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The bee's flight of victory

The western honey bee can be found also in Arabia. Its original geographic range was Europe, Africa, and Western Asia, but with human help, she was distributed worldwide. In this issue, Professor Dr Jürgen Tautz shows what we can learn from the bees.

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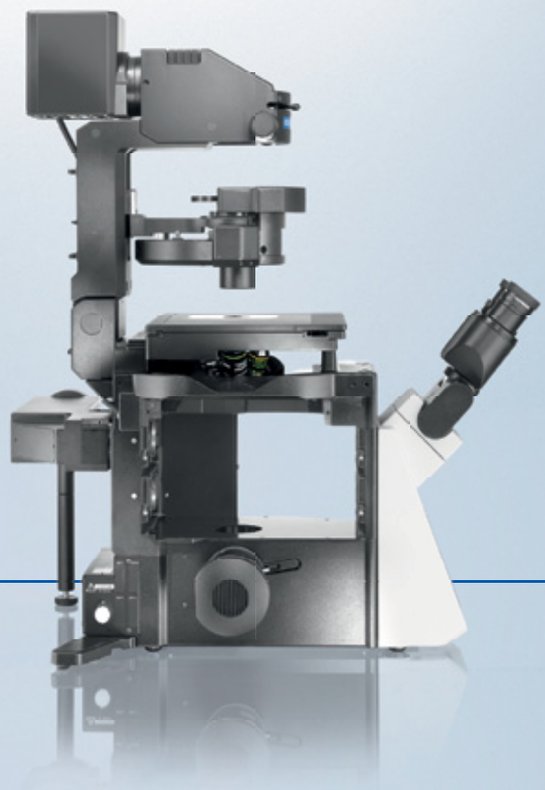


OLYMPUS
Your Vision, Our Future

editorial

Foto: © istockphoto.com | AdrianThomas

Only the Most Important Things

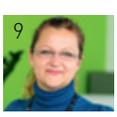
But that goes without saying, considering we really don't have time for incidental issues in this restless age. A fact which was also reflected at the 50th Security Conference recently held in Munich where top international politicians debated on a range of global issues. The list of current "hot spots" in international politics is now headed by the Ukraine, Syria, Iran and Thailand. In his opening speech, German President Joachim Gauck also appealed to Germany to assume more responsibility for open international order and to make it fit for the future. This task involves a major challenge as the world is changing faster than predicted by the futurologists and the speed of these changes is constantly being underestimated.

But the state of the world is not only determined by crises. The last few decades have seen fast-paced transformation towards peaceful sustainability in the Middle East. Since merging in 1971, an outstanding economic and social infrastructure has evolved in the United Arab Emirates (UAE), giving rise to one of the world's strongest and most interesting economic regions. Additional dynamism was introduced to the region in the form of the Gulf Cooperation Council federation of states creating growth and wealth by developing modern industries. But this is not entirely without loss. The other side of the coin of a high standard of living in highly-developed economies is represented by illness as a result of longer lives or unhealthy lifestyles. Diabetes and corresponding heart disease or cancer are the greatest challenges to be faced by the health sector and science. The Gulf States have recognised this and are investing heavily in health systems and information programmes for the population. The booming health sector offers enormous opportunities for research and industry and products "Made in Germany" are of particularly high regard in the Arab region.

Which brings us to the issues preoccupying us both professionally and personally. After all, health and economic success are of key significance for each individual. The new year – also regarded as of particular importance by the Chinese celebrating the Year of the Horse – has started and at lab&more Orient, this task will accompany us to this year's international trade fairs. It will take us back to Munich to the analytica in early April and bring lots of new ideas for research. We will be there and would like to present to you in this issue just how extensive the range of themes is. In this context, we would also like to offer our particular thanks to Prof. Fares M. Howari who will provide you with an up-to-date insight into research at the University of Abu Dhabi. And this goes very well with an event of ever increasing importance – the ArabLab – which kicks off the year for the international laboratory sector and which we are very much looking forward to again this year.

