optics and medical technology, it is our goal to transfer new molecular imaging techniques from research to their practical use in laboratories, doctors' offices and hospitals and to safeguard Germany's position as a leading healthcare market with the aid of this future-oriented technology. Optical technologies will be key pacemakers in this process.

I hope this issue of Innovation *finds you in the best of health!*

Best wishes

Dr. Michael Kaschke
Member of the Carl Zeiss AG Executive Board

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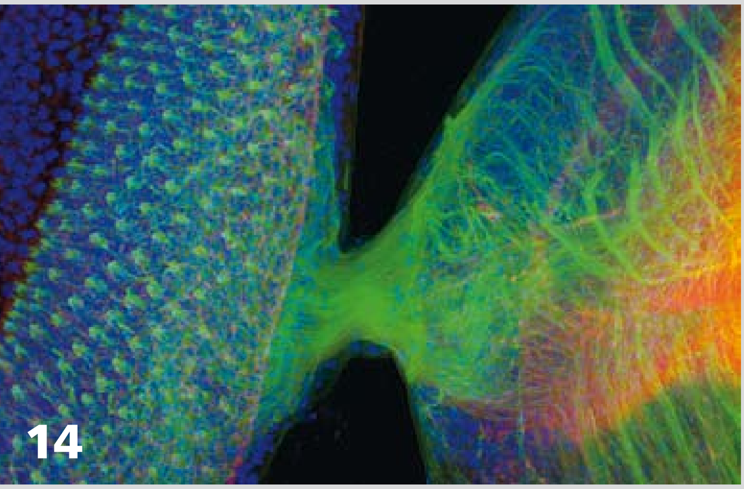
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It is considered a revolution in medicine: molecular imaging helps us to better understand the human body.

Cover Story: Future-oriented Medicine

New projector systems in planetariums invite the audience to take part in virtual adventures into the dark depths of the cosmos.

Images from another world – Mongolia.

Watching videos at total ease – with the cinemizer from Carl Zeiss.

Movies for Your Vest Pocket

The *cinemizer* from Carl Zeiss puts movies at the end of your nose

A long-distance flight, an awful TV lineup at a hotel, a late train – business trips can be boring. With the *cinemizer*, Carl Zeiss has landed a winner: an innovation that puts movies from portable players right in front of your eyes and looks just like a pair of sunglasses. The *cinemizer* simulates a 115 cm display at a distance of two meters, giving the wearer an authentic movie feeling with a private viewing. The smooth adjustment possibilities on both sides for different prescriptions enable people with visual defects to also enjoy this exclusive experience. Loudspeakers integrated into the earpieces ensure a good sound. The high-performance battery guarantees four hours of movie enjoyment. You can watch your favorite videos and movies anytime, anywhere. Simply connect the *cinemizer* to the iPod using the practical clip or connect it to another mobile video player via a cable. The main advantage: there are no uninvited guests such as the person sitting next to you. Optimized for iPod with video, the *cinemizer* can nonetheless be connected to other devices, such as your home DVD player or a game console, thanks to an additional jack. Gamers and movie enthusiasts can indulge in their passion without turning other family members into unwilling participants. The *cinemizer* celebrated its world premiere at this year's MacWorld Expo in San Francisco in January.

Wonderfully Fossilized

Living deep-sea oyster discovered

Successfully hidden: a primitive oyster.

Oysters are sometimes located in the strangest of places. Not only in Frank Schatzing's book "The Swarm", but also in the ocean. The deep sea oyster hid under overhanging rocks for decades so successfully from the dragnets of researchers that it was considered extinct until the 1970s. By chance, paleontologist Max Wisshak discovered a significant cluster of hundreds of oysters near the Azores at a depth of 500 meters on a video taken with his research submarine Lula. At the site of filming, he discovered living deep-sea oysters and thus a scientific sensation. The primitive oyster was probably 100 years old and had annual rings made of lime. Wisshak analyzed these layers of lime under the microscope, a ZEISS *Axiophot*. From their composition, he was able to identify fluctuations in the water temperature and other environmental parameters such as nutrient content. He is currently researching how these oysters can be used as a climate archive for the North Atlantic.

Movies and Pixels

The ARRI AG can do both: analog and digital

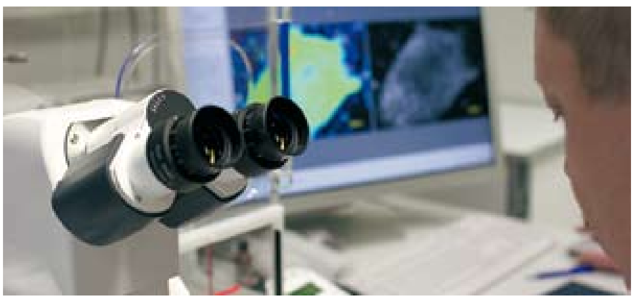
ARRIFLEX 35II, 1946

Movie buffs prick up their ears with great interest when they hear that ARRI is now building digital cameras. The company that has been working with Carl Zeiss for 70 years is gaining a second foothold with this new technology.

In 1917 August Arnold and Robert Richter founded the firm "Arnold & Richter Cine Technik" in a former shoemaker's workshop in Munich. Today, ARRI is the world market leader in the field of analog movie cameras. The new digital technology is not intended to replace the proven analog technology, but to supplement it. In the future, other magnificent movies such as The Lord of the Rings and Perfume will also be filmed with analog cameras. However, digital cameras offer new possibilities. "We are utilizing these capabilities," says ARRI Product Manager Marc Shipman-Müller, "but, of course, we are continuing to build cameras for 16 and 35 millimeter film."

Cancer Research at Its Best

Carl Zeiss opens application center at the German Cancer Research Center



Dynamic cell processes under the microscope.

Cancer is the second most common cause of death in Germany. The German Cancer Research Center (DKFZ) in Heidelberg focuses its activities on research into the malignant growth of cells. The goal of the DKFZ is to systematically research the mechanisms that lead to the onset of the disease and to determine risk factors. With the opening of the application center last summer, Carl Zeiss is supporting the research work of the DKFZ at the technology park in Heidelberg which is one of Germany's most important biotechnology locations and one of the global leaders. Research can be performed on complex dynamic processes in the lab rooms with a laser scanning microscope, high-quality light and stereo microscopes and automated microscope systems. Scientists develop new approaches for the prevention, diagnosis and treatment of cancer based on the results of these examinations. Carl Zeiss not only provides technology: workshops give scientists an opportunity to learn the latest microscope techniques and enhance their know-how. Furthermore, the Advanced Microscopy Forum regularly provides information on current topics in research, science and development.

The Perfect Light Color

O-INSPECT checks LEDs in the new BMW Museum

Architecture is always a reflection of the times in which it is created. Munich is just one example: in 1972 the young Federal Republic of Germany wanted to present itself as a cosmopolitan and attractive state for the XX Olympics. This was also echoed in the architecture: the Olympia Stadium with its tent-like roof, the spacious Olympia Park or the high rise BMW building with its famous "Four Cylinders" and the neighboring BMW Museum – it was all pioneering, contemporary architecture. 35 years and many millions of visitors later the redesigned museum has reopened in the spring of 2008 after four years of renovation work – with LED illumination of the glass facade tested by Carl Zeiss.

A major component within the newly built pavilion beside the museum is a glass facade with LED illumination extending over 3000 square meters. This lighting configuration was created by Zumtobel with the support of the LED specialist Ledon: harmonious light ensures uniform illumination of the glass surface. The color temperature of the light emitting diodes must be adapted so precisely that it can exactly reproduce the light color of the media facade. The most difficult part of this light configuration is the need to create optimal uniformity of the glass facade despite the different distances of the individual LED platelets. The challenge confronting Carl Zeiss: none of the 2.5 x 2.5 millimeter large points of light should fail. The solution: the optical and tactile inspection of the digital light source with *O-INSPECT*. The measuring machine tests the LEDs in high volume serial production – and all at astounding speed and with amazing accuracy.

Resplendent in a new light: the renovated BMW Museum.

Analysis Over the Shoulder

MAVUS® facilitates work on plant and machinery in distant countries

Engineer with the MAVUS® system.

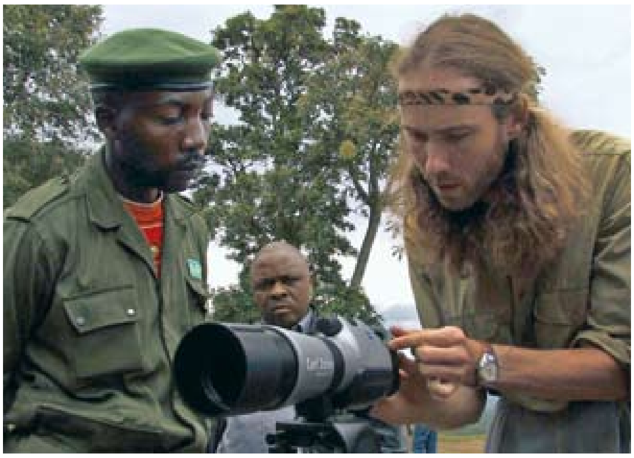
For a long time, it seemed like an almost insurmountable problem: plant and machinery are built in the home country and shipped to a far-off region of the world, where they are then put into service and maintained – preferably by experts from the original country because very few other people have their know-how. Long and expensive business trips were the result. However, this can now all be changed: *MAVUS* (the abbreviation of the German for Mobile Audio-Visual Support Service), a cooperation venture of Carl Zeiss and the HEITEC systems house, facilitates collaboration between the expert at the home service headquarters and a service engineer on site. How does this work?

An advanced camera and headset, which are attached to an ergonomic support on the engineer's head along with a monocular *Head-Mounted Display (HMD)*, are used to transmit high resolution freeze frames or live images to the expert in real time online. He or she analyzes the situation in an "over the shoulder" approach and provides the on-site engineer – visually on the *HMD* and via voice communication – with information about what should be done.

The benefit: excellent availability of experts, fast reaction times, efficient startups, minimal downtimes – and low travel costs.

An Eye on Gorillas

Carl Zeiss equips game wardens with binoculars and telescopes



Wildlife filmer Matto Barfuss (right) is committed to conserving an endangered species of apes.

Mountain gorillas are an endangered species. Approximately 300 of them live in the Virunga Mountains National Park in Congo. This is half of all the mountain gorillas remaining in the world. Rebels repeatedly hunt them – out of a desire to kill, out of a desire to make a profit. They murder the adult animals and take the young. Poachers have an easy time of it. Animals in national parks are used to people and are particularly over-trusting. Game wardens must protect them – not an easy task in this spacious region. Artist and wildlife photographer Matto Barfuss, who filmed the mountain gorillas for two years, launched a relief operation for game wardens. Carl Zeiss is doing its part by donating high-performance binoculars and telescopes that Barfuss delivered to Africa himself.

A video of the handover to the game wardens is available at www.zeiss.de/innovation

Under Extreme Conditions

New sports eyewear offers distortion-free vision

Professional sport has developed at tremendous speed over the past few years: sophisticated training methods, targeted nutrition and optimized sports equipment are propelling career athletes to new dimensions of excellence. There is room for even better performance, but for one thing there is not: leaving anything to chance. This also applies to the development of the new sunglass models for road and cross country cycling which are often subjected to extreme conditions.

The eyeglasses took just under two years to develop, a period during which professionals tested the fit, optical quality and sun protection of the models. The result of the collaboration with the sports outfitter GIRO: fashionable sports eyewear with 100 percent UV protection which guarantees totally distortion-free vision over the entire lens, combined with a special surface coating. The polarizing, exchangeable lenses are repellent to water, dirt and oil and are available in seven different tints. Clear lenses are also offered for night driving to ensure that cyclists enjoy full visibility during every cycling tour.

Tested by pros: GIRO sports eyewear.

Accurate Down to the Micrometer

Jet engine manufacturer relies on ZEISS coordinate measuring machines

The precision of parts is decisive to the quality of the finished product. Munich-based MTU Aero Engine relies on measuring machines from Carl Zeiss to inspect its parts. In September 2007, MTU received the 25,000th measuring machine built by Carl Zeiss: a *PRISMO navigator*. This coordinate measuring machine with integrated rotary table measures jet engine components with accuracy down to the micrometer. Karl-Heinz Klügl, head of Incoming Goods Inspection at MTU Aero Engines, stated during the handover that “We are proud to have the 25,000th ZEISS machine available for our incoming goods inspection. The high demands on MTU engines, which will also be used in the Airbus A380, require reliable measuring results. Furthermore, we value the reliability and durability of ZEISS machines.” Klügl emphasized that all parts are measured with measuring machines from Carl Zeiss directly in incoming orders.

Quiet as a Church

Mouse

The popularity of birdwatching is increasing: Once ridiculed, birdwatching is becoming the new leisure time hobby for people who want to take it a little more slowly.

Always on the Lookout for Rare Birds

The blackcap is a useful creature: it can be easily identified by its “monks' hood” and ideally adapts to changing living conditions.

As many other birds, this small songbird no longer winters in Spain, but heads north to Great Britain. It goes where the food is: the British are enthusiastic feeders. Of course they do not do this simply because they are nice. The British love birdwatching as do many people in other countries. Great Britain has the world’s largest bird-lovers club with more than one million members and newspapers that employ their own bird columnists. At first glance, birdwatching is a peculiar sport in which there are neither winners nor losers, only observers who are as quiet as a church mouse. Real birders get their thrills by observing as many different birds as possible and checking them off a personal list.

These hobby ornithologists arm themselves with spotting scopes, binoculars and field guides in their attempts to conquer this list and are always on the lookout for rare birds which are usually far away and shy by nature. Recently, birdwatchers have received support in their arduous work in the form of new technology.

Digital photography, digiscoping in this case, makes it possible.

