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1/2004 ▶ On Minnesang in the Database ▶ Getting a Grip on the Computer World ▶ A Hand Full of Technology with Fingertip Control ▶ When Small Organisms Have a Big Effect ▶ An Insect's Life in a Scented World

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In this issue

Compressed Air for a Robotic Hand

Artificial hands are needed for a wide variety of applications. The important thing is, to simulate the human hand's great mobility and dexterity. The hand developed by engineers from Aachen is distinguished by its specialised grasping and holding abilities. It is also the first hand that is not powered by an electric motor, but instead operates using compressed air. **Page 9**

Insights into an Ecosystem

Living soil crusts extend from the deserts to the tropics and from the Arctic to the Antarctic. Not only do they form remarkably diverse and resilient communities, but they also provide the soil with effective protection against erosion by wind and water. The preservation and regeneration of these crusts thus plays an important role in the conservation of the global landscape for the future. Basic research in biology can make a contribution to this. **Page 16**

The Effect Scents Have

Insects have a highly developed sense of smell. This gives them their sense of direction when hunting for food or searching for a mate. A detailed study of the olfactory system in honey bees and soldier ants has been conducted to discover how scents are processed in the brain. The results obtained from this study can also be partially applied to the human olfactory system. **Page 21**

Invitation to the Middle Ages

Manuscripts are cultural and historical records of great significance. This includes the "Renner" manuscript, which was completed around 1430 in Nuremberg (Page 12).
Cover photo: Universitätsbibliothek Heidelberg

Impressum

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Clinical research in Germany is in need of stimulating impetus. This is why the Deutsche Forschungsgemeinschaft in cooperation with the Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung, BMBF) has introduced the new "Clinical Studies" programme. Its purpose is to promote clinical researchers in a concerted effort and to facilitate networking. This is all done for a good reason! The importance of clinical research is obvious: People everywhere follow health care research with great interest, and even with specific expectations, because they have high hopes concerning the results of such research for the prevention, diagnosis and treatment of disease. At the same time, it has been known for many years that while the state of clinical research in Germany is first-rate in some areas, it is less than satisfactory in others, especially in patient-oriented research. This is particularly noticeable from a structural perspective and in terms of the international competitiveness of the research undertaken. These deficiencies become apparent in a study by the Boston Consulting Group which indicates that Germany takes one of the last places, behind Denmark, Great Britain and the Netherlands, in a ranking of countries by the number of publications (relative to population) reporting on clinical studies. This is so despite the fact that Germany, with a great number of specialists and top-notch medical facilities, in principle has all the proper conditions for conducting patient-oriented research. In 1999 the DFG already unambiguously stated this fact in its white paper on "Clinical Research" which provided an overview of the state of German clinical research, analysed its deficiencies and suggested improvements. In the meantime the recommendations made by this white paper have now begun to be implemented. Tangible and creative momentum has resulted from the associated analysis. One example is our "Clinical Studies" programme.

What does the term – "clinical studies" – actually mean? Clinical studies are systematic research projects that, after first having obtained the informed consent of the participants, are undertaken in accordance with a clearly defined study protocol at various locations, sometimes on a worldwide basis, and correspondingly require a large number of patients.

However, the objective of the new "Clinical Studies" funding programme is to support not only studies with large patient pools, but also those focusing on smaller groups of patients. The pharmaceutical industry has no direct economic interest in these latter research projects. One such example is the treatment of malignant brain tumours of which only about 3,600 occur each year. In other words, the funding programme is aimed exclusively at science-driven clinical studies. These differ significantly from drug approval studies in that they focus on a clinically important scientific question and are conceived and published by independent experts in the clinical sciences. Experience has shown that many questions can only be successfully explored independently of the pharmaceutical industry and with the financial resources provided by public research funding institutions.

The proper implementation of clinical studies requires a high degree of professionalism; this is currently the exception rather than the rule at the participating clinical institutions. With this in mind, the funding programme aims to significantly improve the existing research culture and to provide the know-how to participating university hospitals for organizing and executing international clinical studies that are as excellent as they are innovative. The observance and implementation of internationally recognized research standards (e.g., the "Good Clinical Practice" Guidelines of the International Confer-

ence on Harmonization) is a decisive factor and an important benchmark. Within the framework of this programme, the DFG will fund clinical studies of non-pharmacological therapies as well as studies focusing on clinical diagnosis and prognosis. In a complementary effort, the BMBF has undertaken the task of supporting projects evaluating pharmacological treatment methods and meta-analyses involving the systematic examination of clinical studies.

The DFG and the BMBF expect their coordinated and harmonised approach in this area of research to achieve particularly long-lasting and effective results. Proposal submission is a two-stage procedure for quality assurance reasons. In the first stage, applicants submit draft proposals, which are evaluated by an international and independent group of reviewers. If approval is granted by the reviewers in the first stage, the complete and detailed funding proposals can then be submitted in the second stage where they will again be discussed by a group of reviewers.

The programme is intended not only to support research excellence, but also to make medical research more well-known to the world at large than has previously been the case. The recently launched reform process in medical research requires more than just new programmes and initiatives. It demands nothing less than a complete change in the mindset of those responsible for its implementation at university hospitals. In this context the new funding programme will also increase the prestige of clinical studies conducted at these locations. The opportunities for up-and-coming researchers in the clinical sciences still need to be significantly improved! Structural hurdles still impede the proper development and the career paths of those with scientific talent: the absence of time for science with an overload of clinical care tasks, the absence of structured training in the sciences and unsatisfactory career prospects for clinical researchers when compared with the possibility of serving as a department head. Another important factor is the chronically inadequate funding that is available for clinical research.

As described and recommended in the white paper, the most important and momentous political reform measure remains the separation of hospital care on the one hand from teaching and research on the other. Ultimately, this would mean a division of medicine into two different academic careers. However, this would require a less hierarchically structured division of labour for clinical researchers with significantly smaller associated areas of responsibility. Furthermore, there are two more basic conditions that are absolutely essential for achieving internationally competitive performance in German clinical research: namely, the recognition of specialisation and an understanding of the long-term nature of this type of clinical research. The "Clinical Studies" programme now being launched as a joint initiative of the BMBF and the DFG will try to meet these demands. And in doing so, it will consider the special requirements of this type of research in Germany.

Prof. Dr.
Johannes Dichgans

Stimulation for Clinical Research

New funding to correct deficiencies in medical research: The DFG and the BMBF launch "Clinical Studies"

Prof. Dr. Johannes Dichgans
Vice President of the
Deutsche Forschungsgemeinschaft

Johannes Dichgans, Department of Neurology, University of Tübingen, is one of the Vice Presidents of the Deutsche Forschungsgemeinschaft. The membership of the Executive Committee of the DFG consists of one President and eight Vice Presidents, as well as the Chairman of the Donors' Association for the Promotion of Sciences and Humanities in Germany (Stifterverband für die Deutsche Wissenschaft).

Another Kind of Heart Murmur

New possibilities options in medical diagnostics: the magnetic signals of the human heart are recorded to assess its state of health

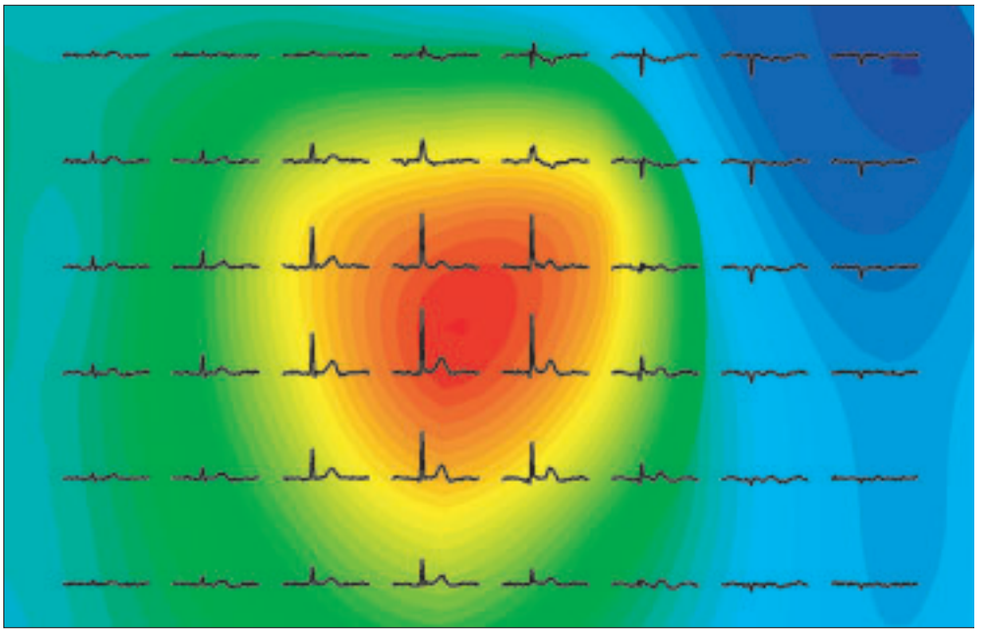
Heart diseases are a significant problem in industrial countries and increasingly also in developing countries, with a large percentage of deaths being attributable to them. A number of procedures are available for diagnosing heart disease, the most familiar of which are listening to heart sounds and recording electrocardiograms (ECG). In recent years a promising new method of heart diagnostics has increasingly become a subject of research: magnetocardiography (MCG). Rather than recording electrical heart signals like the ECG, MCG records the associated magnetic signals. This harmless and contact-free method yields information comparable or even superior to the ECG. Currently, magnetocardiography is not yet commonly used because it relies on magnetic field detectors that require cooling close to absolute zero – an expensive and cumbersome procedure. Last year, our research team at the University of Fribourg in Switzerland developed a new technique that works at room temperature, making MCG use possible outside of special high-tech medical centres.

From a physicist's point of view, the physiological processes in the heart can be modelled in a very simple way. The heart is visualised as a blood-filled muscle in the shape of a hollow cylinder, with the top and bottom being closed by the heart valves. The muscle cells are surrounded by a saline solution, which is slightly charged relative to the cell interior. A nerve node is located at one cylinder end and produces an electrical pulse about once per second. It inverts the voltage between the cell interior and exterior locally, causing the muscle cell to contract. During this discharge a small part of the electric current reaches neighbouring cells that also discharge and contract as a result. This causes the hollow cylinder to contract and push the blood into the circulatory system while creating a weak ion flow called a primary current. The electrical circuit is closed by a distributed return current through the surrounding medium. Typical currents are only about one to ten microamperes.

A physical law states that the primary current is surrounded by a magnetic field with field lines that concentrically surround the current's path. The return current's field is negligible by contrast. During the heart's contraction, a pattern of approximately circular field lines is found outside the chest exiting from one side and re-entering the chest a short distance away.

However, this physicist's model is oversimplified: in reality the heart consists of four chambers, none of which is cylindrical. There are two separate circulatory systems – one for the lung and another for the heart and the rest of the body. Also, the mechanism of pulse generation is significantly more complex. As a result, a complex, but characteristic interdependence on time and location is found in the magnetic field of a healthy heart.

The magnetic field of the human heart is very weak: directly outside the chest the strongest signal peaks barely reach a millionth of the strength of the Earth's magnetic field. Consequently, magnetocardiography requires highly sensitive magnetic field detectors. Since the 1970s superconducting quantum interference devices (SQUIDs) have normally been used for biomagnetic measurements. However, these suffer from the significant disadvantage that depending on construction type they must be cooled to -196 degrees Celsius or even -269 degrees Celsius. This leads to comparatively large expenditures for energy and



Magnetocardiography records the heart's magnetic signals without touching the patient. The curves show the spatial and temporal distribution of magnetic field strength.

logistics, because expensive liquefied gases must be used as coolants.

A simple magnetocardiogram can be recorded by holding the sensor directly in front of the chest and registering the magnetic field's change with time. At first sight these curves look similar to those of an ECG. An image of the spatial distribution of magnetic field strength, obtained for example by sequential measurements at several points in front of the chest, or by using a grid of several simultaneously measuring sensors next to each other, contains more information. The way in which the field distribution changes during a heartbeat is an important diagnostic aid. Compared to the heart's field, typical interfering magnetic fields of elevators and other iron-containing or electrically operated devices as well as the rapid fluctuations of the earth's magnetic field can be a thousand times stronger. It is therefore essential to suppress the effect of interfering fields. Normally, this is achieved by performing the measurement in a magnetically shielded room. Gradiometers – several sensors placed one behind another – provide an alternative to expensive shielding chambers. In the simplest case, one sensor is located immediately outside the chest and a second one a few centimetres away. The heart's magnetic field decreases rapidly with distance from the chest, so the second sensor basically only records the interferences. Since these are about equal on both sensors, in the difference signal only the heart's signal remains.