Jörg Peter Matthes
CEO, Publisher

content



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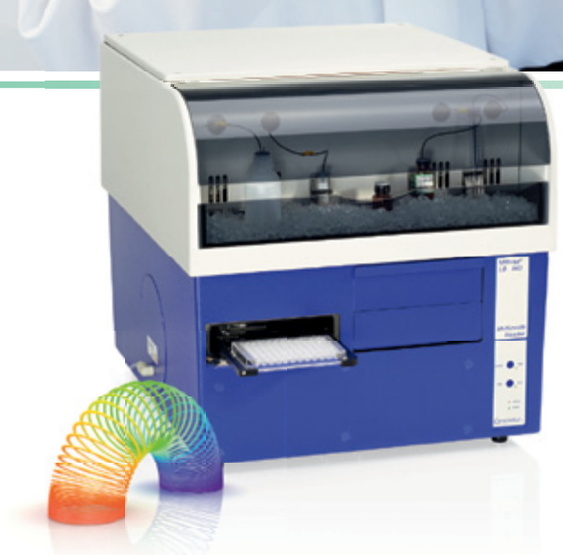

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cooperations

BASF and Petroleum Institute

Research Co-operation on Gas Scrubbing

Research co-operation agreed (from left): Tareq Sahoo, Vice-President Al Hosn Gas and Head of the PI Gas Sub-Committee; Dr Ismail Tag, Provost of the PI; Oliver Cullmann, BASF; Ralf Schröer, Deputy German Ambassador in Abu Dhabi
Fig.: BASF

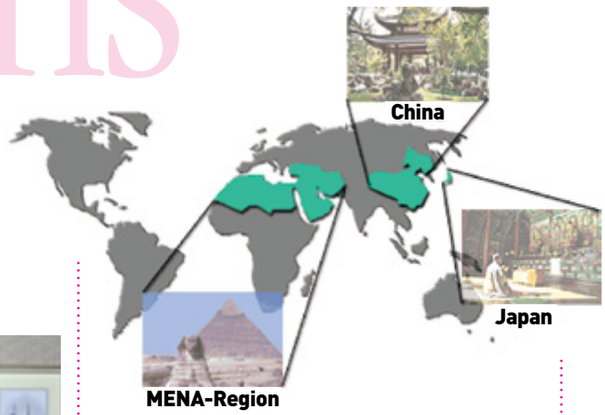
Within the framework of research co-operation, BASF and the Petroleum Institute (PI), Abu Dhabi, wish to develop new methods for removing aggressive sulphur compounds from so-called acid gases. Research by BASF and PI aims to focus on methods involving minimum energy consumption. Some examples include membranes which are already used for removing hydrogen sulphide (H_2S) and carbon dioxide (CO_2) from acid gases, as well as utilising adsorbents.

"We look forward to this collaboration as it will see the Petroleum Institute integrating its outstanding know-how in the research, development and production of membranes and sorbents", claims Dr Jens Rudolph, who is responsible for the Middle East in the OASE® gas scrubbing team at BASF.

Petroleum Institute: Engineer training and research

Based in Abu Dhabi, the capital of the United Arab Emirates, the PI was established in 2001 with the support of the Abu Dhabi National Oil Company (ADNOC). The PI concentrates on training engineers and researching in the area of the energy industry. With 1,200 students and 200 lecturers, the PI is one of the leading teaching and research facilities in the Middle East. Plans for 2014 include opening a research centre – the PI Research Center (PIRC) – on the PI campus. The gas scrubbing research projects at the PI are financed by the Gas Sub-Committee of the Abu Dhabi National Oil Company (ADNOC).

→ **www.basf.com**



International representatives of the Fraunhofer Life Sciences Group

International representatives

Fraunhofer Life Sciences Group

Within the framework of emphasising intercultural management in the Fraunhofer Life Sciences Group, international representatives of the Group work in their home countries in the MENA region, Japan and China.

Thanks to international representatives in the MENA region, it is possible to adequately apply the various biotechnology methods and processes with regard to peoples' needs. Water management and agrobiotechnology are of particular significance for the MENA region, for instance.

As the East-Asian Economic Community is continually gaining in relevance and Japan, Korea and China are striving towards their own East-Asian identity giving rise to a huge market, the Fraunhofer Life Sciences Group is focussing on this region.

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→ **www.lifesciences.fraunhofer.de/de/internationale_vertretungen.htm**

Cyber safety

Gulf States Called to Co-operate in the Area of Cyber Security

At the annual conference of the Research and Development Foundation in Qatar, experts called on the Gulf States to co-operate in the area of cyber security. Considering the political tension prevailing and increasing industrial espionage, these countries are not sufficiently protected from hacker attacks. And effective protection is only possible through co-operation. Qatar subsequently declared cyber security one of its top three research priorities.