Carl Zeiss has developed an instrument to make picture taking easier. How does this work? A compact digital camera is placed in front of the eyepiece of the spotting scope and held in place with a camera adapter. The new solution for digiscoping takes it one step further: the *DC4 camera eyepiece*. It is mounted to the spotting scope in place of a pure observation eyepiece. It allows birdwatchers to continually observe and take pictures at the same time. The camera is triggered via a remote control. Special software corrects contrast, definition, exposure and color fidelity – even before the image is stored on the chip card. The camera eyepiece achieves 40x magnification.

Many changes are still to come for birdwatchers when a leisurely migration from north to south takes place in the near future. In the winter, the British have the German blackcaps, but they do not yet have the red kites, of which more than 70 percent of all pairs in the world nest in Germany.

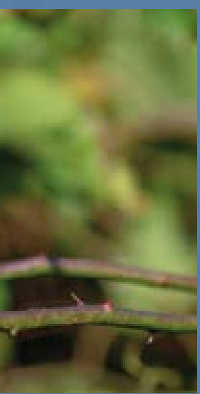
Photo on pages 10/11: Sven Achtermann
Photos on pages 12/13: Stephen Ingrahm

Belted kingfisher

European robin

Gray heron

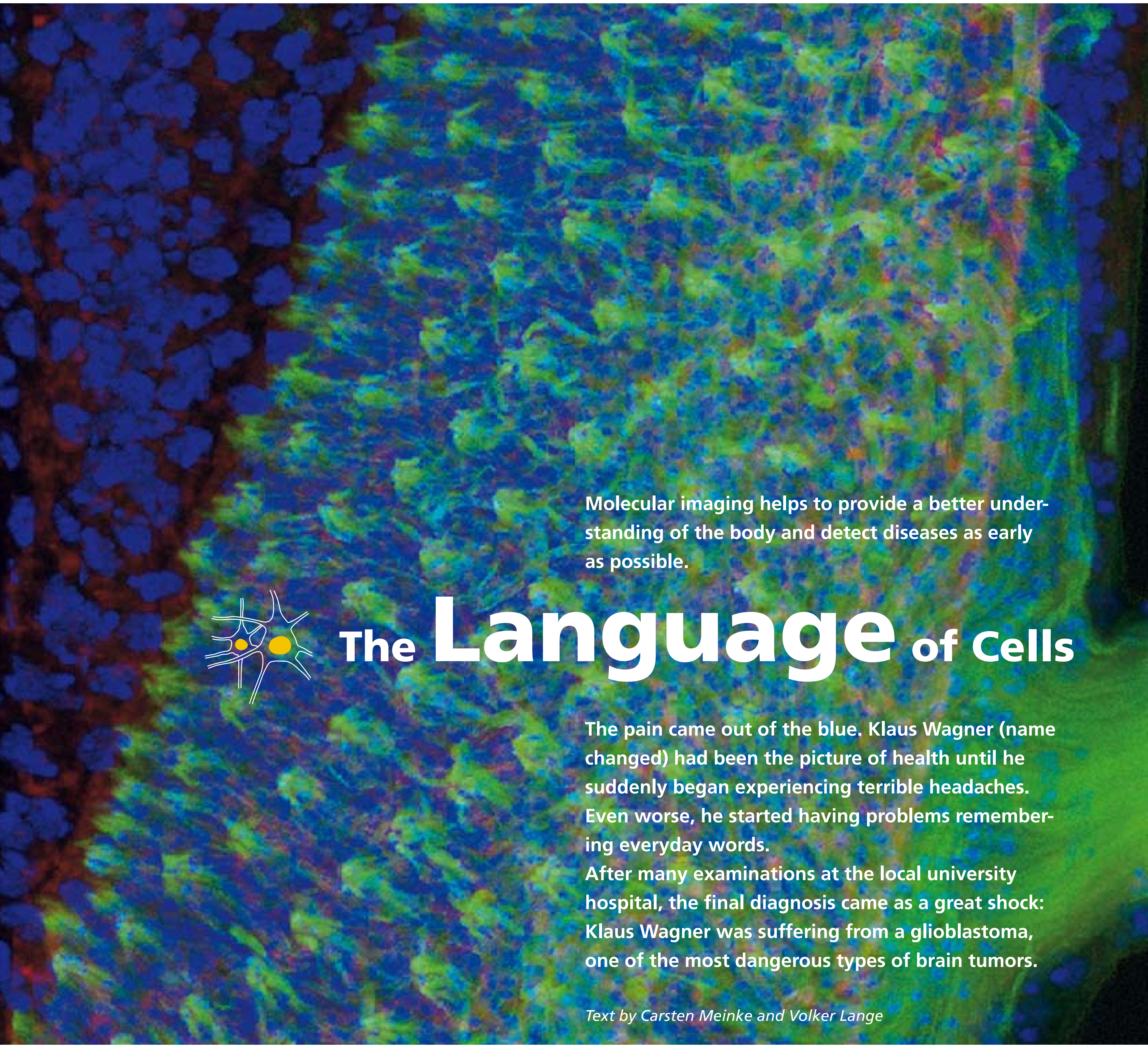
Yellow-rumped warbler



Great egret

Blackcap

Linnet

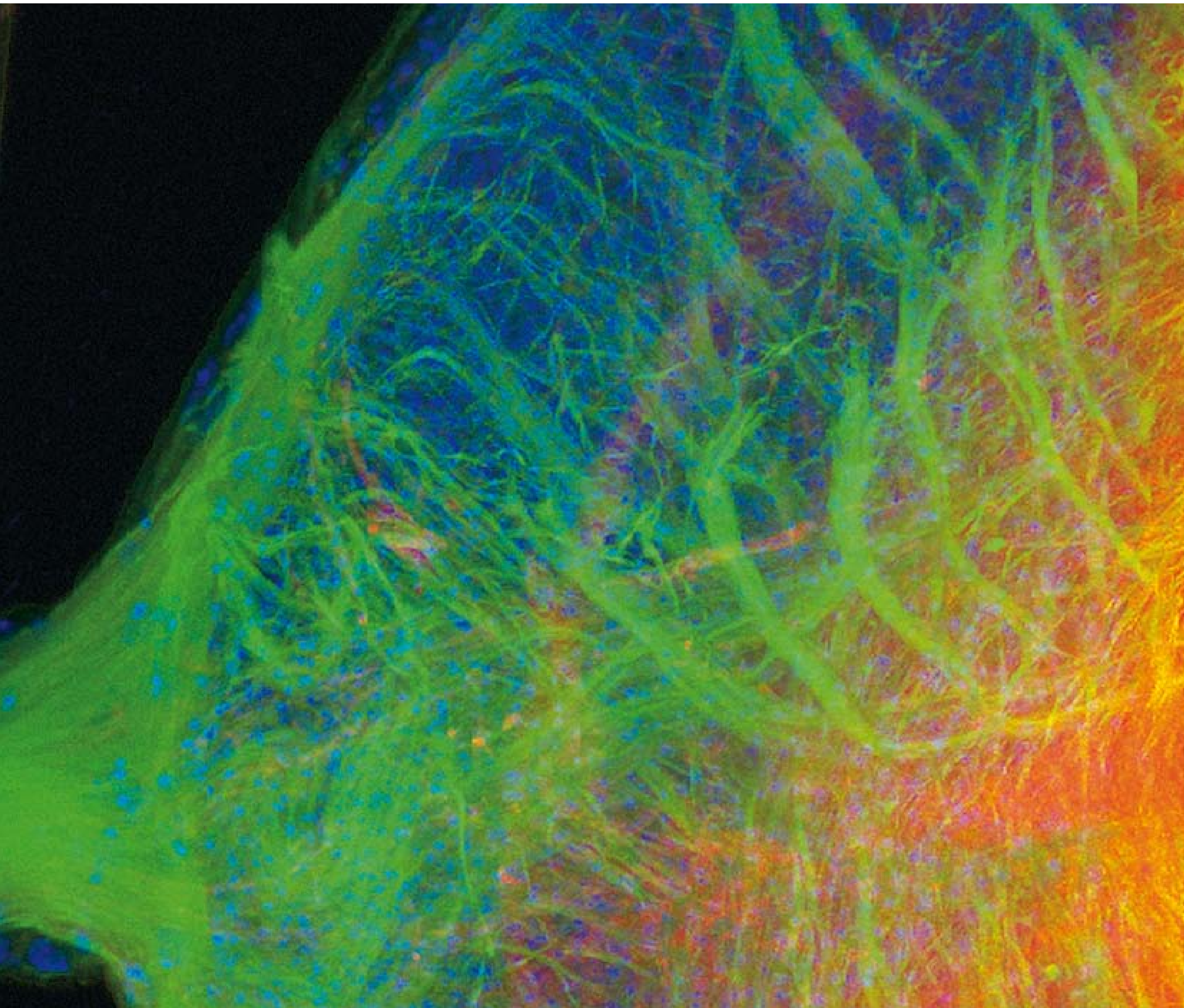


Molecular imaging helps to provide a better understanding of the body and detect diseases as early as possible.

The Language of Cells

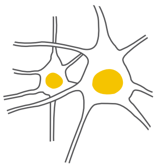
The pain came out of the blue. Klaus Wagner (name changed) had been the picture of health until he suddenly began experiencing terrible headaches. Even worse, he started having problems remembering everyday words.
After many examinations at the local university hospital, the final diagnosis came as a great shock: Klaus Wagner was suffering from a glioblastoma, one of the most dangerous types of brain tumors.

Text by Carsten Meinke and Volker Lange



Cross-section of the hippocampus with YFP fluorescent neurons in green and Arc RNA signals in red.

How Enzymes Stimulate Tissue to Glow



Every year, some 2,400 people are diagnosed with a glioblastoma in Germany alone. Glioblastoma multiforme, the precise name, is extremely malignant. Most of the tumors are enveloped in a type of capsule and can therefore be easily distinguished from healthy tissue. However, the glioblastoma infiltrates tissue in a diffuse manner: It has no clear edge and can send individual cells far into the surrounding tissue. Surgical removal of the glioblastoma, called resection, presents neurosurgeons with a difficult predicament:

Picture on page 14/15:
Retina brain complex
(Drosophila larvae)
Green: neural cells (GFP)
Anand Tiwari, Bananas Hindu
University, Varanasi, India

On the one hand, they want to do as little damage as possible to healthy brain tissue, and on the other hand they have to cut deep enough to extend the patient’s life.

Walter Stummer from the University of Düsseldorf and his colleagues from the Ludwig Maximilian University in Munich found a way out of this dilemma. They took advantage of an interesting phenomenon: If the cells of a glioblastoma are only sufficiently supplied with the “5-ALA” amino acid, they create a preliminary stage of the respective molecule which binds oxygen in the blood pigment hemoglobin. Normal brain cells do not do this. This substance, called protoporphyrin IX, can be stimulated to glow. It is fluorescent and can therefore be visually differentiated from its environment.

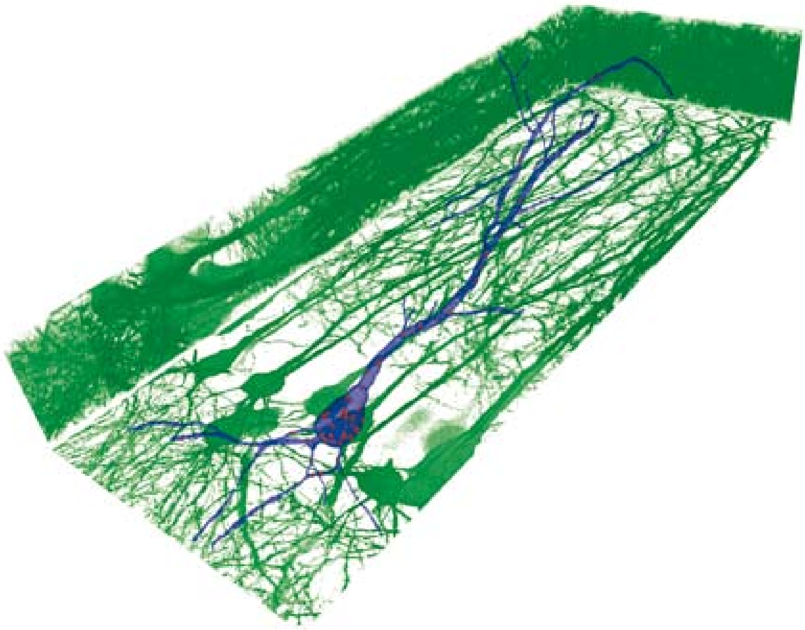
Gaining valuable time. For neurologists, this is of enormous help. Therefore Carl Zeiss developed the *BLUE 400* fluorescence module. It illuminates the surgical area with a deep blue light with a wavelength of approximately 400 nanometers, causing the protoporphyrin IX to fluoresce. A look through the *OPMI Pentero* surgical microscope allows the surgeon to see the degenerated tissue, which has a light red color, while the healthy brain tissue remains dark. Recently, Stummer and his colleagues reported that an especially thorough removal of the glioblastoma is possible with the help of this fluorescence contrast. The life of the patient can therefore be extended by many precious months. The example of the glioblastoma tumor leads right to molecular imaging, a research area that is currently in the midst of revolutionizing medicine. The principle is simple: Scientists are taking advantage of the fact that the various tissue types in the human body possess very specific configurations with enzymes or other key molecules. Each tissue thus has a very special metabolism that differs from that of the neighboring tissue. If the characteristics of a tissue can be made visible, entirely new possibilities arise for researchers and physicians to understand the body and detect diseases at the earliest possible stages. Methods must be found to measure molecular processes in the living body (in vivo). This is a challenging goal, but development is proceeding at full speed.

Since 2005, researchers in the Westphalian city of Münster have been developing methods to make molecular processes visible for cardiovascular diseases. The German Research Foundation (DFG) established a Collaborative Research Center for this purpose as diseases such as heart attack, coronary heart disease and stroke are among the most frequent causes of death in western industrial nations. “Physicians can only indirectly assess the risks for individuals based on various risk factors,” says Michael Schäfers, scientific organizer of the Collaborative Research Center.