A competitive magnetocardiograph must offer a magnetic field sensitivity of one picotesla with a time resolution of milliseconds and a spatial resolution of one to two centimetres. For this purpose, a recently developed variant of the optically pumped magnetometer was chosen. The measuring principle makes use of the fact that every atom in a caesium vapour at room temperature acts like a small magnet. By shining a laser beam through the vapour, all of the magnets in it are aligned. Assisted by a rotating radio frequency field they then rotate about the local magnetic field. The atoms modulate the intensity of the laser beam crossing the vapour in the same rhythm. This rotational frequency is proportional to the magnetic field strength and can be measured by observing the intensity modulation of the laser beam behind the vapour cell. An experimental difficulty is to achieve the required precision at a temporal resolution of only a few milliseconds. To measure the heart's magnetic field, a change in the rotational frequency of only a few hundred-thousandths of one percent must be detected.

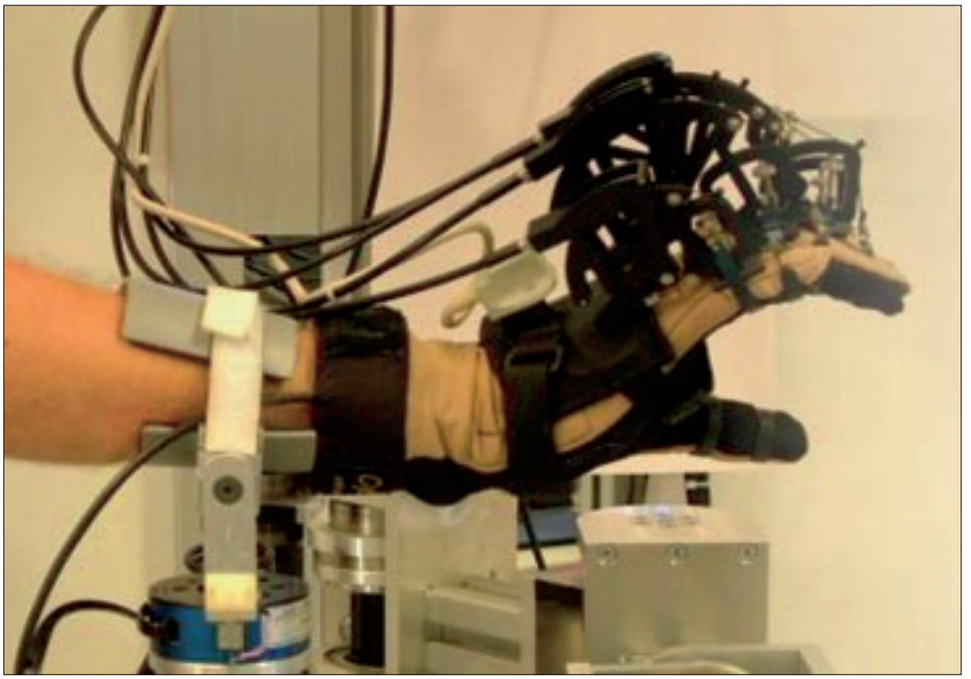
To reduce the effect of external interference in the demonstration set-up, the magnetocardiograph is operated in a partially magnetically shielded room. A further reduction

is achieved with a two-sensor magnetic gradiometer. To produce maps of the magnetic-field distribution, the patient is placed in various positions under the sensor and a short time sequence of the magnetocardiogram is recorded. From this data series a map of the field distribution can be generated for any point in time during the heartbeat.

In many cases the magnetocardiogram supplies information equivalent to that of an ECG, but in recent years clinical research has identified a variety of diseases in which the MCG is clearly superior to the ECG. This is particularly evident in cases in which the ECG looks normal, despite the presence of a cardiac problem, but where the MCG exhibits irregularities. These include, for example, Wolff-Parkinson-White syndrome, as well as the hours immediately after a myocardial infarction. Furthermore, the occurrence of circular currents in the heart, whose presence is suspected in the case of certain severe cardiac arrhythmias, for physical reasons does not contribute to an ECG but does to the MCG. A magnetic map also proved more suited for locating arrhythmogenic centres in the heart muscle than an electrical map, which is important prior to surgical intervention.

So far, the advantages of magnetocardiography have only been brought to bear in a few select high-tech medical centres because the technical, logistical, and financial burden of installing and operating a SQUID-based system is too heavy for an ordinary hospital or cardiological practice. With the new technology, this expense is reduced to such an extent that magnetocardiography will also be affordable and practical for medical practices and remote hospitals. Since magnetocardiography is essentially contact-free, public screening for heart conditions will be possible once the system has become market-ready. The potential advantages to general healthcare are clearly apparent.

PD Dr. Robert Wynands
Dipl.-Phys. Georg Bison
Prof. Dr. Antoine Weis
University of Fribourg/
Switzerland



Getting a Grip on the Computer World

In computer games or other multimedia applications, the user receives only visual and audio sensations. New touch displays help to transmit tactile sensations

Multimedia and computer technologies have become a part of our everyday lives in many ways. Before buying new furniture, we can view it on a computer screen from multiple perspectives in a virtual living room. Also impressive are the virtual reconstructions of famous historical buildings, in which computers and multimedia give the user the illusion of walking through historical rooms that no longer exist in reality. Multimedia computer games enjoy great popularity – and not only among young people – such as auto racing "à la Michael Schumacher". However, with the constant improvement of these multimedia systems, they often begin to show their deficiencies in terms of delivering high levels of realism. With its monitor and speakers, a computer can presently stimulate only two of the five human senses. Other sensations important for "grasping" the world, conveying a sense of motion, force or touch, currently cannot be emulated satisfactorily or at all. Frequently, however, it is exactly these haptic (relating to the sense of touch) perceptions that turn out to be key for a comprehensive, realistic immersion into virtual, computer-generated worlds and environments.

Customers would certainly appreciate not only being able to see their future furniture on the screen but also to feel its surface texture or

The technology makes it possible to see a phantom hand on the screen inserting a virtual radio into a dashboard while controlling the movements and feeling the object with one's own hand.

test the quality of the upholstery. Visits to a virtually reconstructed historical building could be made significantly more realistic if visitors could run their fingers along the architectural details and actually have to exert the force necessary to open or close a door. And of course the same applies for computer games. Computer game manufacturers have recognised the importance of haptic sensations, which is why they sell joysticks and steering wheels giving the player authentic tactile sensations in addition to the familiar audio and visual sensory input.

These examples indicate a recognisable trend in the human-computer interface – from today's multimedia systems to so-called "multimodal" systems, in which the user receives multisensory stimuli and can act and respond by various means. This vision is also at the centre of the research activities of the Collaborative Research Centre "High-Fidelity Telepresence and Teleaction", located in the Munich area. Telepresence refers to a feeling of being physically present with all relevant human senses in a computer-generated, virtual world, or in a real environment that is not directly accessible to the person. The inclusion of the haptic sensory modality in telepresence systems makes it possible to perform more realistic actions in virtual environments or even to perform teleactions, for example via the Internet, across distances.

What does a computer require in order to give the user of a multimodal system haptic sensations in addition to visual and audio stimuli? First it must comprise display devices that are capable of adequately stimulating the haptic sensory channels. Tactile sensations on the fingertips can be conveyed, for example, by miniature vibration elements or using pincushion-like displays composed of numerous individual moving rods.

Robot-like mechanical structures can be used to elicit sensations of force on the fingers, hand and elbow. In addition, special software must be prepared so that the computer can generate the specific haptic stimuli on the displays and coordinate them with one another. Despite certain similarities with high-quality graphics software in the way it can generate three-dimensional visual sensory impressions by computer, corresponding haptic computer programs still place high scientific demands on the respective modelling, programming and computer technology. In the end, the human organ, such as a finger or a hand, interacting with the virtual environment, must be blended in the computer image as a type of phantom, often called an avatar. This ensures that all visual, audio and haptic information transmitted by the computer and perceived by the user conveys a harmonious overall experience – which is the crucial factor for realism.

A few examples of the applications developed and executed at the Munich Collaborative Research Centre show that the "tactile simulation" achievable through multimodality allows a considerably deeper and more comprehensive grasp of computer-generated worlds and objects:

Shortly before the introduction of the euro, it was possible not only to visualise the as-yet-physically-unavailable one-euro coin, but also to allow one to feel it with the fingertips using a haptic coin model and touch displays. Similar techniques

can also be beneficial when used in medical training. For example, it is possible to practice palpating the abdominal wall to locate a beating artery or to detect a tumour.

Another application is associated with "virtual prototyping", that is product development on the computer in the automotive or other industries, such that users cannot only see and hear a car radio in a virtual instrument panel, but can also touch it. By means of a complex hand/arm display, they can feel the weight of the radio when lifting it, experience the smoothness or roughness and the temperature of the housing and finally even feel the force required to insert it in the instrument panel. A recently developed mobile haptic display lets users take a walk through an extended virtual art gallery, while actually moving through a confined area of a laboratory or, in future, even in their own homes. Users can not only view works of art such as paintings or sculptures from all angles, but can even touch them and hold them, which as we all know is rarely possible in a real gallery.

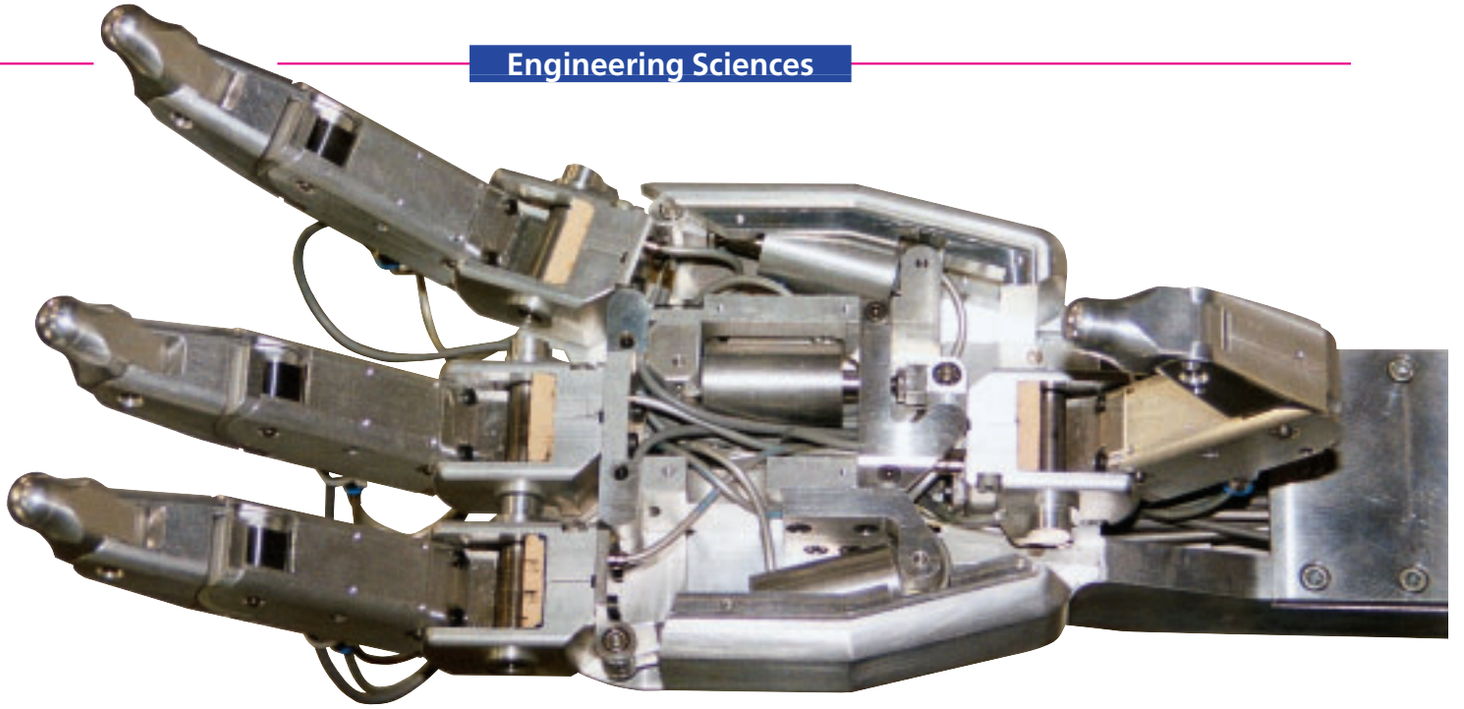
> A long-term research goal is to enable a more comprehensive and intensive perception of virtual environments

At present, however, the intensive international research efforts have not yet progressed far enough that affordable, mass-market haptic display products will be on the horizon yet in the near future. The approaches to multimodality described here have, however, already proven themselves time and again in specific applications, thus demonstrating a broader application potential. They will increase in importance in the near future, for example in intensifying medical training by use of multimodal organ or patient simulators, as well as for "rapid prototyping" in digital product development. Another area that will benefit from multimodality is teleshopping, in which customers will one day also receive haptic sensations of the products whilst browsing through a virtual catalogue. Furthermore, there are also possibilities for the haptic exploration and manipulation of nanotechnological or molecular biological structures.