Please refer to this article on the SciDev.Net online portal:

http://www.scidev.net/global/technology/news/gulf-countries-need-early-warning-on-cyber-attacks.html

→ **www.kooperation-international.de**

MPIP and KACST

Co-operation on Basic Research in Key Technologies

The Max Planck Institute for Polymer Research (MPI-P) in Mainz, Germany and the Saudi Arabian research facility King Abdulaziz City for Science and Technology (KACST) started an intensive scientific exchange in 2013. The co-operation programme will run until 2016 and has a total volume of around 2 million Euros. Researchers from the Desert Kingdom will often be seen in the laboratories of the MPI-P in the years to come. With approx. 3,000 employees, KACST is primarily oriented towards the direct economic requirements of Saudi Arabia whose future alignment is increasingly relying on developing technology as well as oil production and the petrochemical industry.

Prof. Katharina Landfester, describes the goals of the co-operation. Together with Prof. Klaus Müllen, she is actively responsible for the co-operation in the Institute.

Established in 1984, the Max Planck Institute for Polymer Research (MPI-P) is one of the leading international research centres in the area of polymer science.
KACST was opened in Riyadh in 1977 and unites a variety of research areas ranging from computer science to space exploration under the same roof.

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Collaborating partner:
King Abdulaziz City for Science and Technology (KACST)

→ **www.kacst.edu.sa/en/Pages/default.aspx**

Source: www.mpip-mainz.mpg.de

United Arab Emirates University

Scientific Research Grants for 2014 with a Value of (39) Million Dirhams

Dr Ali Rashid Al Noaimi,
Vice-Chancellor, United Arab Emirates University
Photo: © United Arab Emirates University

The UAE University announced support and funding for 116 research grants worth 39 million Dirhams, awarded to a group of researchers at the University who made presentations of innovative research to address important challenges in various scientific disciplines, through three categories; the "University Program for Advanced Research" (UPAR) Competition, the "Center-Based Interdisciplinary Competition" and the "Startup Competition". The latter two competitions were launched for the first time in 2014.

Dr Ali Rashid Al Noaimi, UAEU Vice-Chancellor, emphasised that according to the directives of His Highness Sheikh Hamdan bin Mabarak Al Nahayan, Minister of Higher Education and Scientific Research and Chancellor of UAEU, the University Administration is keen to continue supporting scientific research to strengthen its position among the most prestigious research universities, by encouraging faculty members and researchers at the University to present their ideas, innovations and research projects to contribute to providing innovative and effective solutions for the local community and humanity in general, which was embodied in the University's ranking the first among Arab countries, and (76th) globally among the best universities in the world by the "Times Higher Education World University Rankings 2013-2014".

→ **www.uaeu.ac.ae**

University of Gießen research project in Saudi Arabia

Desalination of Seawater Using Solar Energy

Like many other countries in the Gulf region, Saudi Arabia faces the major challenge of how to safeguard its water supplies in the future – desalination of seawater is one possibility and forms the starting point for the research project at the University of Gießen: seawater is to be desalinated using solar energy and then used in agriculture. The scientists in the team led by Prof. Dr Hans-Georg Frede at the University of Gießen are preoccupied with the question of the level of salt concentration required for seawater so as to avoid damage to crops. Issues relating to feasibility of modern desalination technologies are also up for discussion. Another area of the project involves the use of modern geographic information systems to examine the regions of Saudi Arabia – which is six times larger than Germany – in which such technologies can be applied.

The project avails of 838,000 Euro in funds and is scheduled to run for three years. It is financed by the Saudi King Abdulaziz City for Science and Technology (KACST) research facility in Riyadh. Some of the studies are carried out in the Interdisciplinary Research Centre (IFZ) at Justus Liebig University in Gießen while others are carried out in the coastal region of north-east Saudi Arabia, near Kuwait.

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→ **www.uni-giessen.de**

researched

Molecular biology

Waste Collection in Cells

Even cells need to dispose of their waste. The process responsible for this is called autophagy and can be described as packing waste (red) into a garbage bag (green), and observed in live cells under the microscope (top right).
Fig.: Copyright: Daniel Papinski

Not only our environment needs to be kept clean – our cells do, too. The process responsible for this is called autophagy whose key co-ordinator has been known for some time in the form of the Atg1 protein. The team led by Claudine Kraft at Max F. Perutz Laboratories (MFPL) at the University of Vienna is now drawing an even more accurate image of how "waste collection" occurs in cells. If this process does not work properly, Alzheimer's and cancer can ensue. The researchers demonstrated that Atg1 modifies a selection of proteins distinguished by a particular sequence tag which they deciphered as well as determining the cellular proteins with exactly this sequence. During this process, Atg9 attracted particular interest. When the researchers prevented Atg1 from modifying these components of the "garbage bag", the cells were unable to package their waste (Fig. bottom right).