If it were possible to directly depict the changes (atherosclerosis plaques) in the vascular wall, this would be a victory for cardiovascular medicine, explains Michael Schäfers.

An example: Today, physicians can determine the status of coronary vessels. They inject a contrast medium into the bloodstream through a catheter. An x-ray or MRI then shows if and how much a vessel has narrowed at a specific location. However, this does not allow a definitive conclusion about how dangerous the deposit is, stresses Schäfers. A deposit does not represent an acute risk as long as the fat core is situated under a stable fiber cap. However, plaques in which inflammatory processes are at work are much more dangerous. Not only can a dangerous active ingredient cocktail develop in these plaques, but the inflammation process also dissolves the fiber cap bit by bit. If the plaque subsequently tears and releases its contents, abrupt blood clotting can result. The possible consequence: a heart attack.

"Hot" plaque. It is exactly this inflammation activity that Schäfers and his colleagues strive to make visible. They are using a trick for this. Special enzymes (matrix metalloproteinases, or MMPs) always occur with inflammations. Markings that can be easily detected can be coupled to these MMPs – in trade lingo these are called ligands and labels. The slightly radioactive fluor-18 is such a ligand, for example. If a fluor-18 atomic nucleus degenerates, it releases a positron. If this positron meets its antiparticle in tissue – the electron – then both irradiate while sending out two gamma quants. These quants can be measured with a high degree of sensitivity using positron emission tomography (PET), and the precise location where they were



Transparent image of a neuron (blue) and the associated Arc signal (red): image segmentation and the use of rule-based algorithms enable differentiation of surrounding dendrites (green, maximal 3D projection).

Inside view of a neuron: Arc RNA signals (red) within the dendrite structure localized in 3D.

released can even be calculated. This provides a sort of three-dimensional, infrared image of the tissue:. The "hotter" a plaque is, the more MMPs it will contain and the stronger the inflammation process inside will be. Prof. Dr. Dr. Otmar Schober is the Spokesman for the Collaborative Research Center in Münster:

> *"We want to use this in the future to identify patients who are at a high risk for a heart attack at a very early stage. This will allow us to give them preventive and targeted treatment."*
>
> *Otmar Schober*

The search for optical markers. In addition to the MMPs, the Münster researchers are focusing on another group of enzymes as well, the so-called caspases. These enzymes always spring into action when a cell activates its "suicide program" (apoptosis). A cell "commits suicide" when it is poisoned due to chemotherapy, for example. By radioactively marking caspase enzymes, researchers want to precisely measure their concentration and distribution in the body. In this way, you can determine if a cancer tumor is responding to a medication or not within a few days. This is a great stride forward, as oncologists in the past could only assess the success or failure of chemotherapy if the tumor became visibly smaller.

Now, not everyone is comfortable with the idea of being injected with radioactively marked substances – even if the nuclides therein are mostly short-lived and their activity quickly subsides. Optical processes encounter much less hesitancy in this respect and are also much more cost-effective when they can be used. This is why Christoph Bremer is researching at the Münster Collaborative Research Center whether fluorescent stains can be appended to the ligands instead of radionuclides. Fluorochromes are particularly interesting: they emit light in the longwave, infrared range. The advantage: Infrared light permeates body tissue very well. However, the modular exchange of labels cannot be easily accomplished. A radioactive atom is much smaller than a comparatively large fluorescent molecule group. In cases where a miniscule radionuclide can attach without any problems, a fluorochrome may collapse due to its sheer size. After all, a truck will not fit into a normal garage

Therefore, it may better to look for optical markers from the beginning. Andreas Wunder from the Berlin Charité Hospital relies on visual phenomena such as fluorescence in his work from the outset. The Berlin-based researcher would like to find out what exactly happens inside the brain during a stroke. In Germany alone, 150,000 to 200,000 people suffer from a stroke annually and, in order to know how to treat individual patients, information is needed about what exactly occurs in the brain.

From Wunder's point of view, the advantages of optical processes are impressive: the costs of corresponding methods are comparatively low, the measurements are fast and they are also highly sensitive to detection. Using optical tomography, the optical counterpart to computer tomography, even three-dimensional images can be obtained from tissue samples and small animals.

The disadvantage of optical methods: light transports much less energy than gamma radiation. Therefore, the more tissue it must permeate on the way to the detector, the more it is dispersed. The consequences: the deeper the tissue to be examined is located in the body, the lower the spatial resolution. However, the body possesses a multitude of openings leading to the exterior. Therefore, a fluorescence detector can be delivered very close to the target organ in a non-invasive manner – for example, through the intestine or esophagus.

Attaching to defense cells. This is no easy matter for the brain. Therefore, researchers in Berlin primarily use mouse models although the researchers at the Charité – together with colleagues from the German National Metrology Institute (PTB) in Brunswick – have been able to show that near infrared fluorescence can even be registered through a cranial bone. To this end, they plant fluorescent molecules in the body and attach them to the receptors of defense cells, which play an important role in the

German Federal Minister of Research Dr. Annette Schavan (center), together with the members of the boards of directors of the five participating companies, gave the green light in Berlin for the "Innovation Alliance of Molecular Imaging" (from left): Member of the Board Dr. André Hertkorn (Boehringer Ingelheim Pharma), Karl-Christian Storz (Karl Storz), Dr. Michael Kaschke (Carl Zeiss), Prof. Dr. Andreas Busch (Bayer Schering Pharma) and Prof. Dr. Erich Reinhardt (formerly Siemens Medical Solutions).

activation of inflammation processes. Inflammation processes such as those researched by Schäfers group. It is not for nothing that there is intensive exchange between Berlin and Münster.

At the Hertie Institute for Clinical Brain Research in Tübingen, researchers also want to look inside the living brain. Neuropathologists in the group led by Mathias Jucker and Michael Calhoun are interested in knowing how protein clumps typical of Alzheimer's disease are formed. They hope to learn from the mouse model how the characteristic amyloid plaques grow in nerve tissue and how the "garbage removal" of the brain, the microglia, reacts to it. Today, they can follow this process in real-time with the help of confocal microscopy – through the skull cap and in a living animal.

High detail rendition. Confocal microscopes, such as the *Laser Scanning Microscope (LSM)* from Carl Zeiss, can also "see through" thicker tissue with high resolution. A laser beam is precisely focused on a point. It stimulates the fluorescent targets to glow and this glow is then precisely measured. Point for point, level for level, it reads the sample and thus provides virtual cross-section images with a high degree of detail. The Tübingen researchers are working in an area that is of great importance not only to the patient but also for the entire German health care system.

In Germany alone, an estimated 700,000 people are suffering from Alzheimer's disease, the continued and hitherto unstoppable loss of memory and all other mental faculties. The German Neurological Society estimates that this number will double by the year 2050. After cancer and cardiovascular diseases, Alzheimer's disease and other dementia diseases constitute the third-largest group of diseases whose prognosis is expected to be greatly advanced by molecular imaging.

A dream is coming closer to reality. Of course, diagnosis is one thing. But what if molecular imaging could also be used for treatment? It's an obvious idea – and indeed there seem to be some fascinating perspectives in this realm. The general idea: If a cell, a cellular component or process has already been marked with a label, would it be possible to leverage this to exert control – and in the same breath track the success of the measure? This principle is actually already being employed, namely thanks to those amino acids with which Walter Stummer from the University of Düsseldorf and his colleagues cause glioblastomas to glow. As the scientific world has known for many years, protoporphyrin not only emits fluorescent light, it also produces aggressive oxygen radicals. If the cells are irradiated long enough with light, so many oxygen radicals gather inside that they subsequently activate their suicide program.

This photodynamic therapy is currently used primarily for some skin cancers in their early stages. A range of research groups is working towards also being able to use this therapy for tumors located deep within the body. Others, wish to use the radiation emitted by radionuclides for marking target cells and simultaneously driving them to the programmed cellular death. A combined diagnosis and therapy at the molecular level would have been unimaginable for Hippocrates and his contemporaries. Sauerbruch or Watson and Crick had at least referred to this idea in the realm of science fiction. Today things are different. There are still many hurdles to overcome, be they chemical, medical or technical in nature. Nevertheless, the dream of many medical professionals is within reach, even if it will still take much time and money until the corresponding processes are clinically applicable.

The details

Five Are Stronger

In order to play on the front lines of the molecular imaging game, many core competencies are needed which would overwhelm an individual company. Therefore, "Innovation Alliance of Molecular Imaging" was founded on October 9, 2007.

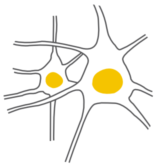
Five companies make up the Innovation Alliance. Carl Zeiss will contribute its expertise as one of the global leaders in the field of optical technologies. Bayer Schering Pharma and Boehringer Ingelheim Pharma will concentrate on the development of molecular probes. Siemens will provide its support in the area of radiological imaging and information systems. The Alliance's fifth partner is the family business Karl Storz, a global market leader in the area of endoscopy.

An estimated 900 million euros will be needed for this project over the next six years. The participating companies will invest 750 million euros, with the German Federal Ministry of Research providing the remaining 150 million euros.

A Medical Revolution

Dr. Michael Kaschke discusses the potential of molecular imaging

Dr. Michael Kaschke, Member of the Executive Board.



Dr. Michael Kaschke is the member of the Carl Zeiss AG Executive Board responsible for Medical Systems and Microscopy. In an interview, he talks about the perspectives of molecular imaging.

Which competencies in particular does Carl Zeiss bring to the alliance?

Imaging methods are among the most important competencies of Carl Zeiss, primarily in the Microscopy and Medical Systems Business Groups. These are supported by our central research & development department.

Is the Alliance also open to other partners? If yes, what additional competencies would you like to see from the new partners?

The five partners who launched the initiative would like to have additional partners: both from research and from industry. It is important for them to bring solutions and products from biotechnology and the life sciences.

Normally companies are in heated competition against each other. Don't you see any conflicts of interest?

No. Quite the opposite: The questions we are working on are so complex that a single company is not capable of finding a solution. Furthermore, the majority of the solutions and products offered by the five partners complement each other; they are not competing against each other. Therefore, imaging techniques, which Siemens and Carl Zeiss are developing, are particularly well-suited to the markers and contrasting agents manufactured by Bayer Schering, for example.

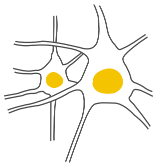
When the alliance was announced, the topic of discussion was not only the possibility of being able to diagnose diseases in good time. Being able to treat these diseases accordingly was a continuous subject. What is Carl Zeiss' role in this?

The objective of the initiative is not only to detect diseases early on but also to determine their causes. This will allow diseases to be treated before their outbreak. Let me explain: proteins are important molecule groups in animals that play a key role in the processes in cells necessary for life. Molecular imaging helps clarify which protein contributes to the onset of a disease. This makes it possible to really understand the cause of diseases. In turn, this information is vital for the development of medicines. I can even imagine that person-specific medicines can be used at a very early stage. In my opinion, molecular imaging is starting a revolution in medicine. Unfortunately, we still diagnose most diseases based on symptoms, i.e. once the disease has already broken out.

Thank you very much for this interview.

The questions were presented by Volker Lange and Silke Schmid

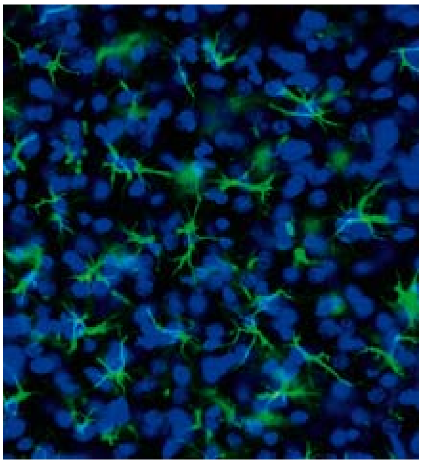
The Direction of Research – a Perspective