In the longer term, it is altogether conceivable that computer-generated multimodality will one day also extend to other sensory perceptions, such as taste or smell. This would make it possible to experience virtual or real remote environments even more comprehensively and intensively.

Prof. Dr.-Ing. Günther Schmidt
Technische Universität München

A mobile haptic display lets users take a walk through an extended virtual art gallery, while actually moving through a confined area. Users can not only view works of art such as paintings or sculptures from all angles but can even touch and hold them.



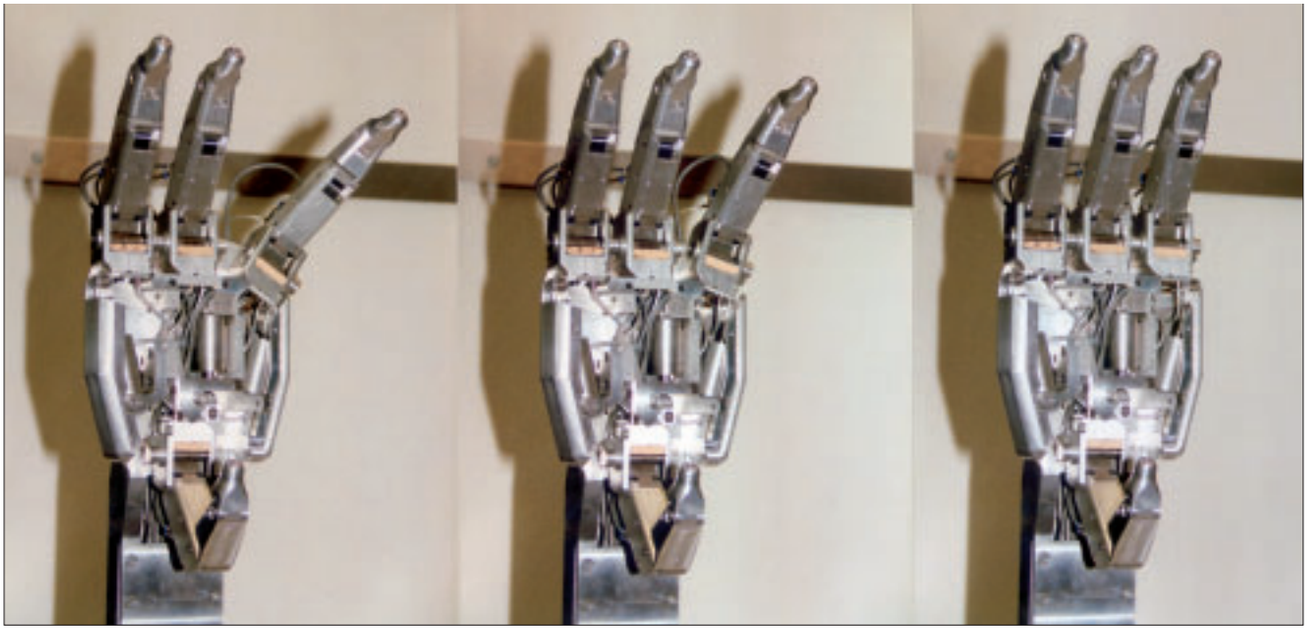
A Hand Full of Technology with Fingertip Control

Whether as prosthetics or robotic hands – artificial hands are used for a variety of applications. A new, pneumatic robotic hand is making a splash with special grasping and holding abilities

It is usually in images of the terrible consequences of war broadcast by the media that we see the importance of prosthetics. Prosthetics replace missing joints and limbs with artificial ones. They have a long, far-reaching history. The first attempts to use artificial hands to ease the stigma of a missing limb were very early. These hands – not yet functional at that time – were usually made of wood, ivory or a workable metal such as bronze or iron. The oldest known surviving artificial hand, which boasts early joint functionality and a technical interior, is that of Götz von Berlichingen (main character in Goethe's tragedy of the same title). After he lost his right hand in a battle near Landshut in 1508 he had an armourer fashion him an artificial hand. He could position its fingers using his good hand and lock in the joint positions. When the locking function was released, spring mechanisms returned the fingers to their neutral position.

Today, in addition to medical uses, artificial hands have found a broad field of application wherever dangerous or life-threatening conditions make it impossible to send human beings. Situations such as chemical plant accidents or defusing bombs make it desirable to duplicate the natural dexterity of the human hand artificially. Using people for assembly and manufacturing is also becoming ever more complicated. The growing variety of products and rising cost pressures in industry generate a high demand for flexible operating equipment that can simulate the abilities of the human hand more cost effectively. Finally, it is possible to provide support for people wherever high precision is needed for hours without fatigue. Such situations commonly occur in the field of medicine, where surgeons must perform lenghty operations with great care. This is an area in which robotic hands can considerably ease surgeons' work.

Thus there are in principle two development aims for artificial hands: the prosthesis, which recreates the appearance of the human hand as much as possible, and the robotic hand which must attain the flexibility and grasp strength of the human hand. Robotic hand development usually results in an appearance similar to that of the human hand. However, in contrast to the prosthesis, this is not primarily for aesthetic reasons, but rather because it is believed that the



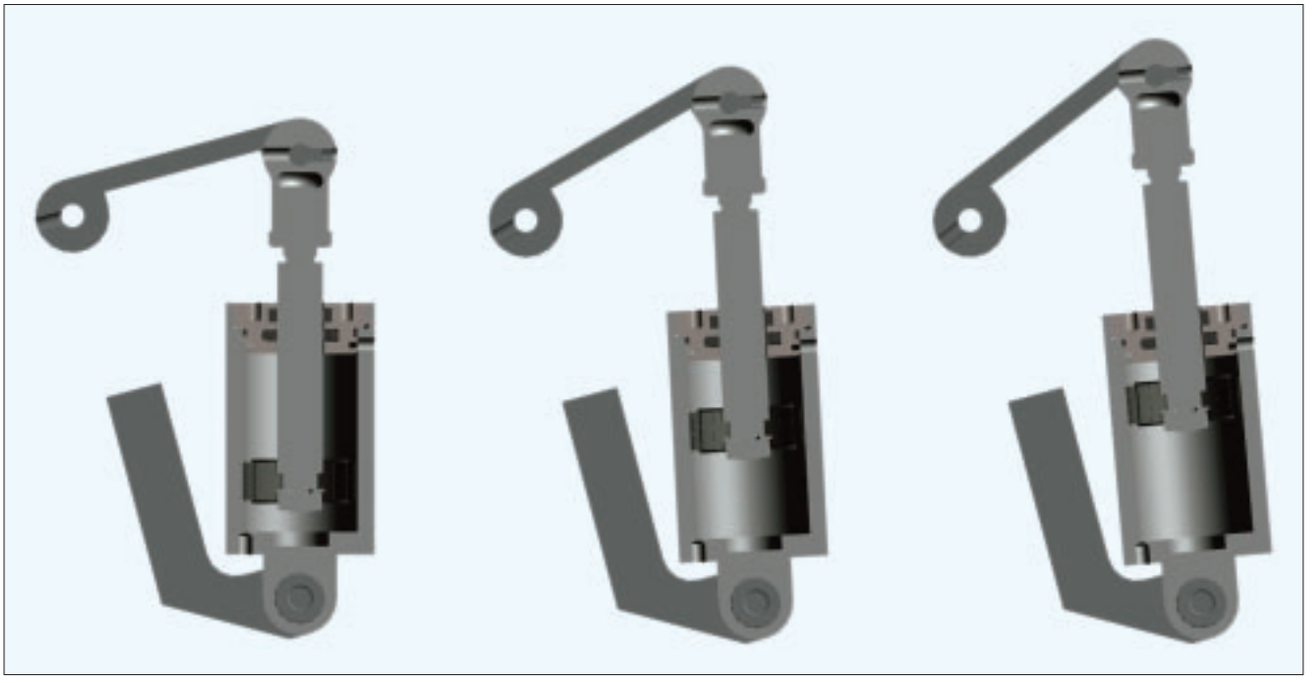
The palm of the "Aachen-IFAS-Hand" contains three cylinder-lever drives. They allow the thumb and the two outer fingers to move parallel to the palm. The piston rod is connected to one end of the proximal joint (the one nearest the hand) and the lever end is connected to the other end and to the back of the hand.

human hand has been refined over the course of evolution into a nearly perfect grasping and manipulating tool.

The "Aachen-IFAS-Hand" is a robotic hand developed at the RWTH Aachen University (Rheinisch-Westfälische Technische Hochschule Aachen), which, while modelled on the characteristics and structure of the human hand, does not try to imitate its appearance.

While the majority of robotic hands developed throughout the world are driven by electric motors or – a few – by compressed fluids, the Aachen robotic hand is the first to be controlled pneumatically, i.e., using compressed air. A pneumatic drive offers a number of advantages over the electromagnetic principle. For one thing, this type of drive does not have to be made of any special materials. Low-density materials such as aluminium or plastic can thus be used, significantly reducing the hands weight. In addition, it is capable of applying strong forces relative to its size with very sensitive pressure control.

Since it uses only air, it is a very environmentally friendly drive principle. Another advantage is that pneumatic drives are very easy to make fire- and explosion-proof, since neither the materials used nor the drive medium can cause or accelerate a fire. Pneumatic energy is very easy to store in containers in the form of compressed air and is generally available in plants and hospitals. Finally, pneumatic drives are very easy to connect since return lines can very often be dispensed



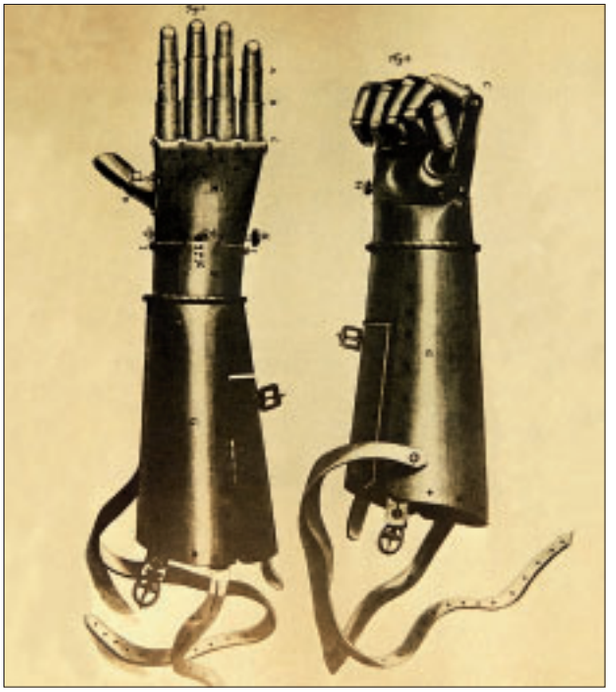
with in favour of direct ventilation into the surroundings. However, pneumatic drives also have a number of disadvantages: The outflowing air causes a certain amount of noise, which may have to be suppressed. Furthermore, pneumatic drives are difficult to regulate due to the compressibility of air, and finally the compressed air used in pneumatic drives must be dry and clean, which requires processing and filtering the compression medium.

The ongoing miniaturisation of pneumatic drives and the sensors used has meant that the "Aachen- IFAS-Hand" could be reduced to one and a half the size of a human hand. However, it only has four fingers. A fifth finger was decided against since only three fingers are needed to securely hold an object. To manipulate an object while holding it securely, one finger must be released and repositioned, making the fourth finger necessary.

The "Aachen-IFAS-Hand" has a total of 11 degrees of freedom, which means that 11 independent movements can be performed. The two outer fingers and the thumb each have three degrees of freedom and the middle finger has two. The outer fingers and the thumb can move parallel to the palm (1st degree of freedom) and also towards the palm (2nd degree of freedom). The 3rd degree of freedom is the movement of the medial joint of the finger. This allows the other phalanx to move towards the palm of the hand.