Source:
www.univie.ac.at
Original publication: Molecular Cell, January 2014, DOI: 10.1016/j.molcel.2013.12.011

Medicine

Collaborative Project on Treating High Blood Pressure

A new collaborative project involving the Charité Medical School in Berlin examines the treatment of high blood pressure resistant to therapy using a special balloon catheter. Funded by the German Ministry of Education and Research (BMBF), the project entitled "Renal denervation with a coated balloon catheter" is being carried out in co-operation with InnoRa GmbH Berlin, a Charité spin-off, and the University of Saarland.

Contact:
Dr Jörg Schnorr, Radiology Institute, Charité Medical School, Berlin,
joerg.schnorr@charite.de
Source: www.charite.de

Nutrition

Fewer Soft Drinks – Lower Risk of Diabetes

A diet low in sugared soft drinks, meat products and white bread is associated with a reduced risk of type 2 diabetes. This is the result of a major long-term monitoring study examining the dietary habits of people in seven European countries. The study incorporated data on 21,616 men and women, 9,682 of whom developed type 2 diabetes during the monitoring period. In the study, the research team led by Janine Kröger and Matthias Schulze at the German Institute for Human Nutrition (DIfE) examined a total of five specific nutrition patterns with regard to the risk of diabetes.

Original publication:
Diabetologia, 2013, DOI: 10.1007/s00125-013-3092-9
Source: www.dife.de

Bee research

The Weaker Sex

Female worker bees and male drones (top right with larger bodies and eyes)
Photo: Geoffrey Williams, University of Berne

Honeybees are complex social organisms which demonstrate haplo-diploidy. The two female castes, workers and queens, are diploid like humans while male honeybees, also known as drones, are haploid and only have one chromosome set. According to the so-called "Haploid Susceptibility Hypothesis", this difference (haploid versus diploid) makes haploid males more susceptible to disease than their female counterparts as dominant genes on one chromosome copy have the opportunity to mask mutated genes on the other copy in diploid organisms. The research team led by Geoffrey Williams and Peter Neumann from the Vetsuisse Faculty of the University of Berne now shows that male honeybees die sooner and in a worse physical condition than females when infected with the exotic intestinal parasite Nosema ceranae.

The study was a component of the international BEE DOC ("Bees in Europe and the Decline of Honeybee Colonies") project of the European Union and represented collaboration by researchers from the Institute of Bee Health at the University of Berne, the Swiss Bee Research Centre (Agroscope, Swiss Confederation) and the Department of Ecology (Swedish University of Agricultural Sciences).

Source: www.unibe.ch
Original publication: PLOS ONE, 17 January 2014, DOI: 10.1371/journal.pone.008526

Biotechnology

Transporting Live Cells Gently

Scientists are often obliged to exchange cell cultures with colleagues in other institutes, with industrial partners or customers. The material is often transported in a frozen state. Cells can incur irreparable damage during freezing and later defrosting. Researchers at the Fraunhofer Marine Biotechnology Facility have designed an autonomous transport box enabling the careful transport of live cells under optimum culture conditions. Registered for patent, the mini-incubator is lightweight and no larger than a cardboard box. An internal lithium-ferrum battery powers the electronic heating and CO_2 supply while integrated sensors monitor and save these parameters.

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Dr Hans-Peter Spengler, hans-peter.spengler@emb.fraunhofer.de;
Dr Daniel H. Rapoport, daniel.rapoport@emb.fraunhofer.de
Source: www.fraunhofer.de

Bioplastics

Development of Bio-based Plasticisers

Plasticisers are among the best-selling chemicals in the world; by 2018 demand will increase to more than 7.6 million tonnes per year (market study on plasticisers 11/2013, Ceresana Research). In many applications however, phthalate-based plasticisers making the headlines have been substituted by new substances. Material designers at Fraunhofer UMSICHT have succeeded in converting the phthalate-based plasticisers in the wood-based bioplastic cellulose acetate into bio-based and environmentally-compatible plasticiser systems as well as obtaining food industry approval for these modern plastics.

Source: www.umsicht.fraunhofer.de

Biochemistry

Indications of Harmful Effect of Plastics Containing Bisphenol A

Bisphenol A impairs the function of proteins decisive for growth processes in cells. This is reported by researchers at the Ruhr University of Bochum and the Bergische University of Wuppertal. Abbreviated as BPA, the substance is present in many plastic products and is suspected of being harmful to health. To date, it has been assumed that Bisphenol A binds to hormone receptors thereby unleashing its harmful effect. The team of chemists and biochemists discovered that the substance also has an effect on the so-called small GTPases. Scientific studies indicate that BPA could be conducive to cardiovascular diseases, breast and prostate cancer as well as neuronal diseases. The use of plastic food containers containing Bisphenol A should therefore be restricted, according to recommendations by the researchers.