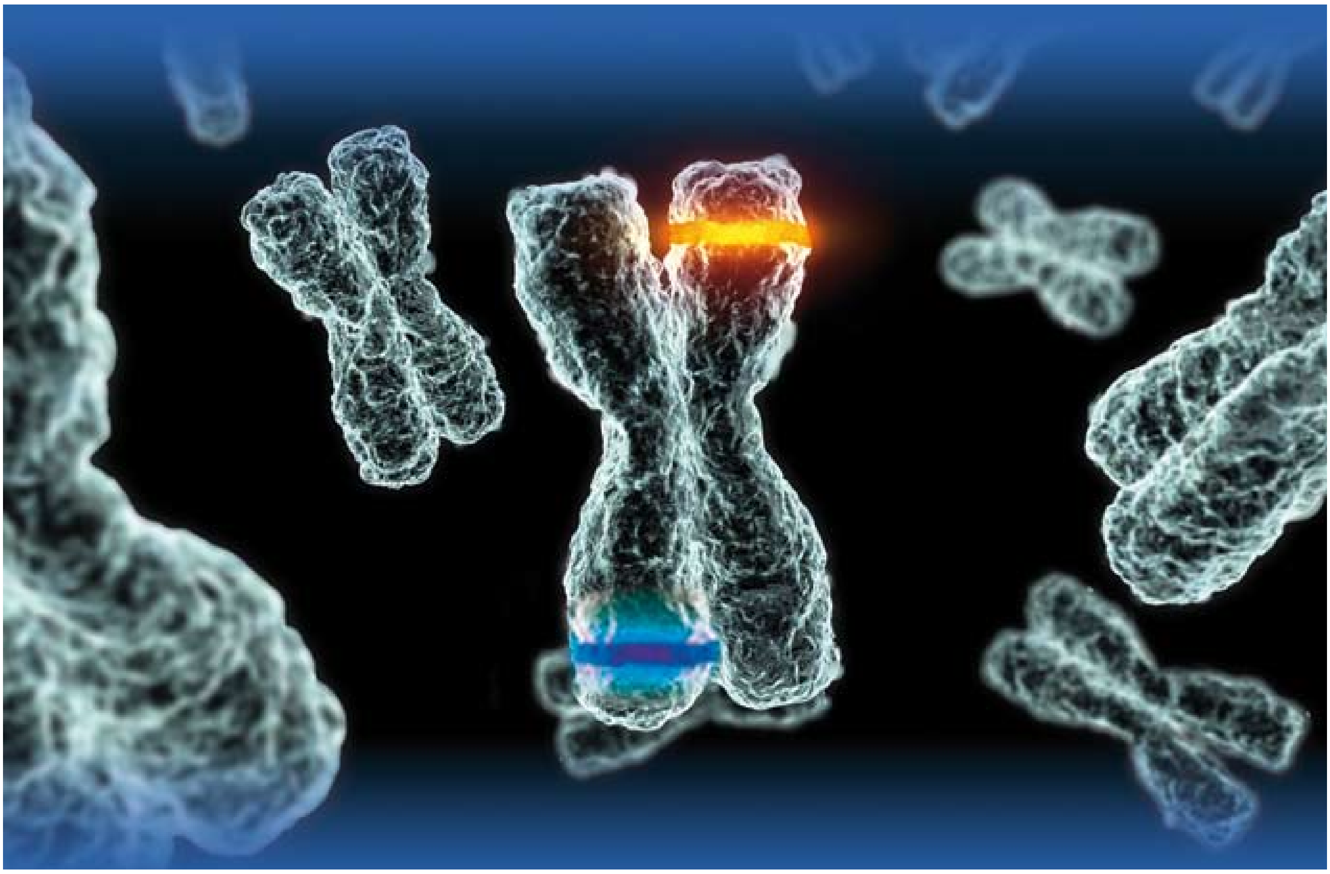
Strictly speaking, molecular imaging is not a new area of research. Nuclear physicians have been using scintigrams for decades to search for inflammation processes and tumors. For example, a patient can be injected with radioactive iodine that is exclusively concentrated by the cells of the thyroid. Using a suitable camera, the radiation can be rendered visible, thus providing information on the metabolism in the affected area.

However, those who search for the term "molecular imaging" in the Pubmed professional article database will notice a remarkable development. The first article containing this phrase appears in the year 1986 and describes a crystallographic analysis of the tobacco mosaic virus. In 2002, shortly after the publication of the "rough draft" of the human genome, 161 articles about the topic were published and in 2007 this number rose to 650. No wonder: molecular imaging is booming.

Enormous economic importance. This is also true from an economic perspective. Molecular imaging offers a wealth of new approaches for research and industry. And often the two areas overlap. An example: Nobel Prize recipient Prof. Manfred Eigen from Göttingen was originally interested in finding out how the reaction speed for very fast chemical processes can be determined. From this he developed an optical process to verify individual molecules. Together with a spin-off of the Göttingen-based Max Planck Institute, the Hamburg-based company Evotec and Carl Zeiss, the first commercially available fluorescence correlation spectrometer *ConfoCor* (see page 25, "The details") was manufactured in 1995. Since then, it has become possible to use this process to automatically filter out active ingredient candidates for a new medication from a quantity of substances. This is also due in part to the *ultra high throughput screening (uHTS)* method developed by Carl Zeiss. The original basic research turned into application research, which has enormous economic significance to pharmaceutical research. And this is only a new starting point for the broad field of medical and pharmaceutical research. If you consider the demographic development in industrialized nations and the new tasks for medicine that stem from this development, enormous growth potential emerges. This can also be gathered from the "Study regarding the Situation of Medical Technology in Germany Compared to Other Countries," which was published by the German Federal Ministry for Research in 2005. The study's authors estimate that the worldwide demand for medical products increased by 8.5 percent between 1991 and 2001. Within one decade, the global trade volume more than doubled from \$30.1 billion to \$67.7 billion.



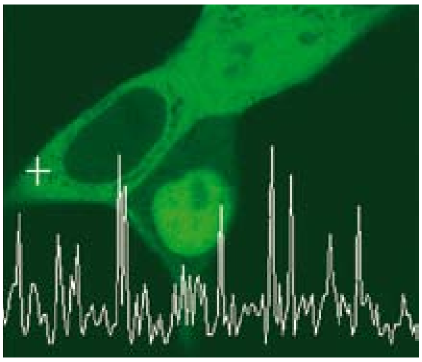
Brain cross-section (multichannel image with ApoTome).



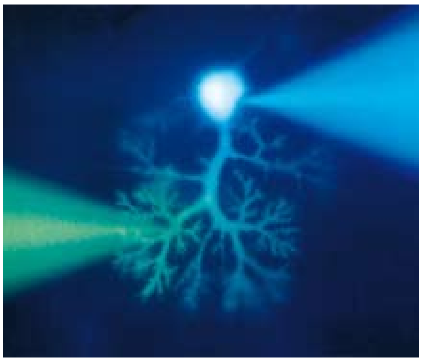
CAD view of complete chromosomes.

Many experts are convinced that the lion's share will fall upon molecular imaging. Market research company Kalorama Information estimates that an application-suitable PET label for the amyloid plaques of Alzheimer patients would have a market value of around $1.8 billion – during the patent-protected phase alone. Such perspectives have startled companies and research institutes around the globe.

High-pressure research. It is not a coincidence that the Center for Molecular Imaging Research (CMIR) was founded at Harvard University in Boston in 1994, for example. Based on the square footage of its laboratories, it has experienced equally explosive growth since that time. Several years after the founding of the CMIR, competition came from California in the form of the Molecular



Fluorescence fluctuation analysis



Neuron in the cortex of the brain, fluorescence

Imaging Program at Stanford (MIPS). Both centers are financed not only with public funds, but also draw on monies provided by industry. Intense research is also being carried out in Japan, Korea and Singapore.

It could seem belated that five leading companies, among them Carl Zeiss, established the German "Innovation Alliance of Molecular Imaging" in 2007 together with the Federal Ministry for Research. Perhaps that ship has already set sail? Michael Schäfers from the University of Münster does not think so at all. He believes that Germany is essentially well-positioned in the molecular imaging area.

"Although the American centers are very capable when it comes to basic research, our advantage still lies in our comprehensive clinical expertise."

Michael Schäfers

It is exactly this intensive cooperation between research and practice that is a not-to-be-underestimated advantage in making the leap to medical application.

A long wish list. However, clinicians would have to work closely together with their colleagues from other disciplines, says Schäfers: "It is not enough to have a medical issue. We also need the tools to work on this issue." And this is where industry comes in. The wish list of practitioners like Michael Schäfers or Berlin researcher Andreas Wunder is long: for example, suitable animal models had to be found, ligands and labels had to be synthesized and the required detection techniques had to be developed. And then, of course, there is the need for a software system so that the collected data can be visualized and analyzed. Then, German research in the area of molecular imaging will reclaim its rightful place: at the top of the winner's podium

The details

Search for active ingredients on the fast track

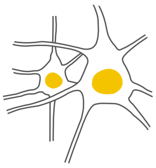
Ferreting out active ingredients for medications was still extremely costly several years ago. The objective was to filter out from large quantities of molecules those specific substances that might be able to form the basis for the development of new active ingredients.

Thanks to ultra high throughput screening (uHTS), today more than 100,000 samples can be examined daily. In so-called microtiter plates with a few microliters of sample volume, protein structures that play a key role in a disease can be systematically examined. They are tested for their interaction with potential active ingredients. As with molecular imaging in medicine, fluorescent probes also play a central role here. If they dock on to the sought molecules, weak luminescence can be measured. This occurs at lightning speed and can be precisely quantified. For example, an innovative uHTS process was developed by Carl Zeiss in Jena together with pharmaceutical company Roche and then sold to Hamburg company Evotec in 2005.

"Nowhere near the End of the Possibilities"

By Dr. Andreas Wunder,
Researcher at the Berlin Charité

Heidi Cartwright, Circuit Collage, Prince of Wales Medical Research Institute, Randwick, Australia, 2000



Optical technologies are essential to medicine and biomedical research. In the past, they have made valuable contributions to clinical diagnostics and in decoding biological processes. This led to the development of numerous endoscopic and microscopic techniques that provide important information on the internal workings of the body and permit research into the biological processes of cells or tissue samples with high spatial resolution at a cellular or subcellular level.

Intensive Research and Development. In recent years, researchers have increasingly succeeded in displaying biological processes non-invasively at the cellular/molecular level using optical methods. The term molecular imaging is being increasingly used to describe several partially competitive imaging technologies that enable the visualization of biological processes in intact organisms.

In the future, this will lead to earlier and more exact diagnoses, as well as more specific therapies for diseases. However, this requires intensive research and development which is also the objective of the molecular imaging innovation alliance launched in October 2007 in Berlin.

The mouse model. Let us take an example of what we are working on at the Center for Stroke Research in Berlin (CSB) at the Charité: how can you non-invasively display inflammatory processes in the brain following a stroke? We are first working on a mouse model for this purpose. Initially, highly specific marker substances must be developed to visualize inflammatory processes in the brain. The first step is to identify suitable molecular targets that play a key role in inflammatory processes. The second step involves developing molecules (ligands) that very precisely bond to the identified targets. In the third step, these ligands are marked for imaging, e.g. with radioisotopes for nuclear medicine or fluorescence dyes for optical imaging.

Optical methods provide enormous advantages in the development of such marker substances. However, they are not only ideal tools for the evaluation of targets and ligands in model systems, but are also suitable for use on patients as long as the target tissue is not too deep in the body. This is where optical procedures reach their limitations. On the other hand, optical methods are known for their high level of sensitivity: very minute traces of a fluorescence dye can be detected. As a result of the wide variety of microscope techniques, optical methods offer the possibility of examining the distribution of a substance non-invasively and also with high spatial resolution at the cellular or sub-cellular level. Thus, stroke-induced inflammatory processes can be examined non-invasively at the cellular level following the injection of a fluorescently labeled inflammatory marker and after removal of tissue samples (ex-vivo).

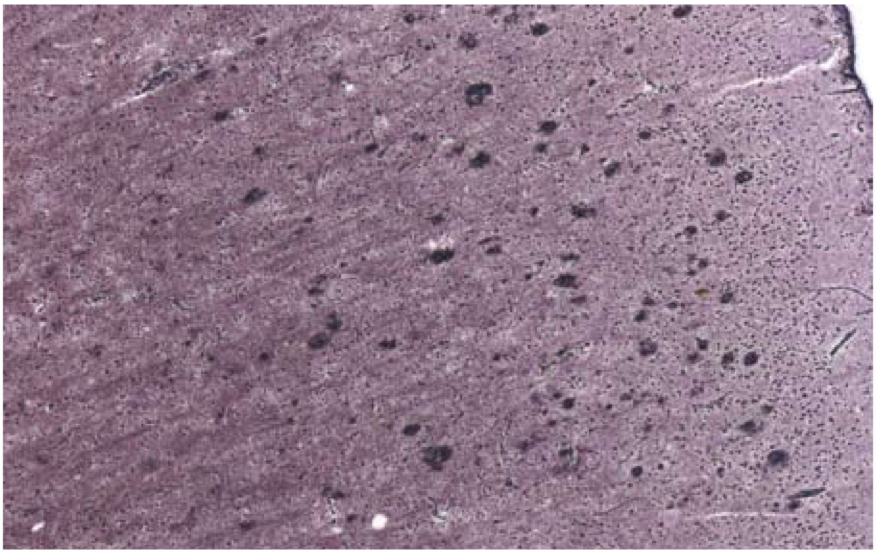
Deep into the brain. An example of this is white light and fluorescence images of a mouse with a stroke in the left hemisphere (see page 29). We injected the mouse with a fluorescence dye with which the stroke-induced inflammatory processes can be imaged. The high fluorescence intensity above the hemisphere affected by the stroke (see page 29, fluorescence image of the head of the mouse, lower left) can be seen in the living mouse even deep into the brain and through the cranium. This image was recorded in only a few seconds.

The removal of tissue samples shows that the fluorescence dye actually images the inflammatory processes in the brain. We succeeded in verifying the marker in the tissue affected by the stroke (see page 29, brain section; the color of the stroke tissue is clearly less intense than living tissue after staining). Furthermore, using a microscope, we were able to verify the specificity of the marker at the cellular level for certain inflammatory cells after preparing thin tissue sections and specific cell staining The yellow-edged cell is an inflammatory cell that has bonded with the marker

The person

Dr. Andreas Wunder

Dr. Andreas Wunder is Group Leader of the Molecular Imaging Work Group in the Experimental Neurology Department at the Berlin Charité.
Andreas Wunder (43) studied biology at the University of Kaiserslautern. Later he qualified as a professor at the Mannheim Hospital in the area of experimental medicine.
From 1994 to 2002, he was a scientist at the German Cancer Research Center (DKFZ) in Heidelberg. He then worked for two years as a Research Fellow at the Center for Molecular Imaging Research (CMIR) at the Harvard School of Medicine. He returned to Germany in 2004 and then conducted research at the Regensburg University Hospital. Since 2005, he has been working at the Center for Stroke Research (CSB) in Berlin.