The joints of the human finger are named according to a simple pattern: The joint that connects the finger with the palm is called the proximal joint (proximus, Latin: nearest). The next joint is the medial joint (medialis, Latin: middle), and the last joint is called the distal joint (distantia, Latin: distance). The phalanges are named in the same way. The middle finger of the "Aachen-IFAS-Hand" cannot move parallel to the palm and so only has two degrees of freedom. It was designed this way to prevent the fingers from colliding.

Three different types of pneumatic drives were implemented to use the degrees of freedom and allow the fingers to move. They are a normal cylinder, which pivots the proximal joint by means of a lever (movement parallel to the palm – 1st degree of freedom), a swivel drive, which flexes and extends the proximal joint (flexing and extending relative to the palm – 2nd degree of freedom) and a belt drive, which moves the medial joint (flexing and extending with respect to the proximal phalanx – 3rd degree of freedom). The cylinder-lever drive is found inside the palm, while the swivel drive is attached to the palm and to the cylinder-level drive and makes up the proximal joint. The belt drive is located in the first phalanx. This is a pneumatic cylinder with no piston rod, whose linear movement is converted into a pivoting movement by a downstream belt-roller system. In this way, the movement of the deflection pulley is mechanically measured and used to drive the next finger segment. The 4th degree of freedom of the human finger, which makes it possible to move the last phalanx, was not reproduced with a pneumatic drive. It is not really necessary, since the last phalanx of the human finger cannot be moved independently of the other phalanges. That is why the last phalanx on the "Aachen-IFAS-Hand" is fixed at a 45-degree angle to the medial phalanx. This position allows for nearly any conceivable grips and manipulations. To control the finger positions, the hand is operated in a closed-loop position control. To grasp and hold objects, a force control loop is used, which ensures that the desired grasping or holding force is maintained. A typical grasping task is performed using both control loops. The fingers are first brought to the object using position control. When the pressure applied in the drives exceeds the value specified for the grasping task as a result of the resistance of the surface of the object, the force control loop takes over. The force control, which uses the pressure within the drives, must be very sensitive: too little force will cause the object to slip, while excessive force can damage or destroy the object.



The oldest existing moving prosthetic hand belonged to Götz von Berlichingen. He had it made after losing his right hand in a battle in 1508.

A total of 22 pressure sensors and 11 angle sensors integrated within the hand supply the two control loops with the information they require (the pressure levels in the drives and the joint angles). Two pressure sensors are required for each degree of freedom because each drive has two chambers, each of which can be subjected to pressure.

The signals from these sensors are processed in real time with measurement and control hardware and converted into position signals for the hand's pneumatic drives.

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Prof. Dr.-Ing. Hubertus Murrenhoff
RWTH Aachen

On Minnesang in the Database

The mediaeval German manuscripts at the Heidelberg University Library are cultural and historical records of great significance. Comprehensive cataloguing is making the collection newly accessible for research

Extraordinarily famous among the manuscripts at the Heidelberg University Library is the Codex Manesse, also known as the *Große Heidelberger Liederhandschrift*. It is a significant collection of German Minnesang (Middle High German song texts) and records a total of 5400 stanzas of Middle High German love poetry. An important factor in the fame of the Manesse is its full-page coloured miniatures introducing the songs of the 140 *Minnesingers*. It also contains the famous portrait of Walther von der Vogelweide. The manuscript came into the possession of the Count Palatine of Heidelberg in the late 16th century and disappeared in the confusion of the Thirty Years War. Its recovery in 1888 from the possession of the Bibliothèque Nationale in Paris and its return to the Heidelberg University Library was celebrated as an event of great national significance.

Less well known are the nearly three hundred vernacular medical manuscripts now being newly catalogued in Heidelberg. They are largely collections of medical recipes, some of which were written down by the Elector himself. One notable example is the twelve-volume "Book of Medicine", personally compiled and set down by Elector Ludwig V of the Palatinate (1478 to 1544). Many of the authors of the approximately 150,000 recipes can, however, no longer be identified. This is undoubtedly folk medicine, practiced by laymen. It is connected only partly with the Latin medicine taught at the universities, which was mainly theoretical in nature and still largely based on ancient knowledge.

Many of these collections are intended as a comprehensive weapon against all of the diseases of the human body *"a capite ad calcem"* – from head to toe (or literally "from head to heel"). But one particular reference to the Heidelberg court must not be overlooked. Several recipes deal with alleviating the consequences of excessive eating and drinking – a problem with which the common people of this time were not burdened. But in fact Elector Friedrich IV of the Palatinate, born in 1574, died as early as 1610 from the consequences of his drunkenness. The following was a preventive treatment at that time: "Place a bit of saffron tied in a small cloth in wine or water, give some of this to a sober man to drink and he will not become drunk during the day". The luxurious life at court could bring on gout, known in the Middle Ages as *podagra.* The cause of this affliction could be treated with the prescription "Whoever has *podagra,* wine is forbidden to him. He must drink honey water". Another approach was to alleviate suffering that was already present. A gouty big toe or painful hand could be helped by acorns thrust in ox gall: "From this make a plaster and tie it on the foot or the hand to drive out the *podagra*".

From these two types of manuscripts, the Codex Manesse and the medical recipes, one can get an impression of the range of the 848 German manuscripts at the Heidelberg University Library. The Codices Palatini Germanici make up the oldest collection of vernacular records of this magnitude. Until 1623, these manuscripts were part of the world-renowned Bibliotheca Palatina at Heidelberg's Church of the Holy Spirit. This library was founded

The illustration shows God, depicted here as an architect, creating the world. It is from a three-volume German Bible and originated around 1477 in the manuscript workshop of Ludwig Henfflin. The workshops tried to speed up the production of manuscripts by using several scribes and illuminators. This miniature of *Minnesinger* Walther von der Vogelweide is the most famous picture from any German manuscript.

Vorred

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upon the death of Elector Ottheinrich (1502 to 1559), whose will called for the university collection to be combined with that of Heidelberg Castle. In September 1622, during the Thirty Years War, the Calvinist elector palatine residence was captured by Catholic League troops. The victorious Duke of Bavaria, Maximilian I, presented the library to the pope as a war trophy. The next year it was transported over the Alps on the backs of mules. In 1816, during a politically favourable period after the fall of Napoleon, Heidelberg Library director Friedrich Wilken was able to persuade the Vatican to return at least the German manuscripts. The Latin, Greek and Hebrew codices that can be traced back to Heidelberg University and all printed works of the same origin remain in Rome to this day.

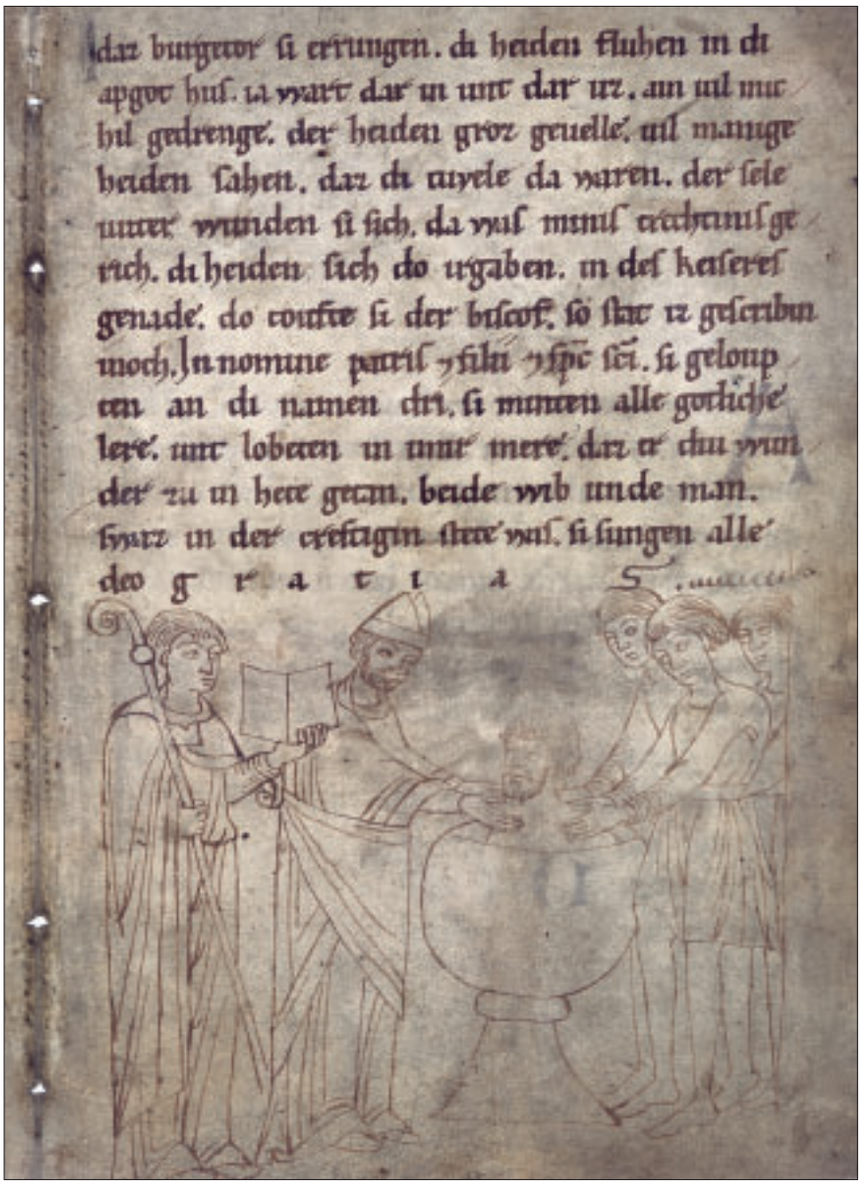
A project to re-catalogue the Codices Palatini Germanici has been underway since 1996. This is the third generation of cataloguing. A brief index appeared in 1817 after the return of the manuscripts in 1816. Then around 1900, two specialists catalogued the collection and divided it into an older section of German studies and a younger one of Palatinate history. After a hundred years, all of these publications are obsolete. More than a third of the collection has already been re-catalogued at this time.

The Deutsche Forschungsgemeinschaft has funded the cataloguing of mediaeval occidental manuscripts since the 1960s. This programme has so far resulted in over 150 printed catalogues. The "Guidelines for Cataloguing Manuscripts" are used as a compulsory standard. They are intended to ensure that the individual libraries in Germany create uniform catalogues.

The manuscript database "Manuscripta Mediaevalia" contains, in addition to the index data, complete descriptions of the manuscript as well as some fully digitalised manuscripts, including some material from Heidelberg. The results of the cataloguing now underway in Heidelberg are entered in this database as the project progresses.

What is meant by the term manuscript description? A manuscript, in contrast to a printed work that is part of an edition, is a unique object in every respect. Depending on the complexity of a codex, a manuscript description can comprise anywhere from half a page to several dozen pages. An attempt is made to make the external elements and the content of the manuscript accessible for research.

Each catalogue entry consists of three parts: an external description, a history of the manuscript and a breakdown of the contents. The external description deals with the physical form of the object. This includes information on the base material, generally paper or parchment, the quire formula, which gives the structure of the book block, the script, the book decoration and the binding. The Heidelberg Codices Palatini are primarily paper manuscripts. The provenance of a manuscript begins with its ori-



The Song of Roland (left), written around 1170 in Regensburg by the cleric Konrad tells the story of Charlemagne battling against the Moors. The Heidelberg manuscript contains the oldest version of this song and is illuminated with 39 high-quality illustrations.

The "Renner" manuscript, completed around 1430 in Nuremberg, bears witness to the Christian Gospel and is Bamberg schoolmaster Hugo von Trimberg's magnum opus. The round picture shows the world as the product of Creation. The phoenix, rising from the ashes, portends the coming of Jesus Christ.

gin, which in the best case is documented with a scribe entry or can be determined by investigating the script, watermark, binding, dialect and other aspects. The Heidelberg history of the Codices Palatini Germanici ends temporarily in 1623 when they were transported to Rome.

In many cases, no light can be shed on the early history of a manuscript. This is even the case for the Codex Manesse. While there is plenty of evidence for its creation in Zurich during the first thirty years of the 14th century, the history of the manuscript is completely unknown from then until just before it was moved to Heidelberg in the 16th century.