Source www.ruhr-uni-bochum.de
Original publication: Journal of Medicinal Chemistry, 2013, DOI: 10.1021/jm401291q

Algae as Biodiesel Source

Characterization of Algal Organic Matter and their Biofuels Potential in Abu Dhabi, United Arab Emirates

Prof. Dr Fares M. Howari, Applied Sciences and Mathematic,
College of Art and Sciences, Abu Dhabi University, Abu Dhabi, UAE

The need for alternative fuel sources is urgent as evinced by the worldwide declining of major hydrocarbon reservoirs, the high demand on hydrocarbon and associated environmental problems. Algae based biofuels or biodiesel are among the strongest options to serve as an alternative source of hydrocarbon. Biodiesel burns 50% cleaner than conventional petroleum-derived diesel [1] and can be used in any diesel engine with little to no modification [2]. The United Arab Emirates (UAE) has set a goal of reaching 7% of energy demand provided by renewable sources by 2030, and algae based fuel are one of the options. UAE especially Abu Dhabi has strong potential for biofuel production from algae. It is mainly because UAE coast has favorable environment and geological conditions necessary for commercial production of this fuel. It has: 1) large barren coastal landscape, 2) plenty of sunlight, 3) saline water, and 4) presence of coastal and inland sabkhas (salt-flat areas) that has thick algal mat cover.

Though bio-fuel is not a new and has been in production in countries like USA and some other European countries; it has been mainly produced from soybean (USA) and rapeseed (European Countries). Producing bio-fuel from algae is relatively a new approach which is creating interest among the scientific communities all over the world. Bio-fuel derived from micro-algae has many advantages over bio-fuels produced from soybean or rapeseed. Most primarily, algae grow naturally and abundantly in coastal areas near the seas and also in the sabkhas. Unlike soybean or rapeseed, one would not have to water or provide fertilizers to grow algae. This reduces the environmental impact on Earth. By just replicating the natural conditions, algae can be cultivated for production of bio-fuel. Selecting the right technique and procedures coupled with the use of appropriate instruments, algal oil can be extracted and thus produce bio-fuels from algae becomes possible. Is this enough? If one sees it from a laboratory point of view, the main aim might be to just successfully extract algal oil no matter how minimal the quantity compared to the raw materials needed. But once investors or industrial engineers want to convert it into a commercial venture, then lot of factors come into play. The most important factor is the yield. This research has two folds the first focus on characterization of algae, and the second assesses the feasibility of algae culture in Abu Dhabi. Highlights from the first part will be presented in this short article.

Objective and application

The objective of this ongoing research is to find out if it is economically viable to harvest the algae growing naturally in Abu Dhabi coastal areas and the sabkhas in order to extract oils from them to convert into biofuels. It is therefore necessary to identify and classify the algal species growing naturally in the sabkhas and coastal areas of Abu Dhabi to assess their potential as an oil producing crop and ultimately as alternate source of fuel. The main application of this research is to provide investors with facts and figures about the commercial harvesting and production of biofuels in order to show that it can be a profitable entity. There are many species of algae available and each one can provide different quantity of oil for biofuels. It is therefore