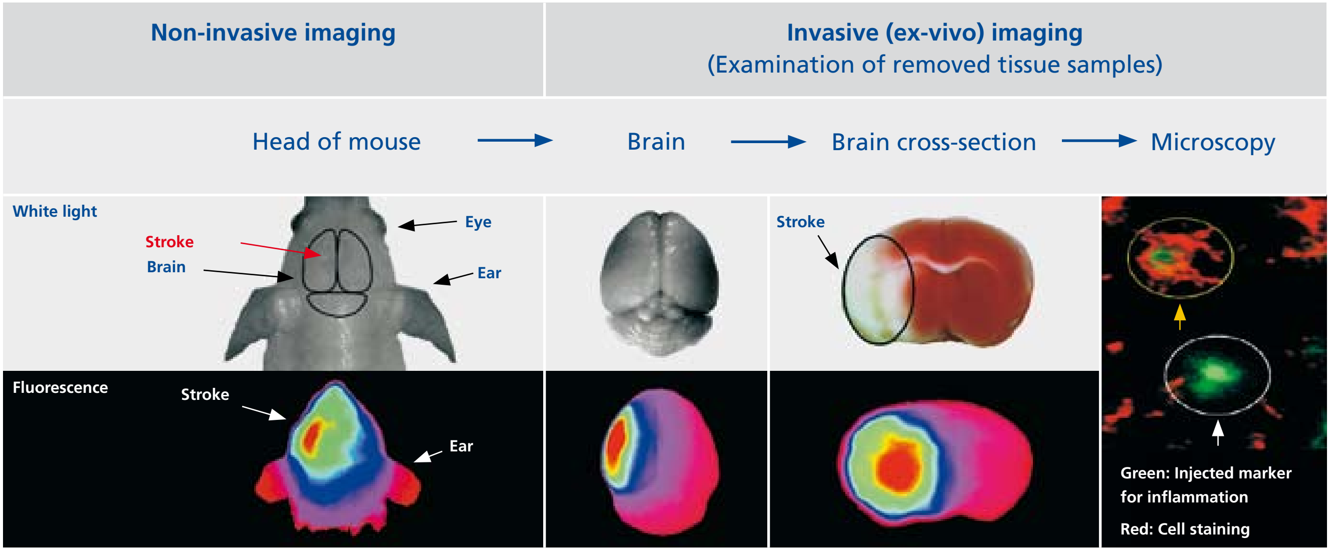


Original preparation by Alois Alzheimer, 1907, presenile dementia, cortex of the brain, Bielschowsky's silver impregnation. MIRAX digital slide scanner.

and that belongs to the stained sub-type. The white-edged cell is also an inflammatory cell, which belongs to another sub-type.

Marking and examining. Optical technologies are not only relatively easy, affordable and fast, they also offer the possibility of examining several biological processes simultaneously. Additionally, the different marker substances are stained with different fluorescence dyes and detected separately (multi-channel imaging). This technique can also be used if marker substances are to be tested for their specificity: with a number of diseases such as tumors or inflammatory processes there is a malfunction of the blood-tissue barrier. This leads to an unspecific accumulation of substances in the affected tissue. Thus, a major part of the detected signal is attributable to unspecific accumulation. In order to estimate this portion, multi-channel imaging can be used to mark and simultaneously examine an unspecific marker substance and the specific marker substance with different fluorescence dyes.

The new filter systems. However, we are nowhere near the end of the possibilities offered by optical techniques. Improved fluorescence dyes that display less bleaching or have a higher fluorescence quantum yield can make the measurements even more sensitive. New filter systems that better separate the excitation light and the fluorescence light or enable improved simultaneous measurement of several fluorescence dyes are also needed. Much will happen in the area of imaging systems in the future. This includes the development of new fluorescence tomography systems that deliver 3D and quantitative data sets and are adjusted to the requirements for use in model systems and the needs of patients. These examples show that optical technologies still have enormous development potential for the future.



White light and fluorescence images of a mouse with a stroke in the left hemisphere after injection of a fluorescence marker for the specific visualization of stroke-induced inflammatory processes.

As can be seen using the high fluorescence intensity above the hemisphere affected by the stroke (see fluorescence image of the head of the mouse, lower left), the fluorescence marker can even be non-invasively detected with high sensitivity deep in the brain through the cranium. This image was recorded in only a few seconds.

After removal of tissue samples, the marker was successfully verified in the tissue affected by the stroke (see brain section; the color of the stroke tissue is clearly less intense than living tissue after staining). Furthermore, using a microscope, it was possible to identify cell types that bind the marker and thus verify the specificity of the marker at the cellular level for certain inflammatory cells after the preparation of thin tissue sections and specific cell staining.

The cell with a yellow border is an inflammatory cell that has bonded with the marker and belongs to the stained sub-type. The cell with a white border is also an inflammatory cell that belongs to another sub-type.

New projector systems in planetariums invite the audience to take part in virtual adventures in the dark depths of the cosmos.

Hurtling boulders of ice and stone compel the pilot of the spaceship to make evasive maneuvers, during which the passengers are jolted back and forth in their seats.

Riding the Comet

Deafening alarm sirens warn of impending collisions, and finally the nucleus of the comet fills the entire field of view of the panorama dome which arches over the viewers' heads. The engines roar for a last time, and billows of smoke blur visibility. This is followed by a truly icy silence. With 200 passengers on board, starship Walther Bauersfeld has landed on the icy nucleus of the Shoemaker Levy 9 comet.

Virtual Space Flights into the Depths of the Cos

During the next few minutes, the armchair space travelers will "age" by more than 50 years. In quick motion, they are propelled on the comet through the solar system until, when flying past the huge planet of Jupiter, they are catapulted onto a new orbit. After a few loops around Jupiter the flying iceberg is ultimately torn apart by the planet's tidal forces and, in the end, the debris plunges into the storm-lashed atmosphere of the huge celestial body. Literally in the last minute, the space travelers can save their skins and embark on a new space adventure ...

The future has already begun. With the exception of the billows of smoke and the jogging effects which can currently only be imitated by space simulators in leisure parks, such a show could already be presented in today's planetariums from Carl Zeiss. Originally, a planetarium was only intended as an instrument that could reproduce the celestial motions in the Earth's sky. At least this was what Oskar von Miller, the founder of the Deutsches Museum in Munich, "ordered" from Carl Zeiss. Professor Walther Bauersfeld, head engineer at Carl Zeiss at that time, surprised his client with the pioneering concept of a projection planetarium. With this ingenious idea, he banished earlier attempts to visualize the heavens and planetary motion into the museum for all time and simultaneously created a self-contained "star theater."

Since then, the opto-mechanical apparatus equipped with many lenses and gears has been enhanced into a complex, highly modern projection system that leaves (practically) nothing to be desired. This can be witnessed not only by visitors to the Olympics in Peking (where the new planetarium was opened on Xi Zhi Men Wai Street in 2004), but also by vacationers to the Austrian town of Judenburg. From 2008, the new technology from Carl Zeiss can also be experienced at various locations in the USA: Peoria in Illinois, Fort Worth in Texas and in Kingsport, Tennessee. In the Japanese city of Nagoya, the *UNIVERSARIUM* planetarium projector is being installed in the world's largest planetarium dome with a diameter of 35 meters as part of a new science center. The new building is due for completion in 2011.

Glass fiber stars – as radiant as the real sky. The glass fiber projection now used for all projector sizes guarantees a realistic star-lit sky, the like of which is difficult to find in today's light-polluted centers of civilization. Thanks to modern electronic control, the planet projectors are no longer brought into (approximately) the right position in a time-consuming procedure using slowly moving gear mechanisms, but are activated digi-

mos

Longing for a night sky: Planetariums are becoming increasingly popular.

tally by step motors. This allows any desired journeys through time and space within a single program – even a ride on the nucleus of a comet or a trip to one of the many moons in the solar system.

These new possibilities of sky and planet projection are supported either by the *powerdome®ADLIP HD* laser-supported, all-dome projection system (All Dome Laser Image Projection High Definition) or by the *powerdome®SPACEGATE* system also developed by Carl Zeiss. Their two or five digital projectors – needless to say, featuring high quality ZEISS *DIGIGON* lenses – illuminate the entire dome surface (360° x 180°) evenly and practically without any discernible transitions. Alternatively, two or four projectors containing SXRD technology (Silicon Xrystal Reflective Display) can be used. They combine SONY's wealth of experience in the field of digital movie projector technology with the ZEISS *DIGIGON* wide-angle lenses specially developed for dome projection.

Complex electronics allow simple operation. Powerful software is required for the precise simultaneous control of the planetarium projector and all-dome projection in pre-produced programs and for live shows in particular. Carl Zeiss offers the *powerdome®* system for this purpose. Behind this name is a comprehensive control platform that combines the opto-mechanical systems with the digital projectors and simultaneously manages all image and sound data. Powerdome® was developed in collaboration with the Fraunhof Institute for Computer Architecture and Software Technology in Berlin and permits intuitive operation, regardless of whether the traditional control panel or a keyboard and mouse are used. This allows practically limitless navigation in the universe, the seamless transition from a terrestrial view of the sky to virtual spaceflights into the depths of the cosmos.

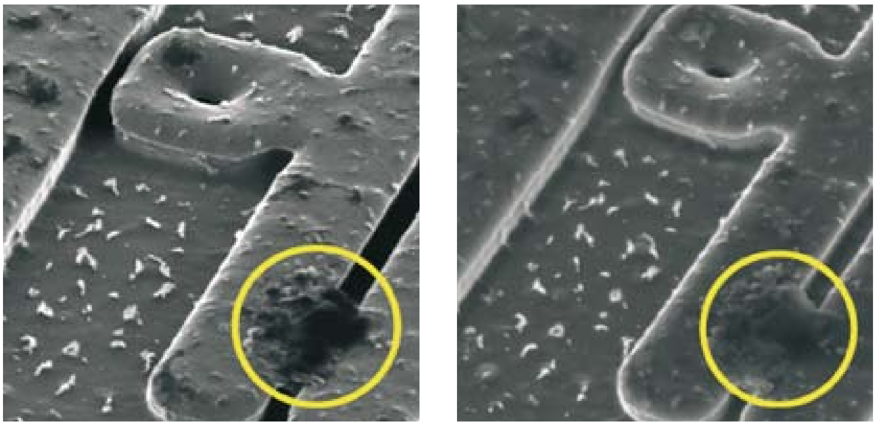
The development continues. The former planetarium originally developed for the newly founded Deutsches Museum in Munich has therefore become a "Universarium" in the true sense of the word. And Carl Zeiss is still constantly devising new ideas for improving and expanding its spectrum of applications. Wilfried Lang, Manager of the Planetariums business unit: "All-dome or full-dome projection is still in its infancy. Carl Zeiss concentrates on projection solutions which promise high image quality. The applications will continue to far exceed current planetarium presentations. These include, for example, possible uses in the entertainment and health fields."

Hermann-Michael Hahn

An Eagle Eye for the Nano World

The new helium-ion microscope generates particularly high-resolution images.

***ORION*™ had to pass its first test right when it was delivered. Because the doors in Building E at the Manfred von Ardenne Ring were not wide or high enough, it was forced to take the more tedious route through the window. Thanks to the active support of dedicated employees, a crane and many wooden pallets, it was possible to nonetheless complete this difficult procedure with the heavy instrument. This new type of microscope that goes by the brand name *ORION* has resided in its rightful place at the Carl Zeiss Innovation Center in Dresden since the end of October.**



Display of a defect on a semiconductor structure with helium-ion technology: the ORION™ helium-ion microscope (left) stands out, in particular, as a result of its brilliant contrast which scanning electron microscopes (right) cannot achieve with their very high resolution.

Behind the stellar name is a pioneering technology that generates helium-ion images from the nano world, in which the dimensions of a billionth of a meter are the measure of all things. The development of this new microscope can be traced to the patented work of ALIS in Peabody, Massachusetts, under the management of Bill Ward. This start-up company was acquired by Carl Zeiss SMT during the summer of 2006 and has now been fully integrated. “With *ORION*, we have launched a truly revolutionary product,” says proud inventor Ward, Chief Technologist of Carl Zeiss SMT in the USA that is now also headquartered in Peabody to the north of Boston. The helium-ion microscope at the Technopark Nord in Saxony’s capital is the only one of its kind in Europe. Together with a microscope based on cross beam technology (CrossBeam 1540 EsB) that uses electron and ion beams for imaging and material processing of the smallest particles and structures, it is the heart of the Innovation Center that will advance the development of future chip generations as part of the joint Nanoanalysis project. In addition to Carl Zeiss SMT, the project sponsored by the German Federal Ministry of Education and Research (BMBF) with a total of 12 million euros also includes semiconductor manufacturers AMD and Qimonda.

Increasingly complex structures in ever smaller dimensions. Imaging procedures have repeatedly provided the foundation for new insights into the natural sciences. Images, whose resolution and contrast set standards, can be generated with an intensive beam of single helium ions. The most important element for the microscope is a durable source for the helium ions in which a sharp tungsten needle is placed in a high vacuum at very low temperatures. The applied high voltage generates an extremely thick electrical field around the needle tip, whose strength is sufficient to ionize the helium atoms flying by. During this process, an electron is released via the tunnel effect on the tip so that positively charged helium ions are created which are accelerated away from the needle. The ion beam is then guided through a column with a series of focusing, adjusting and probing elements before it is bundled on an almost unimaginably small surface with a diameter of only 0.75 nanometers. Here, the beam scans the probe pixel by pixel, similar to a scanning electron microscope. "The gray scale value of each single image element is determined by the number of secondary electrons detected," explains Ward. The potential of the new method can be estimated based on the dispersion pattern created when the helium ions scatter while penetrating the specimen: its cross section is clearly smaller than with an electron beam and ensures the high resolution. In this regard, *ORION* is clearly superior to a scanning electron microscope.

"The size of the specimen is approximately one square centimeter where we can examine up to six of the objects at the same time. The largely automated change takes less than 10 minutes, the processes thus permits very good throughput," emphasizes Dr. Heiko Stegmann, head of the Carl Zeiss team at the Innovation Center in Dresden. Together with partners from the chip industry, the group of scientists is working on the 3D characterization of semiconductor structures and new materials for chip fabrication. "As a manufacturer of innovative microprocessors, we are faced with the challenge of producing increasingly more complex structures in ever smaller dimensions with maximum yield," says Dr. Udo Nothelfer, Vice President of AMD Fab 36, explaining the commitment of the three partners. "With the structural dimensions that we have now achieved, the current storage cells can only be seen under an electron microscope," confirms Frank Prein, President of Qimonda Dresden GmbH and Global Head of Technology at Qimonda AG.