The provenance is followed by details on the most important literature. With such prominent pieces as the Codex Manesse, this requires a critical examination of the vast quantity of literature about this manuscript. The description of the contents of the manuscript lists the individual texts in the order in which they appear in the manuscript. In many cases, it is sufficient to indicate an academic edition here. Particularly lesser-known texts will often not have a usable title in the manuscripts. In such cases, the first and last words, known as the incipit and explicit, are given. For example, the beginning of one text in the Codex Palatinus 212 giving instructions on blood-letting reads: "Master Almansor says that from the blood-letting comes much hurt and much wisdom if one does it at the right time…". In this case, a similar incipit shows that there are two parallel records of this text in different manuscripts. The information provided by the descriptions of the individual manuscripts goes into two indexes: an incipit index containing the first lines of all of the texts, and a person, place and subject index. Without these indexes, a manuscript catalogue with its wealth of detailed information would be completely unusable.

An organic collection such as the Codices Palatini Germanici in Heidelberg is a culturally and historically significant ensemble. The individual manuscripts have, in contrast to collections that have come together by chance, an internal, historically deducible relationship to one another. This is what the introduction to a manuscript catalogue deals with. It attempts to create a synthesis of the individual observations made regarding the individual codices. In this specific case, they give us a fresh look at the castle library of the Heidelberg electors and their sources. The medical manuscripts of the Bibliotheca Palatina can once more serve as an example: their number shows the high value placed on this area of study at the Heidelberg court. Historical libraries thus have a source value comparable to that of other historical records. This applies to an entirely unique degree to the holdings of the Heidelberg Bibliotheca Palatina so rich in tradition.

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Dr. Karin Zimmermann
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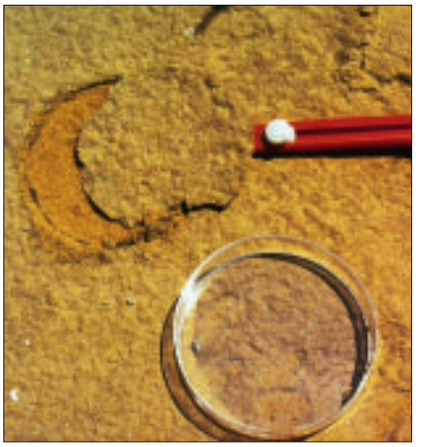
When Small Organisms Have a Big Effect

Living soil crusts exist in all warm and cold arid lands of the world. They not only form remarkably enduring living communities, but also protect the soil effectively against erosion by wind and water

The arid lands of the world are characterised by incomplete plant cover, or even its complete absence, because in the deserts, semi-deserts and steppes of the world, as well as in many arctic regions, there is not sufficient precipitation for closed vegetation cover. Between bushes and plants the soil is open and appears to be bare. But this appearance is deceptive. A more detailed analysis shows that the soil surface is densely populated by tiny organisms. Filaments of blue-green algae, the cyanobacteria, penetrate the top few millimetres of soil. They secrete slimy carbohydrates from their sheaths with which they attach themselves to particles on the ground. As well as bacteria and microfungi, green algae colonies grow on, or slightly below, the surface. But the most conspicuous are lichens, which are often brightly coloured. Lichens are symbiotic communities of fungi and algae. Many species cover the ground in a crusty layer, others are squamulose or scaly, but there are also leaf-shaped, foliose and even shrub-like, fruticose forms. Lichens are anchored with attachment organs: cell bundles penetrate into and through the soil and solidify it with a finely branched web of mycelial filaments. There may also be mosses and liverworts, which also attach themselves to the substrate. The result is a microcosmic community which has a great, often landscape-forming significance, because the activity of these organisms solidifies the soil surface like a close-knit carpet. As a result, the soil particles in the uppermost millimetres or centimetres are no longer loose and mobile relative to each other, but are highly interwoven and glued together. This compact layer of soil and living organisms forms a "biological soil crust".



The composition of living soil crusts is mainly determined by the amount of precipitation.
On a dune in Israel's Negev desert (top): in the lifted round clod the cohesive soil crust, which was formed by cyanobacteria and algae, can be seen. On Cyprus (right): a white crust lichen dominates the soil crust in a Mediterranean shrub community. In the desert in Namibia: students from Würzburg at work during a field trip; the soil is covered by crust-forming lichens.

This crust formation is extraordinarily important for the stability of the soil surface, because it protects against erosion by wind and water. Wind tunnel measurements, taken by the American crust specialist Jayne Belnap, demonstrated that

crusts are not susceptible to erosion. They can withstand wind speeds ten times higher than crustless reference soils without soil particles being blown away. If the protective crust is removed, running water can also wash away far more material. Without this protection many arid and semiarid lands would turn into dust bowls with a constantly changing surface structure. Crusts also play an important role as pioneers in the recolonisation of disturbed soils by plants.

Other properties are also profoundly changed by crust formation. The organisms and their secretions expand significantly together with the soil particles when they are first moistened by rain, sealing the soil surface. This significantly reduces water penetration into the ground. Instead the water flows downhill and allows run-off farms to cultivate plants in desert valleys, as for example in the central Negev Highland. This type of farming was already practised there by the Nabataeans. Even on sand dunes, where most of the water usually seeps away, some water run-off may become established in this manner and so plant cover may form in the dry valleys. Biological soil crusts occur in almost all warm or cold arid lands around the globe. They may be found in the cactus deserts of the Americas, the Eucalyptus savannahs in Australia and the dry grasslands of the Mediterranean. Biological soil crusts are also found in the open polar tundra, at high altitudes and even in Antarctic locations. On a small scale, soil crusts even grow in the gaps of local steppe formations in central Europe.

The composition of soil crust communities is mainly determined by the amount of precipitation. Mosses and liverworts have the greatest moisture requirements, while lichens predominate in dryer locations. In desert areas with a lot of dew and mist, such as the Namib, lichens with green algae prevail, while cyanobacterial lichens are more common in the deserts with little dew near the Dead Sea for example.

A sun-scorched desert surface is one of the most extreme habitats for living organisms on this planet. The boundary layer close to the soil is where the energy exchange takes place, where the highest temperatures occur during insolation and the lowest during nocturnal radiation of heat. High temperatures of up to almost 70°C have been measured even in ground lichens in the Kaiserstuhl hills in south-western Germany, where winter temperatures may drop to -20°C. In hot

A leafy whitish ground lichen colonizes a soil crust together with mosses in the northern Harz mountains near Goslar, Germany. Lichens, algae and cyanobacteria densely covering the ground on the Colorado plateau, USA (below). Bacteria and lichens fix nitrogen from the air and thereby contribute to fertility in North American desert soils.

Soil crusts with dominating crust lichens and a high percentage of a brownish-red fruticose or shrub-like lichen (far top). After mountain bike tires and trampling have destroyed the soil crust (left), water and wind erosion sets in. At the measuring station in the Namib desert photosynthesis and the moisture content of lichen samples are monitored.

deserts and polar regions the maximum and minimum temperatures are even more extreme. Soil crust organisms must therefore have great resistance to heat and cold.

The most critical factor at a soil crust location is water. High insolation and low humidity will repeatedly dry out mosses, lichens and algae. As poikilohydrous, i.e. intermittently moistened organisms, they are very resistant to drought. Even after years of desiccation under experimental conditions, they remain viable. This in itself is not sufficient, however: any productive metabolism needs moisture. The organisms must be able to use the limited quantities of water and the all too often very brief moist periods effectively.

Only shortly after rainfall does the desert surface that had not shown any signs of living activity come to life. Filaments of cyanobacteria creep into the light from the uppermost soil layers. They use the brief moist period for their metabolism and growth. As soon as it becomes drier they retreat a few millimetres back into the soil. Thanks to their sensitive sensors they are capable of recognising changes in moisture levels in their environment and, thus, avoiding longer periods of sunlight. Apart from the infrequent rainfalls, soil crust lichens are especially capable of using additional water sources. Mist, or even dew and frost, are sufficient to activate their metabolism. Dried-out green algal lichens can even reactivate their metabolism in equilibrium only with high humidity but without a single drop of water. These properties enable them to exist in the coastal Namib desert, where almost no rain falls, but mist, dew, and high humidity occur regularly. Photosynthetic productivity in biological soil crusts is the most important factor of

their existence. Recording photosynthetic activity at different natural locations and analysis of their responses under controlled conditions provide insight into the ecophysiological functions of these highly specialised organisms.

Hundreds of square kilometres in the coastal zone of the Namib desert are covered by soil crusts. For much of the day they appear grey and parched. Every morning after mist or dew has fallen, however, they awake to new life and the desert takes on a green lustre. Relative to the surface area, the chlorophyll content of the soil crust is similar to that of a beech leaf for example. The maximum rates of carbon dioxide fixation by crust lichens from the air are of a similar order of magnitude. It is fascinating to think that the otherwise apparently dead desert floor awakens to life, as if it were a huge extended leaf. However, this awakening only lasts for a short time, often less than an hour. As soon as the mist has dispersed and the sun begins to shine more brightly, the organisms dry out again completely and become latent. At this Namib location soil crusts are only active for about 10 percent of the total time in the course of a year, whereas central European soil crusts that benefit from extensive rainfall and snow are active for 35 to 65 percent of the time.

In one year a lichen-dominated soil crust community can absorb up to 370 kilograms of carbon per hectare from the air and bind it in plant matter. That is a significant contribution to soil improvement in arid lands with little productivity from flowering plants. This carbon fixation is also of importance on a global scale, but precise details on the extent of biological soil crusts over the entire planet are not currently possible. It is estimated that they cover 5 to 15 percent of the Earth's total land surface. They thus represent a sizeable link in the global carbon dioxide cycle. At many locations it is also very important that free-living cyanobacteria of the soil crusts as well as lichens with a cyanobacterial partner fix nitrogen from the air and so increase soil fertility. In North American desert soils an average annual nitrogen input of up to nine kilograms of nitrogen per hectare from soil crust activity has been demonstrated. This fertilisation benefits entire ecosystems that suffer from nitrogen deficiency.

Under natural conditions biological soil crusts are omnipresent in the world's arid lands. However, humans have become their worst enemy. Particularly in their dry state, crust communities are very sensitive to mechanical impact. They break and crumble under human feet and animal's hooves in cases of overgrazing, they are ground up by car tires and tank tracks. Human beings have been pushing their activities ever deeper into arid lands for some time – to use the last pasture reserves, for construction or for off-road tourism. The fragile soil crust layer is being destroyed on a large scale and the soil is then laid bare to wind and water erosion. This may have devastating consequences and it is essential that we become aware of this danger.

An important task of modern landscape management in arid lands is the protection of soil crusts. In the USA and Australia extensive programmes for their protection are already underway, but the regeneration of destroyed crusts is a long, drawn out process because of their slow growth. Pure cyanobacteria crusts are formed relatively quickly, but it takes many decades before a lichen-rich crust community recovers from destruction. Since artificial planting has not been very successful so far, management is restricted to encouraging and preserving existing soil crusts. From the deserts to the tropics and from the Arctic to the Antarctic we often – quite carelessly – step on the carpet of biological soil crusts. They constitute a complex ecosystem with many highly specialised organisms living in a complicated equilibrium. Biologists, soil scientists and landscape ecologists are trying to understand the structure and function of this sensitive living skin that spans the arid lands of our planet as both protection and provider.

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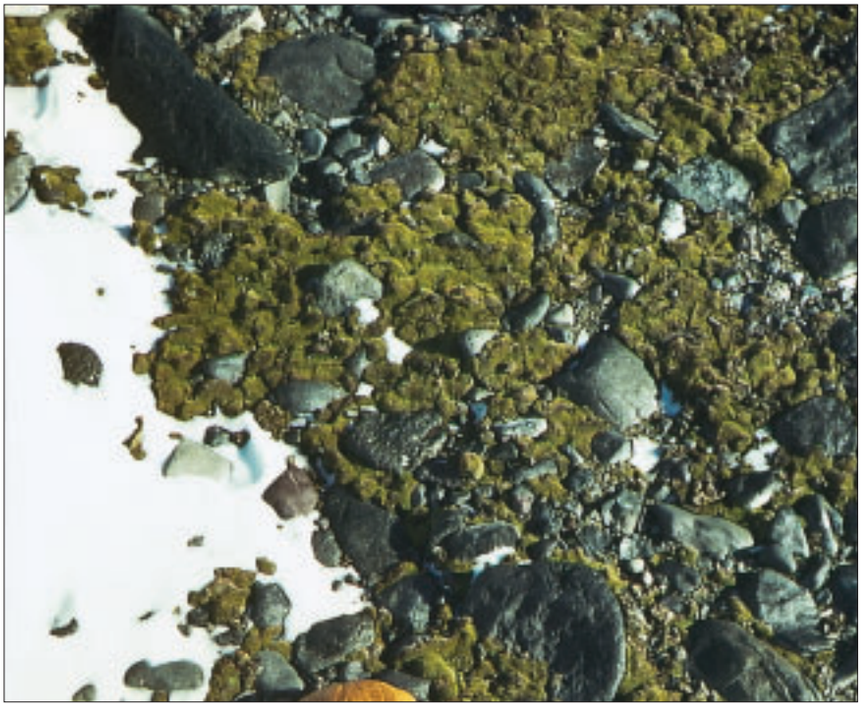
Mosses and green algae in Antarctica. They cover and stabilise the soil surface in ice-free areas where melting snow provides moisture.