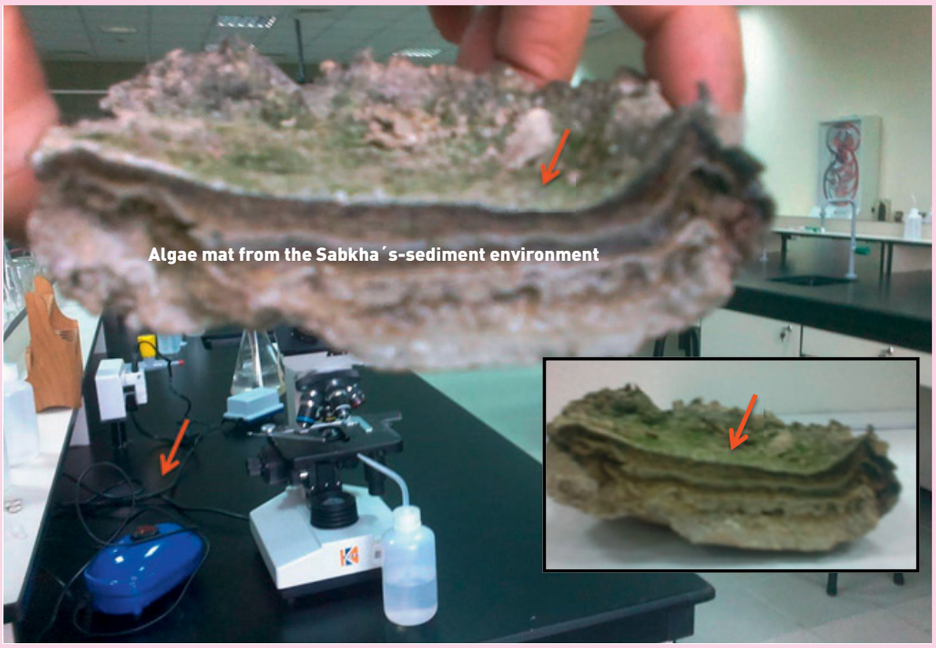


Fig.1 Algae mat from the Sabkha's-sediment environment

Fig.2 Naturally grown algal mat in selected areas, Abu Dhabi

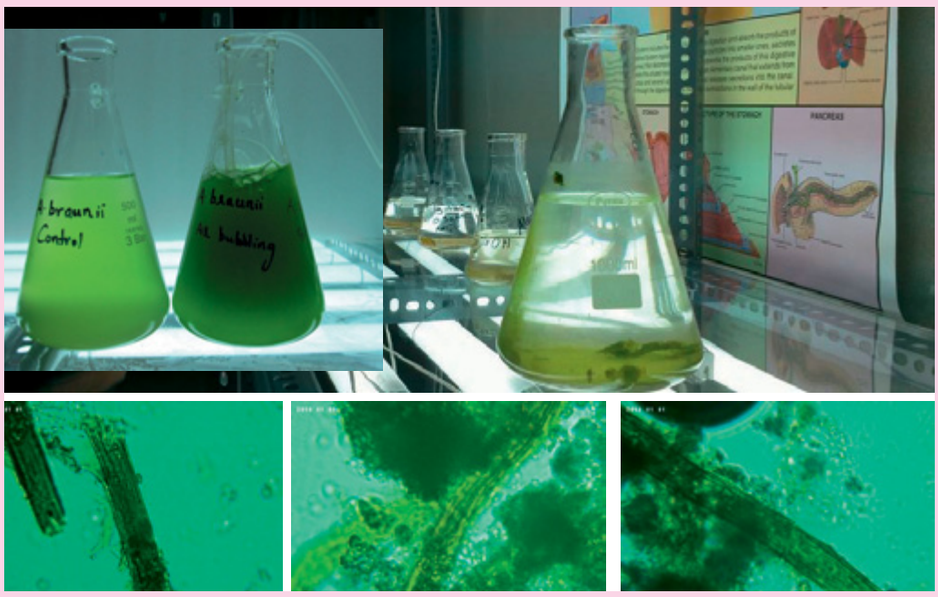
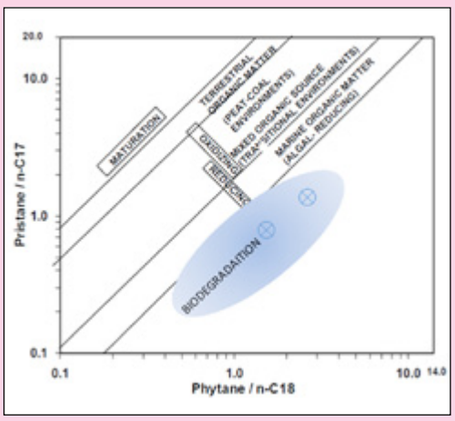