Biological specimens and semiconductors. The new cutting-edge tool is not only available to the project partners but all interested companies and institutes in greater Dresden. All of the approximately 250 employees of the Silicon Saxony Network, which includes the technical university in Dresden and the Fraunhofer Center for Nanoelectronic Technologies (CNT), for example, can ask and receive answers to nanotechnology application questions. Furthermore, biological specimens from the natural science and medical institutes at the University of Tübingen (NMI) are currently being examined in Dresden.

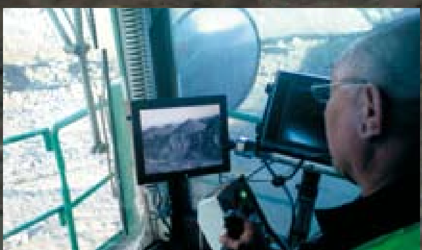
Strategic Alliances. The use of the new precision instrument from Carl Zeiss is not limited to leading micro-electronic companies in Europe. There is also enormous interest from across the Atlantic. Systems have already been installed at key customers such as the National Institute for Standards and Technology in Gaithersburg, Maryland. Harvard University in Cambridge, Massachusetts, also relies on technology from Carl Zeiss for its Center for Nanoscale Systems (CNS). Harvard has ordered eight electron and ion microscopes from Carl Zeiss SMT, including an *ORION*. "This order, which also means a long-term strategic partnership for our company, is a great honor and accolade," says Dirk Stenkamp, Member of the Board at Carl Zeiss SMT. Hopefully the "scientific heavyweights" will also fit through the doors at the CNS.

Extremely heavy, leading-edge instrument: the ORION™ helium-ion microscope

Klaus Jopp

See in the Dark

See what is hidden to the human eye: the UCM.



The monitor displays the surrounding area.

The new *UCM* thermal imager camera makes invisible infrared radiation visible

A gray-brown blanket seamlessly covers unending grooves and craters. Thick dust absorbs the sunlight. Oversized excavators with their heavy buckets rumble around the mining site like giant toys, scraping off the top layer of rock and freeing the layers of coal. The fossil fuel lies near the surface, making strip mining possible. The world's enormous hunger for coal forces the monster excavators and dump trucks to work non-stop, 24 hours a day, 365 days a year: South Africa is in a rush for resources. More than 28.2 million tons of coal reserves have been verified in the country, with estimates reaching up to 115 billion tons. South Africa is the world's sixth largest producer of coal and the fourth largest exporter. Mining conditions are favourable: strip mining and shallow depths make the local coal an internationally important export commodity – when the conditions are right. Darkness, dirt, dust and fog rob the sight of the drivers of the giant excavators and 200-ton dump trucks. This is not only dangerous but inefficient. The giant machines must be able to safely maneuver, and excavate and transport the coal. The uncooled *UCM* (uncooled module) thermal imager from Carl Zeiss has been recently integrated into the driver's compartments in a box no larger than a hand to make

visible what the human eye cannot see. The *UCM* detects minute temperature differences and displays them as a visible image. Uncooled in this sense means that the infrared detector in the *UCM* does not have to be cooled and is immediately ready for use.

The miniature camera features thermal resolution of 0.06° C and optionally displays the thermal images in black/white or false color in real time. The high sensitivity of the 200 g device enables it to generate informative images even when normal cameras are blind: at night or under poor lighting and weather conditions. Unlike x-rays that penetrate objects, the infrared radiation used by the *UCM* captures the spectral region between 7-14 micrometers and thus even the minutest, invisible thermal differences between every object. A meaningless raw image is transformed into a picture and displayed on the screen. The *UCM* uses so little energy that it can be powered by a battery.

More information at:
www.zeiss.com/innovation

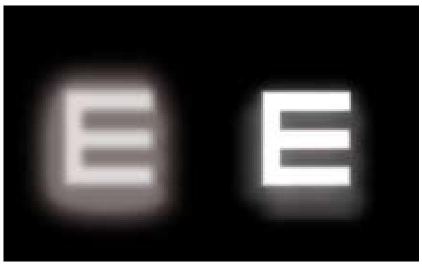
Discovering Complex Defects in Vision

View of a road without i.Scription® lens optimization.

With new measuring techniques and a totally new type of lens optimization for practically all ZEISS eyeglass lenses, it is now possible to reduce complex defects in vision.

Everything appears to be crystal-clear in daylight. However, when the light starts to fade, things begin to blur. This is something that quite a large number of eyeglass wearers experience, especially when driving. The reason: normal eyeglasses can correct only simple visual defects, and this is primarily due to the fact that only these can be detected by standard eye exams. A technique incorporating wavefront measurement and the *i.Scription®* lens optimization developed from it makes it possible to also detect complex visual defects, allowing eye care professionals to provide their patients with considerably better correction than in the past. From the scientist's viewpoint, the eye is a truly abysmal visual instrument. "If someone offered me an optical instrument with such errors, I would certainly turn it down," said Hermann von Helmholtz. In the 19th century the doctor and natural scientist invented the ophthalmoscope for examining the retina and the ophthalmometer for measuring the curvature of the cornea, and therefore knew exactly what he was talking about. Eyeglasses had already been invented a long time before in 1750. They were used to correct shortsightedness, farsightedness and astigmatism, an abnormal change in the corneal curvature. These are simple visual defects which can be effectively corrected with eyeglasses.

About half of humankind does not enjoy optimal vision. Most of these people are shortsighted or farsighted, but not every visual defect can be explained with excessively long or short eyeballs or a malformed cornea. More complex refractive errors, so-called higher order aberrations, exist in all optical systems. They also occur in the eye and are specific to each individual person. Traditional (subjective) refraction, the process used to determine what lens powers are required, reveals simple defects only. Here, the patient is required to



Vision is always multidimensional: a comparison with and without i.Scription.

The same road with i.Scription® – with considerably sharper definition.

identify increasingly smaller numerals and letters on a brightly lit chart which is responsible for making the pupils smaller. Therefore, only visual performance in optimal light conditions is taken into account. Higher order aberrations are of major importance when the pupil is fully open. This explains why eyeglass wearers may have no problems during the daytime, but see everything blurred or feel dazzled in poor light or at night when their pupils dilate.

In wavefront measurement, Carl Zeiss scientists found the key to a considerably more detailed method of determining visual performance. This paved the way to more precise eyeglass correction. With the *i.Profiler®* measuring system, eye care professionals can use wavefront measurement for lens optimization. The *i.Profiler* projects low intensity light rays onto the retina which scatters them back again. If the system identifies a deformed wavefront, this indicates aberrations in the eye. The *i.Profiler* determines the distribution of the aberrations across the entire aperture of the pupil. The visual defect, or ametropia, is measured to the nearest one hundredth of a diopter – 25 times more precise than in the past. These measured values also reveal what the conditions are like in poor light and darkness and what higher order aberrations the eye displays. The *i.Profiler* data and the values obtained in traditional refraction are used to calculate *i.Scription* lens optimization. Lens designers at Carl Zeiss have developed a special algorithm for this purpose: *i.Scription* provides eyeglass wearers with a considerably enhanced visual experience in many cases. For example, the happy owner of a pair of glasses featuring *i.Scription* optimization expresses her satisfaction in the "Besser sehen" blog as follows: "Especially now when it's starting to get dark earlier, I can see with astounding clarity. I would recommend it to anyone: it was well worth it." Looking back at his three months of using the new technology, her eye care professional Niels Rebin, who operates a Relaxed Vision Center in Liechtenstein – *i.Scription* is only available in these centers – writes the following: "I must say I'm really impressed." Impressed, as he then adds, at how impressed his patients are.

You can find eye care professionals who offer *i.Scription* at: www.zeiss.de/i.scription

Ursula Walther

All with the Light of a Matchstick

Images from Mongolia – photographed with the Zeiss Ikon

Four times larger than Germany and only 2.5 million inhabitants, one third of whom live in the capital Ulan-Bator – that is Mongolia, the steppe landscape between Russia in the north and China in the south. Breathtaking landscapes stretch from the foot of the four thousand meter high Altai mountain in the northwest to the Gobi desert in the southeast.

Photos from Sven Zellner

Mountain forests, grasslands and semi-deserts. Half of the country is covered by it. Since 1990, 5.3 million hectares have formed one of the earth's largest biosphere reservations. The region is shared by snow leopards, Gobi bears, Bactrian camels, saiga antelopes and 400 people living in a handful of settlements. These settlements generally consist of a few "ger," as the yurts are known in the Mongolian language. They are barely discernible in the endlessness of this vast landscape. They seem to cower away from the flickering haze of the 40 degree midday heat under the huge expanse of the sheltering sky, away from the yellow-gray clouds which herald the advent of the fine, all-pervading dust of the next sandstorm.

Understanding the Language and Way of Life

A return to its cultural roots. In 1990 Mongolia was the first state in Asia to abandon communism and 70 years of a centrally planned economy. Under a democratic constitution, the population re-embraced its old culture and tradition. Some of the inhabitants resumed their traditional form of existence and occupation as livestock raising nomads. Perfectly adapted to the barren landscape and extreme climatic conditions, they had lived and survived freely and without ties before being collectivized and compelled to lead a sedentary life.

Sven Zellner was attracted by this special breed of human being – self-confident, open and hospitable. Here, the German photographer found new friends. He returns to visit them time and time again. He has come to understand how they live and their language. This makes it easier for him to embark on his many excursions and explorations, far away from the beaten track. Sometimes he uses the mail bus, sometimes he travels in one of the heavily loaded trucks that link places and towns over long distances. Occasionally, when his friends make it possible, he takes a cross-country approach with their expert guidance.

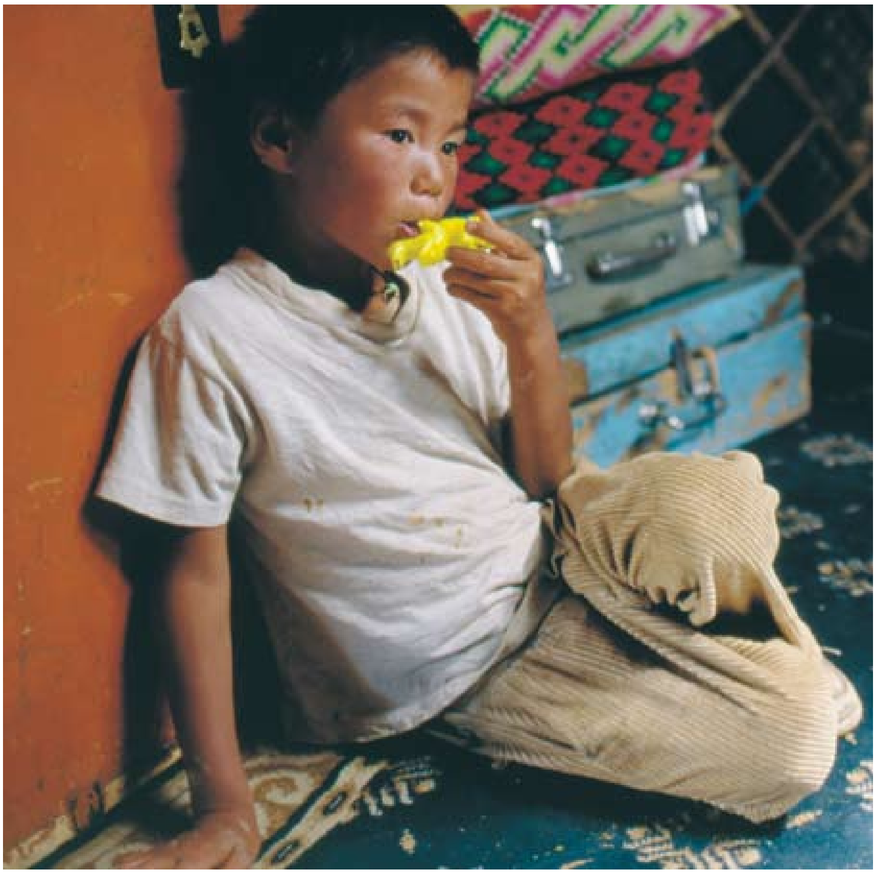
Having a break in the dangerous quest for gold. The gold-diggers force tunnels and shafts into the rocky ground of the Gobi.

After the wrestler has won in the Naadam, a Mongolian festival, he presents himself to the public.

Note in his diary : "No roads, no signposts, not even dirt tracks! Nevertheless, my companions find their way with admirable certainty. We reach a maximum of 30 kilometers an hour and are constantly shaken around in our jeep. Water bottles and apples, our provisions for the journey, are stacked in heaps on the floor. Now and again, nomads pass by, with their entire possessions on the backs of their camels. Sometimes we can also see a herd of animals on the horizon. As dusk draws in, we head in that direction, reach the yurts of their owners and are greeted with great warmth and hospitality. The simple dinner consists of boiled mutton, accompanied by a type of yogurt and cheese from the milk of their sheep, goats, camels and horses. During the night, the animals are kept close to the "ger", away from the howling wolves in the background. We eat and sleep on the floor of the ger which has only one large room. In its center a fire blazes in a simple tin container. The dried dung of the animals is used as fuel. There is practically no firewood available in the steppe. Water is obtained from deep wells. The sparing use of resources is an absolute must. This is why our usual morning hygiene rituals are slightly shorter than usual. We then proceed into the first rays of the morning sunlight ..."