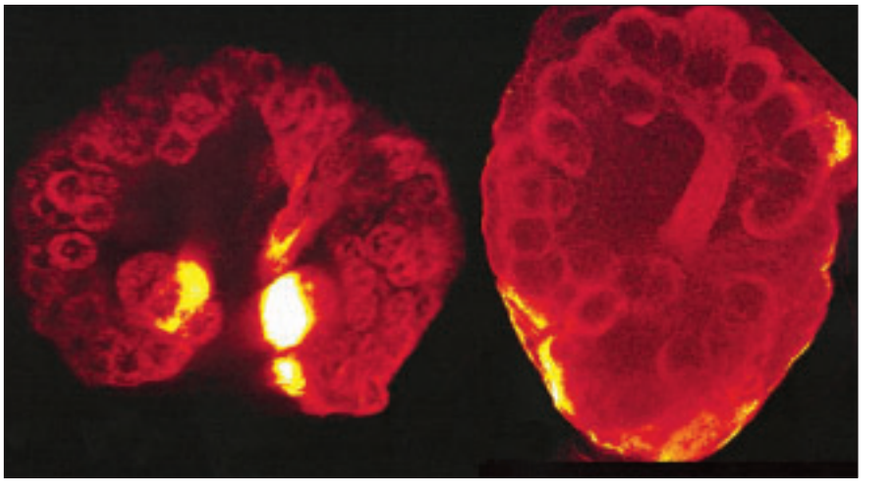


An Insect's Life in a Scented World

Whether searching for food or a partner – scent plays an important role for insects. How scents are processed in their brain is answered by studies on the olfactory system in honeybees and robber ants

Insects have a pronounced sense of smell. For example, bees learn to recognise the scent of nectar-rich blossoms so that they will fly to those flowers from which they can collect the most honey for their hive. Scents also play an important role in insects' search for a mating partner. The silk moth female attracts males with sexually attractive substances over long distances. The males smell these chemical messages and fly against the wind to the female. The partners can even find each other in the evening twilight. Social insects, such as bees, ants and termites, use scents for communication. We all know about ant roads: the animals follow a scent trail on the ground to their destination. These messenger substances produced by the animals themselves and used to communicate with members of their species are called pheromones.

For animals there is a critical difference between environmental scents – such as a blossom scent for the bee – and pheromones. Environmental scents cannot be predicted, but pheromones, in a sense, constitute a part of the species' memory. For a scent of this type to fulfil its function, a certain genetically determined meaning must be attributed to it (i.e., when the animal smells this scent a particular behaviour is triggered). This behaviour is context-dependent, because a sexually immature animal will not react to a sexual pheromone. In the correct context the scent will cause stereotyped behaviour without the animal ever having learned to recognise the scent. Evolution "wrote" the link between scent and behaviour into the genes. This is entirely different in the case of environmental scents, as for example blossom scents by which bees are lead to a nectar-rich diet. Bees must learn these scents over the course of their life.

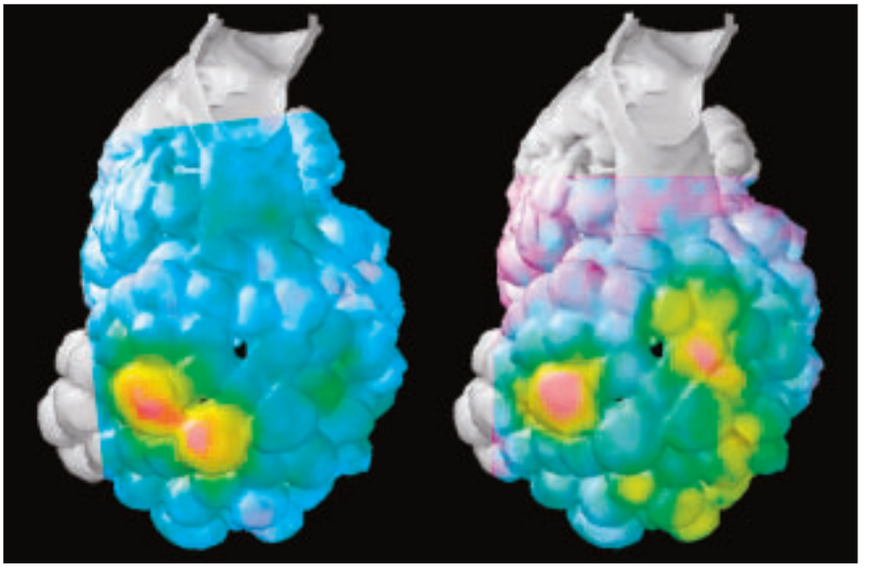


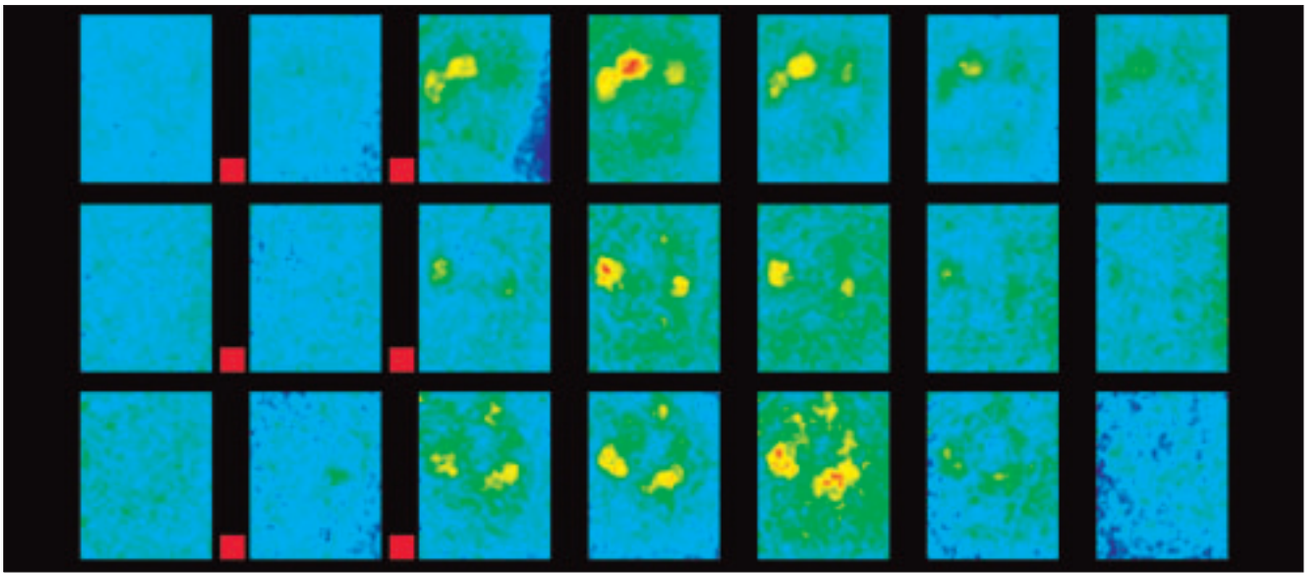
In insects the olfactory receptors are stimulated by various scents. The resulting impulses are sent to the brain via neural appendages. The optical sections depict antennal lobes of an ant (left) and a honeybee (right)

Scientists have examined the question whether the brain processes these two scent classes differently. On the one hand, can the genetic memory for pheromones be found in the brain and, on the other hand, can we understand the "olfactory system" that enables the honeybee to reliably recognise every blossom of the world? Researchers have pursued two basic ideas: to understand the processing of scents in the brain, the activity they trigger must be measured. And to understand the difference between the processing of environmental scents and pheromones, species are examined that make significant use of pheromones and are exposed to many different environmental scents. For this purpose, social insects are particularly suited because many of the signals necessary for life in communities require pheromones. Honeybees and robber ants, which are natives of Central America and closely related to the Central European wood ant, were studied. Numerous pheromones of known chemical composition and their triggered behaviours have been described for these species.

In insects the olfactory receptors are primarily located on the antennae. There are around 60,000 receptors on each honeybee antenna. These cells are stimulated by vari-

ous scents, which are sent to the brain via long neural appendages, the axons. The antennal lobe of the bee is an organ that is similar to the human olfactory bulb. It looks somewhat like a blackberry. Each of its berries constitutes a functional unit, a glomerulus. When the animal smells a scent, a characteristic pattern of activated glomeruli is generated in the antennal lobe. The olfactory information is not located in individual glomeruli, but is based on their pattern as a whole. A combination pattern of this type can code many thousand scents with only a few glomeruli – the bee has about 160. The hypothesis: pheromones should produce a predictable and constant pattern for all individuals of the species, because they are determined by evolution. A greater variability should be assumed for environmental scents, because they only become meaningful through experience. Therefore, the same scent should cause differing patterns among individuals.





With the so-called optical imaging method the patterns caused by scents in the antennal lobe can be measured. The antennal lobe is of varying size in different insect species: in the bee it has a diameter of about 0.25 millimetres, with the individual glomeruli having diameters between 20 and 50 micrometers. The ants studied have somewhat smaller antennal lobes and glomeruli. To measure the scent patterns, the scientists first fixed the animals in a plastic chamber so that the head could not move. Then they cut a window into the head capsule so that they could see the brain and dyed the brain with a pigment that changes its colour when nerve cells become active. The researchers used fluorescent "calcium green" dye, which reacts to calcium. Active cells increase their intracellular calcium concentration which causes an increased fluorescence. These changes could be measured under the microscope with a special camera. Since the insects could still smell perfectly, the scientists were able to determine the response patterns to various scents in each test animal. First, the characteristics of the patterns produced by the scents – that is, pheromones and environmental scents – in both species were examined. This showed that the coding principle described above is the same for both species and both scent classes: each scent produces patterns based on several, not necessarily neighbouring glomeruli. Is the variability among individuals larger for environmental scents than for pheromones? To answer this question, a measure had to be developed. A certain characteristic of honeybee glomeruli proved useful:

In a maze of scents a honeybee finds its favourite flower. Its blackberry shaped antennal lobe consists of glomeruli that enclose a common centre. Certain fragrances stimulate specific glomeruli. On the left: the response to the scent nonanol. On the right: the response to oil of cloves. The reaction to different scents, recorded in sequence for one second, exhibits characteristic patterns.

they differ in size and shape. Some are round while others are elongated. They are also located in a characteristic pattern relative to each other. In different animals the glomeruli can be recognised and named because of their external characteristics. A digital atlas of the glomeruli was then produced and used to map the scent responses of the honeybee. This made possible the numerical recording of the pattern for each scent in each animal. For example, the scent nonanol resulted in strong activity in glomeruli 17 and 33 in one animal. When compared to other individuals, it turned out that this pattern is universal and nonanol always stimulates glomeruli 17 and 33. The patterns occur so constantly that the causative scent can be identified from them. This result applied not only – as anticipated – for pheromones but also for environmental scents that have no significance for communications within the species. The initial hypothesis was clearly refuted. But how do bees handle the incredible diversity of flower scents? Apparently, the millions of possible combinations of active glomeruli that result from their different response characteristics are sufficient for orientation in different environments without having to learn those scents of current relevance.

However, it is known that a memory trace for scents is present in the antennal lobe. If a bee is offered a scent and sugar water, it learns the relationship between scent and reward and, when it smells the scent the next time, will extend its proboscis in anticipation of the sugar water. This is classical conditioning. Several regions in the honeybee's brain participate in this learning process, among them the mushroom bodies and also the antennal lobe. If the scent-dependent patterns are measured during this learning process, the result is unequivocal: when the bee is learning a scent, the resulting pattern is enhanced, but the participating glomeruli remain the same. In this manner, the bee can probably more quickly recognise this scent and better differentiate it from other scents. The "olfactory system" is structured so that it can react to millions of scents, while learned scents are recognised more easily.