Fig.3 Treatment of algae collected from water bodies, Abu Dhabi



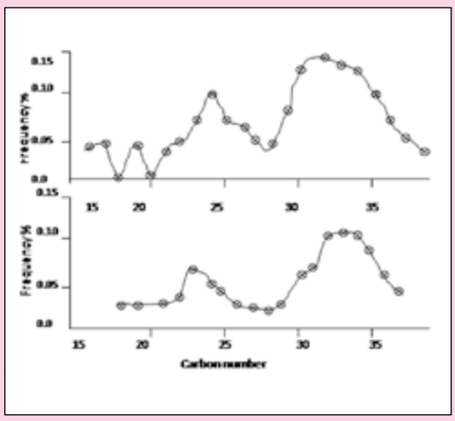


Fig.5 Carbon number and maturity of organic matter

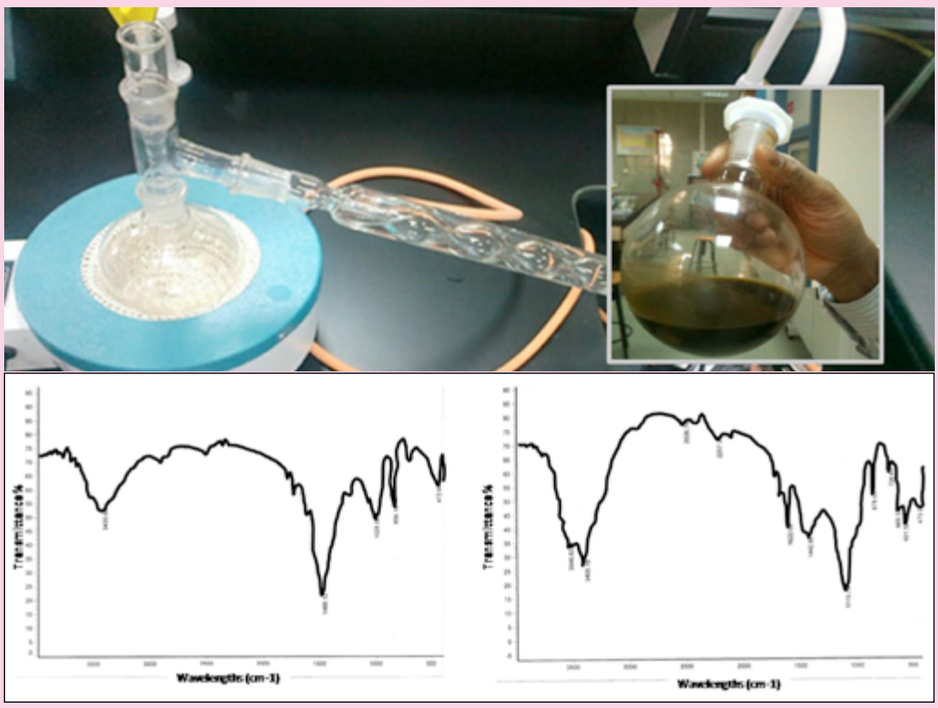


Fig.4 Functional group in algal mat of Abu Abu Dhabi

necessary to harvest those species which can yield large amounts of biofuels. This short article will highlight only the technical part of this ongoing research project that emphases on the quality and characterization of algae organic matter.

Characterization of algal organic matter

The present study assessed the potential of coastal algae in UAE for biofuel potential. Algal samples were collected from irrigation return flow, from sea shore, and mangrove fields. We placed the pieces of algal inside a glass petridishes (14 x 2 cm) and in glass trays (30 x 22 x 5 cm) wetted the bottom part with tap water to prevent their dehydration and incubated at 25 +/- 10 C. To augment the illumination in lab, illuminated stand were designed to enhance algal growth. Dimensions were 200 x 200 x 50 cm. Frames of the stand were perforated angle post (bolted with shelving arms). Illumination source is 1.2 ± 0.2 Klux light intensity total of 24 long fluorescence tube lights. The shelves of the stand were fixed with 8 mm tampered clear glass with the size of 50 x 100 cm. Isolations and purification were done by serial dilution followed by plating and individual colonies are isolated and inoculated. The study focused on green algae and the dark type algae communities that are associated with the Sabkha's environment (Fig. 1–3). Toward this end, the following tasks were carried out: i) isolation of algae culture, ii) screening of algal culture for biodiesel and iii) extraction of biodiesel. The dry mass factor, lipid content, etc were determined. The biomass of algae was measured by counting their amount under a microscope and the ratio of their amount, and other methods reported in literature [3].

The black and organic part of the algal mat from the sabkha's sediment have been carefully separated and weighed.Then were filled in a cellulose thimble and taken for Soxhlet extraction. We used different solvents for the extraction: 1) chloroform – methanol mixture (2:1 ratio), 2) methanol – chloroform mixture (2:1 ratio), 3) chloroform alone, 4) methanol alone, and 5) hexane. After the extraction, the samples are undertaken for distillation and separated the different types of organic material from the Algal mat samples. The extracts were analyzed using GS/FID (Varian CP-3800GC) as well as with Nicolet FT-IR spectrometer.