In the late summer of 2007 Sven Zellner visited the "Ninjas", the gold-diggers of Mongolia. The name is an allusion to the "Ninja Turtles" because the men are reminiscent of these comic figures when carrying their large metal gold panning dishes on their backs. But maybe the term means even more! Hidden to everyone and usually illegally, the gold-diggers fight what they consider to be a battle for a just cause. Sven Zellner photographed them with his *Zeiss Ikon* during their work, or during a cigarette break, seven meters under the earth. The light of a matchstick had to suffice as a light source.

Future problems: "Ninjas" reveal a problem that endangers the nature of the steppe landscape and the culture of the Mongolian nomads: when one of the Earth's largest gold deposits was discovered in the Gobi region, but the state did not have the means and technology for the mining process, the mining rights were sold to foreign companies. This foreign exploitation triggered outrage in yurts right across the company. An unwritten law of the steppe says that everything that is offered by the barren earth belongs to those who live on and from it. It should be shared fairly. This sharing process is the ancient principle of survival and hence an important value in how the inhabitants see themselves and their existence. The nomads demand their share of the natural resources. Some are starting to dig for gold on their own initiative and are forcing unsafe shafts and tunnels into the earth. The number of accidents is increasing.

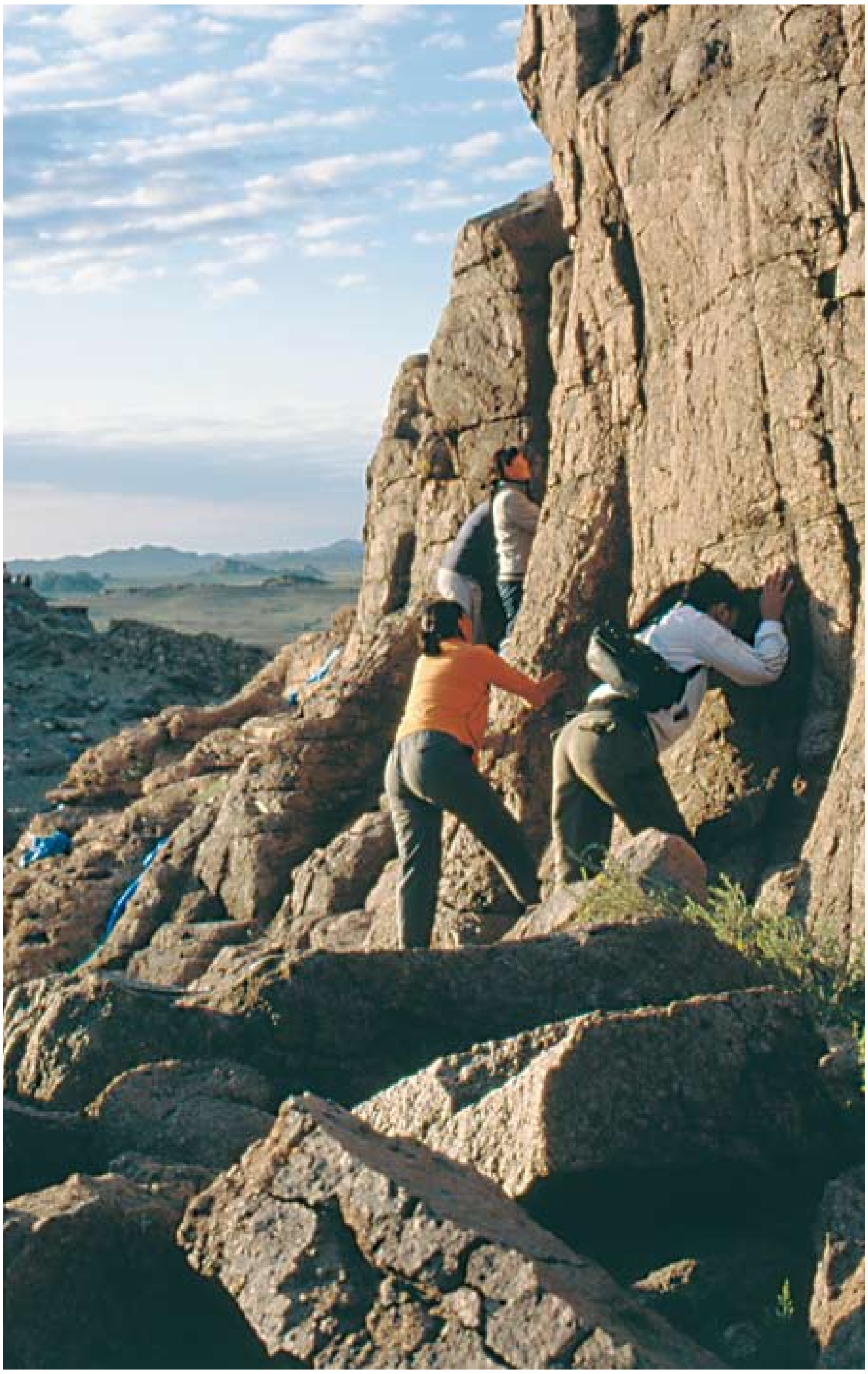


Tired and exhausted: a nomad child after finishing its work in the yurt.

A further source of concern is also the high water consumption and the use of poisonous chemicals involved in both industrial and manual gold mining. The consequences are already evident. There is a shortage of drinking water, and the unique flora and fauna are suffering.

The photos taken by Sven Zellner in Mongolia were created with a *Zeiss Ikon* and the *Biogon 2.0/35 mm* and *Sonnar C 1.5/50 mm* lenses. Sven Zellner swears by the robust quality and good handling properties of the camera, which has never let him down – even after adventurous journeys through sandstorms or heavy downpours. He uses it primarily for spontaneous documentation. His images reflect not only impressive landscapes, but also – and with the same sensitivity – the reality concealed behind the more beautiful side of this attractive country.

Manfred Schindler



A bright location: the rocks on the Kahn Bogt Mountain.

The person

Sven Zellner

Discovering countries and cultures and capturing their uniqueness for longer than a fleeting moment is the goal of photographer Sven Zellner, 30.

His travels have led him to almost all corners of the earth: Mongolia, Armenia, Israel, Latvia, Poland, Brazil, Tasmania. Australia, USA and Canada.

The former student of the University of Television and Film in Munich has received second place in the renowned BBC Wildlife Photographer of the Year Award on two occasions (1995 and 2000). Zellner has published his photographs in numerous books and magazines. He also works as a documentary and movie cameraman.

Current projects of Sven Zellner include a new collection of photos on the subject of Mongolia, photographic work for a music video and a movie project as a cameraman in the USA.

The Right to Sight

Carl Zeiss is supporting a center for ophthalmology in India.

Poverty leads to blindness, and anyone who is blind stays poor. This is the vicious circle that the inhabitants of developing countries can only escape through external aid. Many people could retain their sight if preventive action were taken in good time beforehand. This costs money and demands commitment. The good message is: the commitment is there, and the money too.

Every day more than 600 patients are treated in the institute.

Both come from the World Health Organization (WHO), the International Association for the Prevention of Blindness (IABP) and from companies like Carl Zeiss. Their vision for the next twelve years: preventable blindness is to be overcome by the year 2020, as everyone has a right to sight. One adult goes blind every five seconds, and one child every minute, according to the Christoffel Mission for the Blind in Germany. 80 percent of these people could be spared this fate through prevention and early surgery. The WHO and IABP therefore created the "Vision 2020 – The Right to Sight" campaign in 1999. The goal: In 2020 no one should go blind for reasons that can be eliminated or prevented. Making sure the vision does not remain a utopia.

Vitamin A deficiency. Half of all blind people suffer from cataract and could be cured by surgery. In industrialized countries this procedure has been routine for several years now. In developing countries it only costs about 30 euros, but it is nevertheless unaffordable for many people. Children often lose their sight through infectious diseases such as river blindness or conjunctivitis. They also suffer from cataract, and premature babies frequently display retinal damage similar to that caused by diabetes. The most common cause of blindness in children is a vitamin A deficiency usually attributable to a lack of money, and often also to insufficient knowledge. Children need clean water, better sanitary conditions, a basic supply of medication and vitamin supplements, and health education. In the developing countries there is not only a shortage of doctors, nurses and eye care professionals, but also inadequate technical and logistic conditions for proper eye care. In Germany, there is one ophthalmologist to every 13,000 people, in Africa one to every million. Therefore, the training of experts is just as important as the setup and expansion of infrastructure.

The dream of treatment for everyone. India is one of the countries most afflicted by blindness. As far back as 1987, Gullapalii N. Rao founded the L V Prasad Eye Institute in Hyderabad, today a center for ophthalmology and medical training. The founder had experienced eye clinics in the USA and was impressed. "It was my dream to offer all Indians this type of treatment right on their doorstep, regardless of their social or economic status." He won the support of movie maker L V Prasad for his idea. Prasad provided premises in Hyderabad and financed the setup of the facility which now bears his name.

Study and scholarships. Today, the L V Prasad Eye Institute is one of the most important Vision 2020 institutions. The hospital treats more than 600 patients – also free of charge if they cannot pay – and performs 70 operations every day. The children's ward is the first of its kind in a developing country. At the same time, the institute is a national center for clinical research and is currently working on the world's largest patient study on corneal transplantation. The affiliated L V Prasad ZEISS International Academy for Advanced Ophthalmic Education offers very practical training and a Carl Zeiss scholarship for

Definitely worth seeing in Hyberbad: the Charminar in the Old Town.

the best students. The donation made by the Carl Zeiss Foundation to the institute in 2004 reflects the significance of the work against blindness. The money is being used to train eye surgeons in India.

Ursula Walther

The details

Vision 2020
In Anglo-Saxon countries normal visual performance is called 20/20 vision. This means: if you can see the same letters and numerals as most test persons at a distance of 20 feet from the test chart, you are said to have normal vision. The 20/20 in the name of the campaign therefore has two meanings. By the year 2020, all people should have normal vision if this can be achieved with medical and social measures.

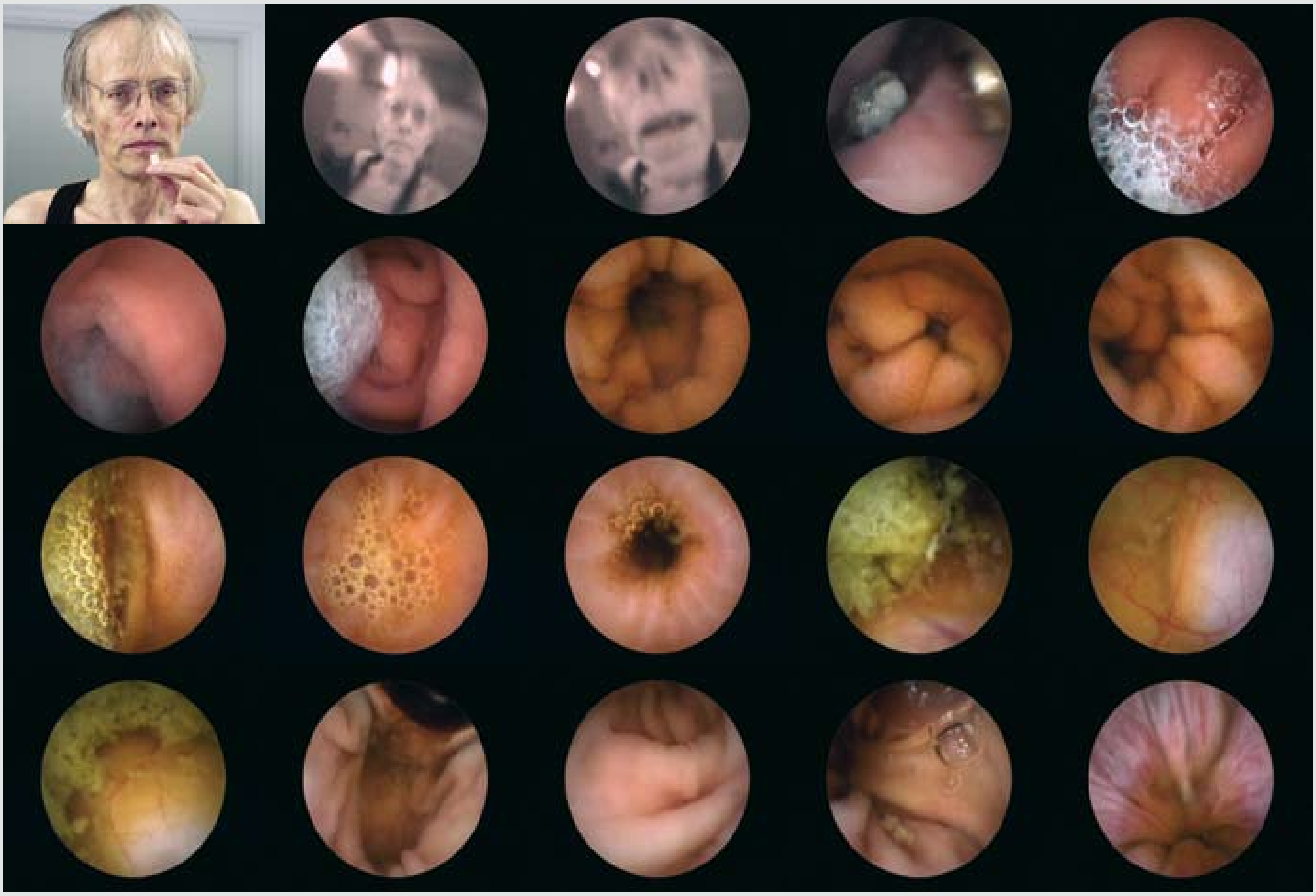
WHO and IABP
The World Health Organization is a United Nations organization. Since its foundation in 1948, it has been committed to healthy living conditions in all countries of the earth. It has a membership of 193 states. Since 1975, the International Agency for the Prevention of Blindness has bundled a wide variety of official and unofficial institutions and groups which are dedicated to the fight against blindness.