The results obtained at the insects' antennal lobe are readily transferable to the olfactory lobe of humans. Both olfactory systems are structured very similarly and there is evidence that scents cause the same activity patterns in different humans.

However, the antennal lobe in insects, like the "olfactory bulb" in humans, is only the first station of scent processing. When we, as humans, are transferred into a mood that we believed long forgotten or the odour of spoiled milk deters us from drinking it, many other regions of the brain other than the olfactory lobe are also participating.

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Rhesus Monkeys and Reproductive Strategy

A male rhesus monkey leaves his birth group to reproduce. On Cayo Santiago, the "Monkey Island" off Puerto Rico, researchers are searching for the gene that controls the primates' migratory behaviour

At some time during his puberty a rhesus monkey lad will roam – as the German poet Friedrich Schiller put it in his famous "Song of the Bell" – "into life so wild". He leaves the shelter of his birth group and seeks contact to another group. For lack of a better alternative he may even temporarily engage in a pure male bond. But soon the adolescent rhesus monkey notices that females of other groups are very interested in young foreign males. That is the positive aspect of a process known in behavioural biology as "natal dispersal": emigration from the birth group with the objective of reproduction. The downside is that the young men put themselves into great danger while "traversing their world" (Friedrich Schiller). In the first year after leaving the birth group, 20 to 40 percent of male rhesus monkeys succumb in their struggle to survive.

By using molecular genetic methods for paternity analysis it was revealed that emigration from the birth group actually fulfils a biological purpose. On the "Monkey Island" of Cayo Santiago, located half a nautical mile east of Puerto Rico, we examined which offspring was descended from high-ranking males in one social group and which from low-ranking immigrant males. The "Monkey Island" is part of the Caribbean Primate Research Center, with which we have been closely cooperating since 1988. The rhesus monkey colony on Cayo Santiago was established by the American zoologist Clarence Ray Carpenter in 1938. Today about one thousand rhesus monkeys live there in several social groups.

It was demonstrated that high-ranking males in a social group – though particularly sexually active – by no means produce the majority of offspring. Rather, the offspring mostly descended from low-ranking rhesus monkey males who had attempted to join the new group during emigration from their birth groups. This demonstrated that natal dispersal serves to avoid inbreeding and maintain the genetic flow. To pursue such high level goals, however, evolution requires an instrument that can be applied to each individual. The fact that almost all advanced mammals and many bird species migrate to reproduce raises the question of what forces cause the animals to do so. For geneticists it seemed obvious to look for an answer in the genes.

Observations by primatologists aided the search for the gene that controls emigration from the birth group. They noted that the time when young rhesus monkey males leave their birth group varies considerably: some start looking for a new group at the age of three, but others much later. At the age of six years about 90 percent of all males had left their birth group. Several groups of researchers also discovered that the serotonin level (serotonin is a neurotransmitter) in the monkeys' cerebral fluid correlates

Young males in the rhesus monkey colony on the Caribbean island of Cayo Santiago usually seek to join another group. This means life-threatening risks but also the prospect of a large number of offspring.

with the age at which the monkeys leave their birth group. This dependency of migrating age on the serotonin level directed attention to the genes that play a role in the serotonin metabolism. Of particular interest in this context was the gene SLC6A4, responsible for the serotonin transporter.

In 1996 Klaus-Peter Lesch's working group at the University of Würzburg discovered that the short variant of the controlling element of this gene, the SLC6A4 promoter, is associated with neuroticism in humans, a personality trait characterised by anxiety and depression. The short variant of the controlling element causes only about half as many serotonin transporters to be formed as the long variant.

The short variant is also found in rhesus monkeys. On the "Monkey Island" of Cayo Santiago about 8 percent of all animals are homozygous for the short variant (ss – for homozygous "small"), 52 percent are homozygous for the long variant (ll – for homozygous "large") and the remaining 40 percent are heterozygous (ls). We examined the effect of these variants on the emigration age of 532 male rhesus monkeys born between 1970 and 1997 on the "Monkey Island" of Cayo Santiago. It was already known at which age these animals had left their birth group. Comparison with the recorded genetic data revealed a clear link between the genetic variants and the emigration age: homozygous ss males left their group at an average age of 57 months, while homozygous ll males were, on average, 72 months old upon emigration. The average emigration age of heterozygous ls animals was intermediate at 64 months. For the

first time it was possible to demonstrate a link between a genetic and a behavioural characteristic in non-human primates. The long variant causes rhesus monkeys to detach from their birth group later. Male rhesus monkeys thus pursue two different reproductive strategies: homozygous ss males who emigrate early take a significant risk of dying during their struggle to survive outside the birth group (20 percent), but are rewarded with special receptiveness by the females of the new group. Homozygous ll males who emigrate late initially incur a lower risk by remaining with the birth group for longer and also procreating there. If they subsequently decide to emigrate from their birth group, however, they take an especially high risk of mortality during their struggle for survival (40 percent). We therefore put forward the hypothesis that heterozygous males have a selection advantage over homozygous males.

If this theory were right heterozygous males should have produced significantly more offspring than homozygous ones. However, the results of our ongoing paternity analysis on the "Monkey Island" of Cayo Santiago did not confirm this expectation. There was no difference between the average reproductive success of heterozygous and homozygous males. Apparently nature is pursuing a different strategy than the classical heterozygote advantage to secure the preservation of the serotonin transporter gene variant we examined. In our current research we are attempting to elucidate this strategy. It is as yet uncertain how the differences in the gene under consideration affect personality and behaviour. It is conceivable that the formation of serotonin transporters affects the serotonin level in the cerebral fluid. However, an effect on prenatal brain development is more probable.

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The Fight against Retroviruses

A gene therapeutic approach for treating viral infections places its bets on incorporated enzymes destroying virus particles from within

The immune deficiency disease AIDS which continues to spread worldwide is caused by a member of the retrovirus family. „Retrovirus" is the name given to a large group of diverse viruses whose genetic information is stored in RNA molecules. In a retrovirus-infected cell, a DNA copy of the viral RNA is produced and then inserted into the host cell's genome. Since this is a reversal of the usual information flow from DNA to RNA, the term „retro"-virus was coined. Retroviral infections cause diseases in humans, which are often fatal. One of the aggressive retroviruses is the human immunodeficiency virus (HIV), the agent responsible for the aquired immune deficiency syndrome, AIDS. Retroviral infections, especially HIV infections, pose a tremendous challenge in biomedical research.

In recent years, remarkable progress has been made in developing effective combination drug therapies that can control, but not cure, retroviral replication. However, even when effective, these drug regimens are toxic, they require demanding administration schedules, and resistant viruses can emerge. Thus the need for new gene-based therapies remains. A novel gene therapeutic approach against retroviral infections, called „Capsid-Targeted Viral Inactivation" (CTVI) is showing the first signs of success in an animal model, promising new efficient alternatives for the treatment of these viral infections in humans.

The use of gene therapy in the treatment of viral infections is a relatively new concept and was first suggested by the virologist David Baltimore in 1988. In a general strategy called intracellular immunisation, genes encoding macromolecules that interfere with viral multiplication are introduced into virus-susceptible cells. Although very promising results against HIV infections have been achieved in cell culture and in animal models by employing these strategies, viruses emerged that were able to escape inactivation by foreign macromolecules through mutation.

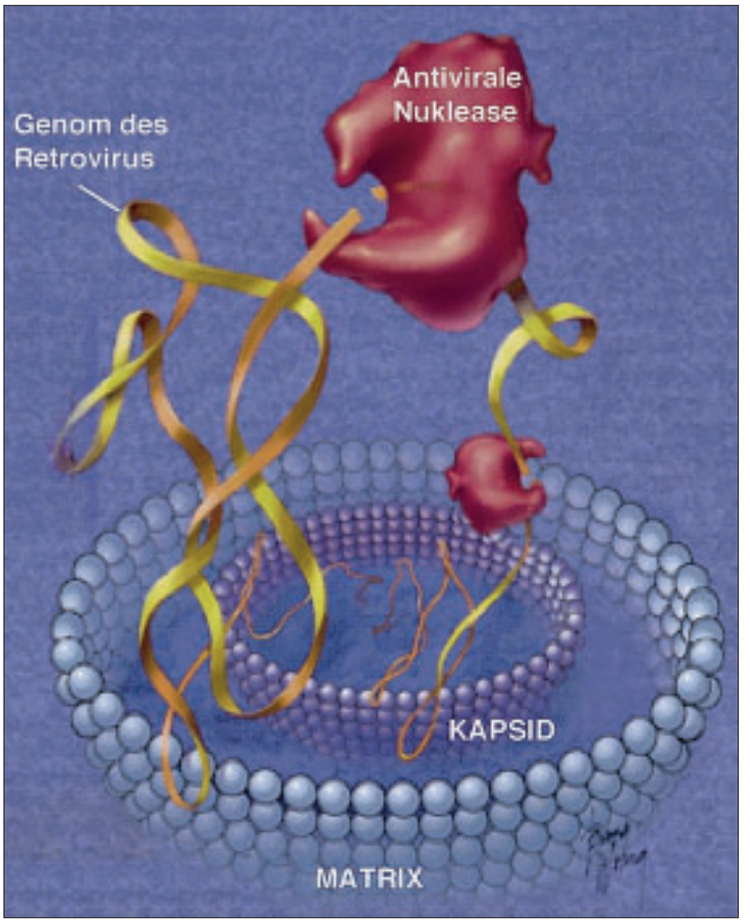
A project developed at the Johns Hopkins University School of Medicine in Baltimore (Maryland, USA) and concluded at the Heinrich Pette Institute for Experimental Virology and Immunology at the University of Hamburg describes a new strategy of intracellular immunisation and demonstrates proof-of-principle of this strategy in an animal model.

A strength of the CTVI strategy is that it is designed to target a step in the viral life cycle that is different from those targeted by most other current anti-HIV gene therapy approaches. Therefore CTVI gives cause for hope that new treatment methods for this disease which remains incurable will be found. The concept of the CTVI strategy was originally developed in Jef D. Boeke's laboratory at the Johns Hopkins University. By using the yeast retrotransposon Ty1, a mobile genetic element whose transposition mechanistically resembles retroviral multiplication, this approach was tested for the first time as a novel means to interfere with viral replication. The strategy was shown to inhibit transposition of the

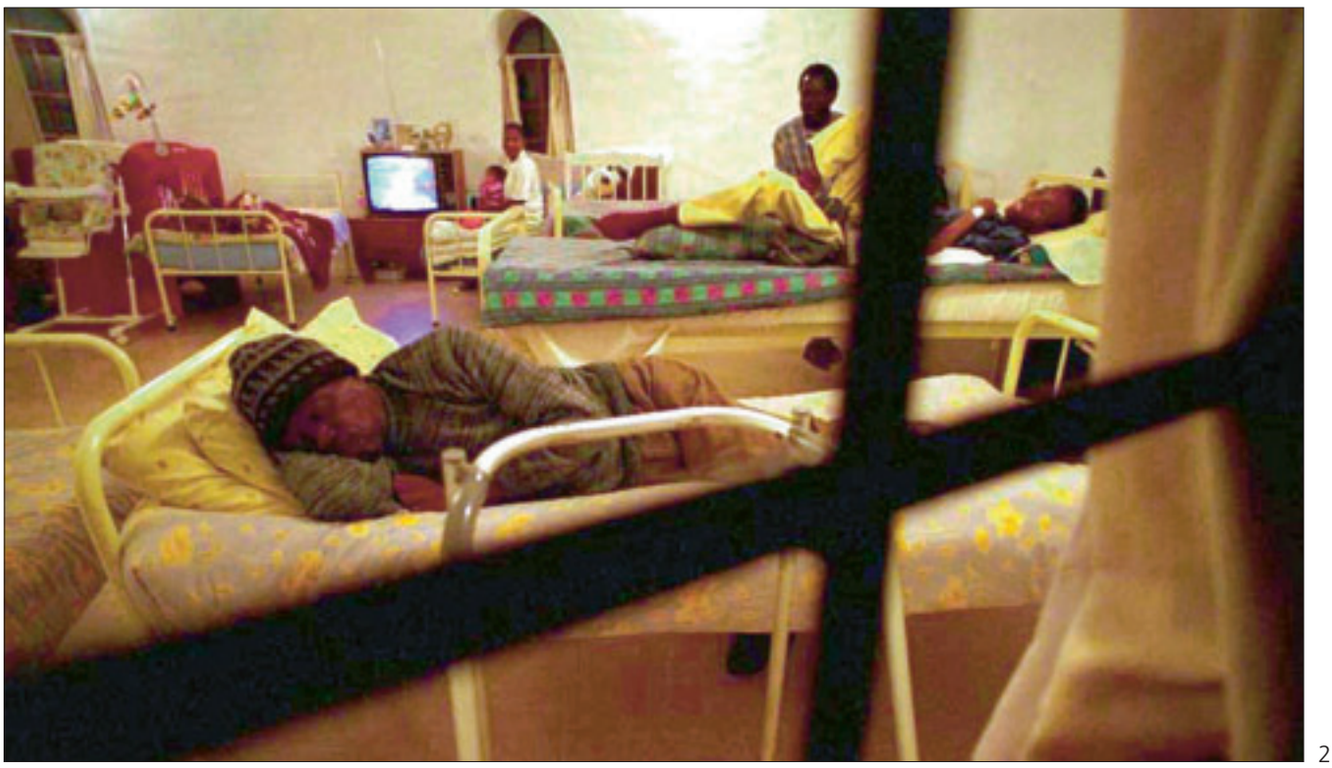
retrotransposon by at least 98 %. In this approach antiviral nucleases (enzymes degrading molecules that carry genetic information) are fused to the viral coat proteins forming the capsid, which surrounds the viral genome.

The process of retroviral particle formation makes the incorporation of deleterious proteins into the retroviral capsid relatively easy. After co-packaging of the viral genome with the deleterious nuclease fusion inside, the core of the assembled virus particle, the deleterious nuclease interferes with viral multiplication by both degrading the viral genome and inhibiting viral protein activity.

To test the feasibility and efficiency of this new antiviral strategy, it was first attempted to deactivate a murine retrovirus causing leukaemia (Murine Leukaemia Virus, MuLV) in cell culture experiments. The nucleases to be tested for their antiviral efficiency were selected for not having a destructive effect on the host cell. In cooperation with the virologist Mark Federspiel of the Mayo Clinic in Rochester (Minnesota, USA), we demonstrated that the selected nucleases did indeed

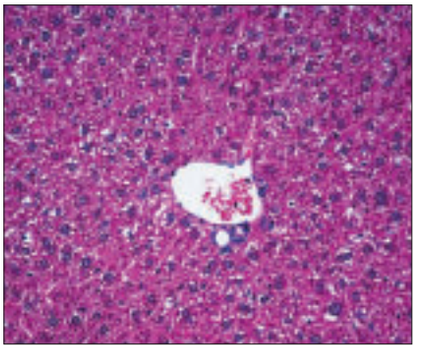


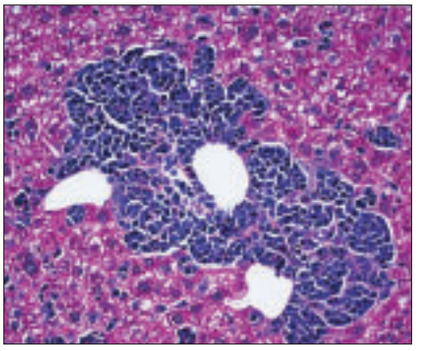
Africa is particularly hard hit by the AIDS epidemic. A destructive enzyme – antiviral nuclease – may help. It is incorporated into the retrovirus particle and blocks the viral production by breaking down the viral genome.

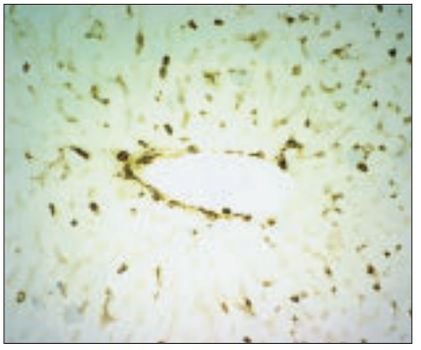


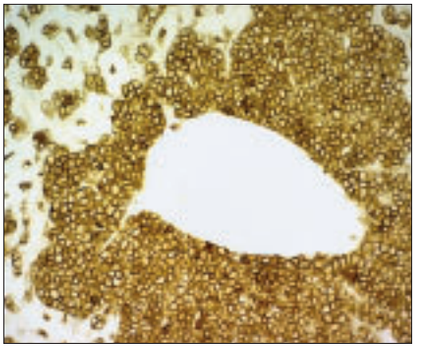
inactivate all infectious virus particles in cell cultures infected with MuLV. The virologists Beatrice Hahn and John Kappes at the University of Alabama at Birmingham used these results to conduct analogous experiments in which the successfully tested nucleases were expressed in cell lines infected with the AIDS retrovirus. The results of these experiments were promising

In genetically modified mice carrying the antiviral fusion protein, the liver's affliction by tumour cells was either strongly reduced or – as demonstrated in the two images on the left – can not be observed at all. In contrast, the images on the right show extended tumour cells in the liver tissue of unmodified mice.









since the number of infectious virus particles released by the infected cells was reduced by 88 to 99 percent. Since the results of such cell culture experiments cannot readily be transferred to living organisms, testing of these strategies in living organisms (in vivo) is indispensable.

Transgenic mice producing fusions of the MuLV capsid protein and the antiviral nuclease (fusion protein) in their cells were specifically bred for these experiments at the Johns Hopkins University in Baltimore. The antiviral proteins were shown to have no harmful effect on the mice, but rather protect MuLV-producing mice, which normally develop certain kinds of blood cancer (lymaphatic leukaemia). In transgenic mice producing the antiviral fusion protein, the number of infectious particles was reduced by up to 10-fold, which considerably delayed the development of leukaemia and resulted in increased longevity in these animals when compared to their normal, MuLV-infected siblings lacking the antiviral fusion protein. It could be demonstrated that the fusion proteins were incorporated into the virus particles of retrovirus-infected mice inactivating the viruses.

Therefore, the mouse model indicates that the antiviral CTVI strategy is not only efficient in tissue culture but could also provide substantial therapeutic benefits in vivo. By altering several factors, it will become possible to significantly enhance the antiviral effectiveness. The results suggest that employing gene therapeutic approaches based on similar fusion proteins to fight HIV and other retroviruses could be of major therapeutic benefit.

The demonstration of CTVI applicability in an animal model presents a multitude of perspectives: In order to make animals resistant, or at least less susceptible, to retroviral infections the methods described here could readily be used to construct improved versions of farm animals that currently suffer from retroviral diseases, including chickens (avian leukosis virus), goats (caprine arthritis-encephalitis virus), sheep (Maedi/Visna virus), cattle (bovine leukemia virus), and horses (equine infectious anemia virus).

However, the greatest challenge is still posed by human retroviruses such as HIV and the leukaemia-causing HTLV-1 (Human T-cell Leukaemia Virus 1). Short of germ line gene therapy, targeting a majority of virus-infected cells by a somatic gene therapeutic approach would be necessary for a robust antiviral effect. The results indicate that even relatively modest decreases in retroviral titers in vivo can lead to significant improvements in clinical outcomes. In transgenic mice this took the form of delayed leukaemia development and increased life expectancy. Since the quantity of viruses present in HIV patients correlates closely to the disease's progress, a two- to tenfold reduction of infectious viruses, as observed in mice, would have a significant positive effect on the course of the disease and would also improve the patients' quality of life.

Building on our research the virologists Gertrud Beterams and Michael Nassal at the Albert Ludwig University in Freiburg have recently succeeded in employing this antiviral strategy against the hepatitis B virus (HBV), which infects humans. By targeting a degradative nuclease into viral particles the number of infectious hepatitis B particles in cell cultures was reduced by 95 percent.

Thus capsid-targeted strategies continue to provide a promising approach for therapy against a variety of viruses that affect humans, directly and indirectly.

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The Deutsche Forschungsgemeinschaft

The Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) is the central self-governing organisation responsible for promoting research in Germany. According to its statutes, the DFG serves all branches of science and the humanities. The DFG supports and coordinates research projects in all scientific disciplines, in particular in the area of basic research through to applied research. Particular attention is paid to promoting young researchers. Every German scientist and academic is eligible to apply for DFG funding. Proposals are submitted to peer reviewers, who are elected by researchers in Germany in their individual subject areas every four years.

The DFG distinguishes between the following programmes for research funding: In the *Individual Grants Programme,* any researcher can apply for financial assistance for an individual research project. *Priority Programmes* allow researchers from various research institutions and laboratories to cooperate within the framework of a set topic or project for a defined period of time, each working at his/her respective research institution. A *Research Unit* is a longer-term collaboration between several researchers who generally work together on a research topic at a single location. In *Central Research Facilities* there is a particular concentration of personnel and equipment that is required to provide scientific and technical services.

Collaborative Research Centres are long-term university research centres in which scientists and academics pursue ambitious joint interdisciplinary research undertakings. They are generally established for a period of 12 years. In addition to the classic Collaborative Research Centres, which are concentrated at one location and open to all subject areas, the DFG also offers several programme variations. Transregional Collaborative Research Centres allow various locations to cooperate on one topical focus. Cultural Studies Research Centres are designed to support the transition in the humanities to an integrated cultural studies paradigm. Transfer Units serve to transfer the findings of basic research produced by Collaborative Research Centres into the realm of practical application by promoting cooperation between research institutes and users.

DFG Research Centres are an important strategic funding instrument. They concentrate scientific research competence in particularly innovative fields and create temporary, internationally visible research priorities at research universities.

Research Training Groups are university training programmes established for a specific time period to support young researchers by actively involving them in research work. This focuses on a coherent, topically defined, research and study programme. Research Training Groups are designed to promote the early independence of doctoral students and intensify international exchange. They are open to international participants. In International Research Training Groups, a jointly structured doctoral programme is offered by German and foreign universities.

Other funding opportunities for qualified young researchers are offered by the *Heisenberg Programme* and the *Emmy Noether Programme.*

Humanities Research Centres were created in the new federal states to improve the existing research infrastructure. These centres have been established for a specific time period and serve to promote interdisciplinary research.

The DFG also funds and initiates measures to promote scientific libraries, equips computer centres with computing hardware, provides instrumentation for research purposes and conducts peer reviews on proposals submitted within the framework of the *Hochschulbauförderungsgesetz*, a legal act which provides for major equipment and the construction of institutions of higher education in Germany. On an international level, the DFG has assumed the role of Scientific Representative to international organisations, coordinates and funds the German contribution towards large-scale international research programmes, and supports international scientific relations.

Another important role of the DFG is to provide policy advice to parliaments and public authorities on scientific issues. A large number of expert commissions and committees provide the scientific background for the passing of new legislation, primarily in the areas of environmental protection and health care.

The legal status of the DFG is that of a private association. Its member organisations include research universities, the Academies of Sciences and Humanities, the Max Planck Society, the Fraunhofer Society, the Leibniz Association, the Helmholtz Association of National Research Centres, research organisations of general importance, and a number of scientific associations. In order to meet its responsibilities, the DFG receives funding from the German federal government and the federal states, as well as an annual contribution from the Donors' Association for the Promotion of Sciences and Humanities in Germany.

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Illustrations

Querbach (p. 2, back); Wynands (p. 4); Bramaz/Schweizerischer Nationalfonds (p. 5); Kron/Kammermeier (p. 6, 7); Nitzsche (p. 8); IFAS (p. 9, 10); archives (p. 11); Universitätsbibliothek Heidelberg (cover, p. 12, 13, 14, 15); Lange (p. 16, 17, 18, 19, 20); Galizia (p. 21, 22, 23); Schmidtke (p. 24); Rawlins (p. 25); Wong (p. 27 a.); dpa (p. 27 b.); Schumann (p. 28)

Layout of pictures:
l. = left, r. = right, a. = above, b. = below

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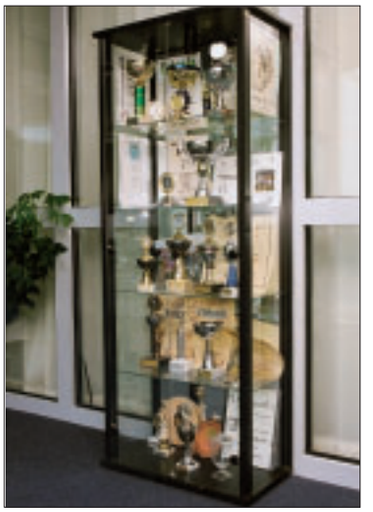

Sport keeps you fit. This applies to the staff at the DFG Head Office too. For over five years the DFG sports club has offered a varied fitness programme. Be it in football or volleyball, whether in gymnastics or athletics – it is impossible to overlook the success of their efforts. The cups and certificates that have been won for various competitions vie for space in this show-case.