Information at:
www.iapb.org

Essay

A Journey Inside

A look at the body's interior in post 1960 art



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Timm Ulrichs,
An Endoscopic Journey
Color video, silent, 86 minutes 42 seconds
Idea: 1971; Realization: 2004

Timm Ulrichs: "I swallow a tiny camera that documents its journey through my digestive tract. Swallowing and excreting the recording device marks the beginning and end of the introspective-autobiographical movie."

Actual recording time: 9 hours.

Gurgling, smacking noises emanate from the video booth separated from the exhibition room by a black curtain. Out of curiosity, a couple of visitors stick their heads in before bravely disappearing into the darkness. The reproduction of this intimate situation is intentional. Behind the curtain is a projection of a journey into the body's interior made by artist Timm Ulrichs (*1940). Those daring to venture inside are met with the circular projection of a forwards movement in a dark abyss that is both mysterious and threatening. To realize this introspective-biographical work, Ulrichs swallowed an endoscopic camera enclosed in a capsule which documented the trip through his digestive tract. Ulrichs first thought of this 86 minute color movie back in 1971. However, the technology required did not exist at the time. The capsule endoscopic procedure that is used for medical diagnostics has only been around for a few years.

> *"Images were unearthed that no travel guide has been able to offer, no Baedecker can explain."*
>
> *Timm Ulrichs*

Medical imaging procedures have made it possible to fulfill mankind's desire of looking into the body. Until the discovery of invisible electromagnetic radiation (x-rays) by Wilhelm Konrad Röntgen, the body was a type of black box. If you wanted to learn more than just the exterior image of a person, you had to dismember the body. However, until the time of the Renaissance, looking into the human body entailed considerable risks. If artists wanted to study the anatomy of people, they were forced to sneak into execution sites in the middle of the night and abscond with the remains of the hangman's work. Even Leonardo da Vinci (1452 – 1519) is rumored to have participated in such illegal autopsies. Art historians have come across an entry in his diaries that confirms these suspicions: "And if you are interested in such things, maybe you are restrained by nausea. And if this doesn't stop you, maybe you are inhibited by the fear of being with the oppressed, dissected and horribly mutilated dead…".

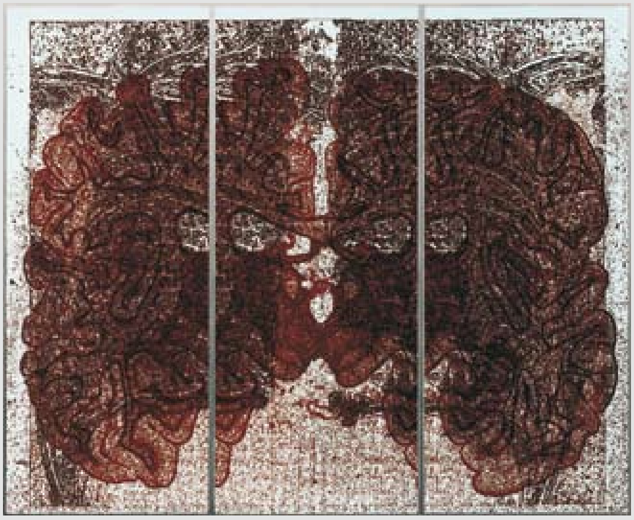
Even later, after autopsies became an accepted part of research, it was primarily the corpses of those sentenced to die that made it to the operating tables of doctors.

The discovery of imaging procedures in medicine also had a profound effect on art. There has be a great deal of interest in natural science methods since the late 1960s as the body moved to the center of artistic activities following socio-political developments. With new art forms such as body art, happening and performances, artists strived to eliminate obsolete moral ideas. Used as artistic material, the naked body became a political tool to make public what was once private. In the beginning, the performances and actions dealt with being satisfied with your body and your sexuality. This changed in the 1980s when the interests of artists began focusing on the dangers to the body caused by diseases.

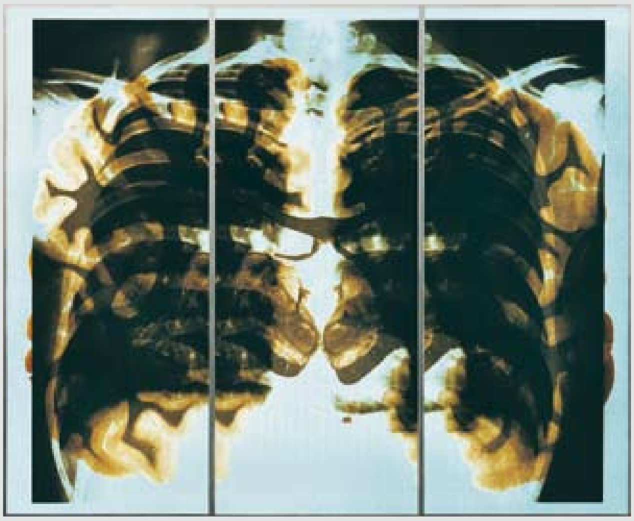
Timm Ulrichs, who gives us an intimate look at his insides in his work "Looking through me – an endoscopic journey" (2004), has been working on bodily related actions since the late 1960s. In "Checked Baggage" (1975-1987), he was x-rayed like a piece of luggage on a conveyor belt at an airport. He later exhibited the photographic findings.

Many artists use x-rays as a metaphor to question the credibility of images. In her work "Global Lines II" (1997), photographer Katharina Sieverding (*1944) shows an x-ray of her lungs onto which she projects a section of her brain. This work initially irritates the observer as it is not possible to clearly distinguish the images. As the daughter of a radiologist, she knows how problematic it is to interpret x-rays. With her work, she not only challenges the visual habits of the observer but also criticizes the truth of medical imaging procedures. Felix Droese (*1950) stated his criticism somewhat more radically when he used thick brushstrokes to write "Everything's a lie"(1990) on two x-rays.

Like an animal, an endoscopic camera attacked the body of Lebanese artist Mona Hatoum (*1952). She arranged the images of a gastroscopy and colonoscopy



Katharina Sieverding,
WELTLINIE I, 1997, A/D/A Process,
Acrylic, steel 300 x 375 cm.



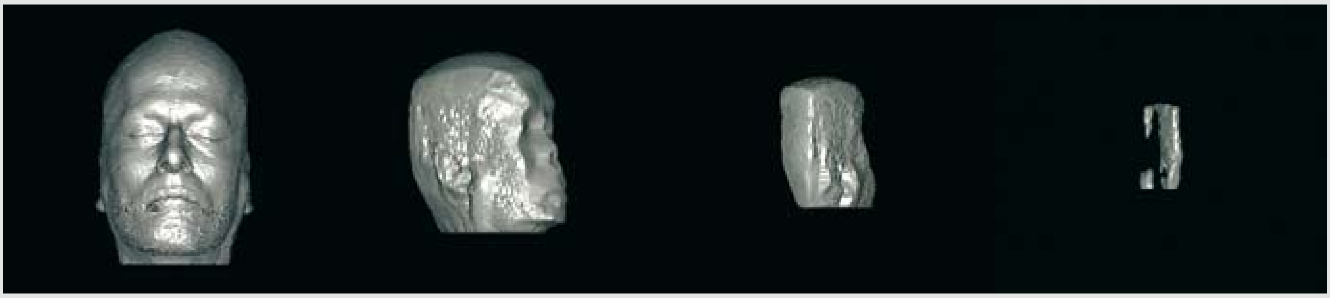
Katharina Sieverding,
WELTLINIE II, 1997, A/D/A Process
Acrylic, steel 300 x 375 cm.

to create an impressive film, "Corps étranger" (1994). The camera initially probed her naked body until it entered an opening and continued its journey inside. In the beginning, the film shows close-ups of her sensory and sex organs which are later replaced with images of the organ walls and mucuous membranes. "I wanted," explained Mona Hatoum, "my work to show how the body is examined, attacked, injured and deconstructed by scientific eyes."

Artists who show their insides in exhibitions always launch a debate, of course, about what is public and what should remain private. Australian performance artist Stelarc (*1946) has probably been the most radical in his work. He declared his stomach an exhibition room for his work "Stomach Sculpture" (1993). He swallowed a 50 x 14 mm capsule combined with a control unit. Inside his stomach, the capsule unfolded to reveal an 80 x 55 mm sculpture that buzzed, peeped and emitted light signals. Everything was recorded using an endoscopic camera.

Images from medicine have always had a particularly fascinating effect on artists. Jean-Michel Basquiat's (1960-1988) drawings were influenced by Gray's Anatomy Textbook. His mother gave him a copy of this American benchmark of medicine in 1968 while he was laid up in a hospital following a traffic accident. Recently, new imaging procedures in medicine have become increasingly important in addition to the pictures in books. In particular, magnetic resonance images (MRI), in which the body is examined and recorded slice by slice, fascinate many artists. This technique inspired Timm Ulrichs to create his film "Journey to the Center of Me" (1987) which is based on the reconstruction of an MRI of his skull.

Marilène Oliver (*1977) used an MRI to measure her entire family. Her 192 x 50 x 70 cm portraits from her "Family portrait" series (2001) comprise 92 equally spaced Plexiglas plates stacked on top of each other. Each of them contains a medical image transferred using the screen printing technique. Although this technique enables you to look at the core of a person,



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Timm Ulrichs,
Journey to the Center of Me; 1995/97; black and white movie, silent, 7 minutes 53 seconds
3D digital visualization of the lowest point of the head of the artist using automatic segmenting and volume rendering (ray casting) based on a magnetic resonance image and fixation of the calculated markers on the scalp using tattoos.

the pure addition of the images cannot reproduce the wholeness. The human body appears in her sculpture only as a dim gray silhouette.

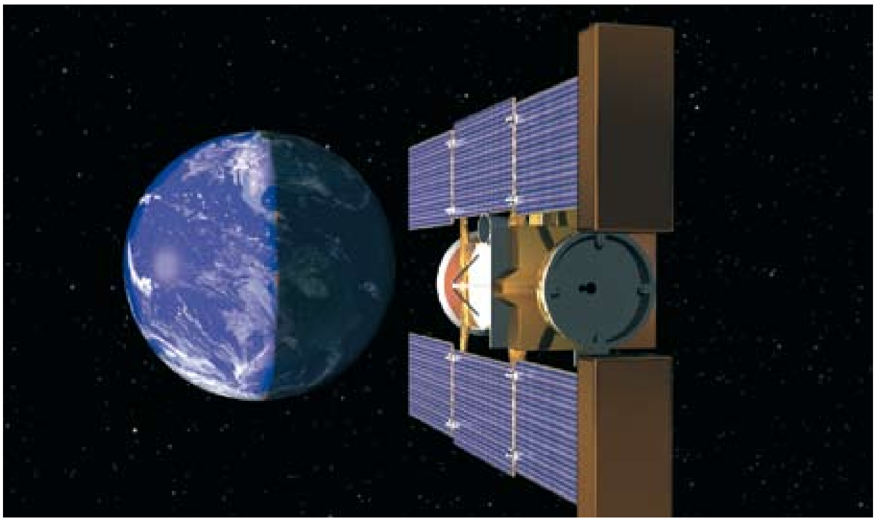
Medical images are produced to convey knowledge about people. However, with the development of new techniques, specialists and amateurs alike are fascinated by the brilliance and beauty of the images of the mysterious inner world. As an "artist in residence," British artist Heather Barnett visited many hospitals and medical facilities to explore the duality of scientific knowledge and the beauty of medical images. She used microscopic images of her own cell structure as a template for her "Cellular Wallpaper" series (2000) to develop wallpaper patterns. The most intimate secretions of her body such as a cervical smear, blood and sweat are examined microscopically and enlarged for decoration. Heather Barnett thus presents existential questions about the origin and meaning of human life that, in the end, cannot be answered through medical images but only philosophically.
Timm Ulrichs, who has dealt with the exploration of people in his artwork his entire life came to the following conclusion:

> *"The deeper we look into ourselves, the more we sink in our physique and psyche, the more mysteriously, abysmally, eerily and strangely we appear to ourselves and we realize what we are: a foreign body."*
>
> *Timm Ulrichs*

Dr. Cornelia Gockel

Born in Düsseldorf in 1963, she is an art critic and lecturer of art history. As a scientific assitant, she teaches at the Academy of Fine Arts in Munich and as a guest lecturer at the University of Newcastle (UK).

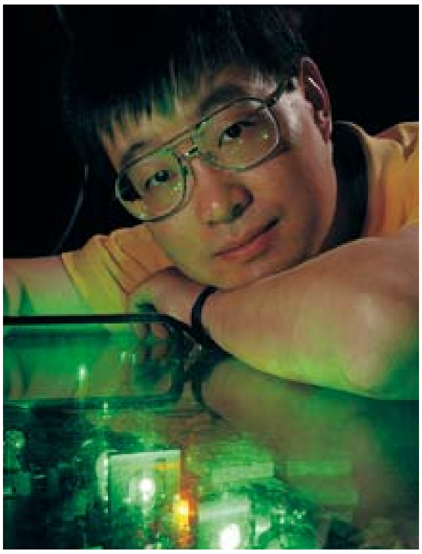
Preview of Innovation 20



http://stardust.jpl.nasa.gov/photo/artist.html

Interview: NASA's Stardust project went on a research expedition to the origins of the solar system 4.5 billion years in the past. One of the "travelers" was Prof. Dr. Falko Langenhorst from the University of Jena and the 2007 Leibniz Award winner who reports on the results in an interview.

Reader survey: Issue 18 marked the relaunch of Innovation. Is it to your liking? A reader survey gives you the opportunity to let us know what you think.



Look at Laureates: Ahmed Zewail and Eric A. Cornell have made it to the top – they received the Nobel Prize. But other winners of the Carl Zeiss Research Award have also been busy – we will report on them regularly in the "Look at Laureates" category beginning with issue 20.

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