Fares M. Howari was born in Jordan and studied Environmental and Earth Sciences at Yarmouk University, and the University of Texas at El Paso. He completed his PhD in 2000/01 from UTEP; then he became a naturalized United States citizen. He worked as post-doc at the Texas A and M University, and then joined UAE University where here served as assistant and then associate professor of environmental sciences. After that, he served as a professor of environmental sciences and engineering; and coordinator of environmental sciences program at the University of Texas (UTPB). He also joined the Center for International Energy and Environmental Policy as Middle East program coordinator, and as an Environmental Scientist at the Bureau of Economic Geology at the University of Texas at Austin. Currently he serves as Professor and Chair of the Department of Applied Sciences and Mathematics at Abu Dhabi University, and Director of Abu Dhabi University Center of Excellence of Environment, Health and Safety. He started his carrier working on technical issues of soil, water and the environment, and evolved to coordinate, and direct large research programs; his interest emerged to include policy and social aspects of natural resources management. In 2004, he received recognition award from Minister of Higher Education and Scientific Research of the UAE, and in 2008, he received the Bureau of Economic Geology, Texas Author Achievement Award.

The analyses of the FT-IR data show (Fig.4) that the prominent peaks in the functional group region are common in all the given samples [4]. Also the data do not show much absorptions in the finger print region which indicates that the samples are pure, and the profile indicates the presence of:

- Hydroxyl group -OH, characterized by the strong absorption centered around 3423 cm-1
- -CH2 groups of lipids is characterized by the absorption seen around 2521–2923 cm-1
- -CH3 groups of lipids are characterized by the strong absorption band at 1443 – 1473 cm-1
- Carbonyl group is indicated by the absorption band at 1629–1787 cm-1

The absorption peaks around 1131 –1200 cm-1 indicate the ant symmetric axial stretching vibrations of carbonyl bonds of the ester. The Carbon Preference Index of the studied samples is more than one which indicate immature recent materials. The reported results from the algal mat are very promising and present the algal mat of Abu Dhabi coast as immature source material of hydrocarbon (Fig.5). Currently we are conducting comparisons between the newly grown algae on the designed stands and algal mat samples. Currently, we are conducting different treatment, and it is believed that the algal mat potential to yield hydrocarbon can be strengthened after treating algae with CO_2. Thus algae treated CO_2 under controlled and field conditions are under study to be used as a reference point for optimal conditions of large scale projects or for deployment of algae-based technology to Abu Dhabi coasts. Our ongoing bench-scale scale studies are essential in order to design an open pond scenario.

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High Precision and Speed

JULABO Temperature Control Solutions

JULABO presents an extensive program of temperature control solutions ranging from -95 to +400 °C. Since JULABO's foundation in 1967 the company has pioneered the development of technology for liquid temperature control. JULABO equipment is used successfully around the world providing application solutions for science, laboratories, technology centers and process industries. During every step of development and production JULABO equipment has to meet high quality criteria and its "made in Germany" technology reliably fulfills customers' requirements.

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JULABO's product range includes temperature control systems for a variety of applications. Heating and refrigerated circulators accomplish almost every temperature control application with temperatures ranging from -95 to +400 °C and are available in many variants. JULABO water baths are high-quality and durable products, with a working temperature range from 20 to 99.9 °C, equipped with the latest microprocessor technology. In laboratories they are ideal for temperature control of samples, incubations, material testing, corrosion tests, cell cultivation or testing of food and beverages. State-of-the-art heating and refrigerated circulators by JULABO rapid and precise temperature control for a wide range of applications. Devices such as jacketed reactor vessels can be controlled within a temperature range from -92 to +250 °C. JULABO recirculating coolers are used for a variety of cooling applications in laboratories and industry. Users may choose from a large range of air or water cooled models with cooling capacities from 0.3 to 20 kW. JULABO also offers specialized equipment for individual applications and an extensive list of accessories for all products.

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JULABO takes pride in offering customers expert advice for pairing the proper JULABO temperature control solution to their specific application. JULABO service and support options include installation and calibration, equipment qualification documentation and application training. These invaluable services ensure customer confidence in the operation and maintenance of their JULABO unit.

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JULABO units function reliably providing years of operation with quality at your fingertips. Every unit meets strict internal requirements and conforms to the highest national, European and international standards. Each JULABO instrument must pass numerous tests in every production phase. A sophisticated quality management program in accordance with DIN EN ISO 9001 guidelines guarantees that only technologically superior products are shipped from our facility. Find comprehensive information on the JULABO program in the current catalog.

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ecology

Light in the Darkness

Learning from honeybees: live observation in the beehive

Prof. Dr Jürgen Tautz, Bernhard Schneider and Kristina Vonend
University of Würzburg Biocenter

Inside a beehive it is warm – and utterly dark. The hive members function like a highly complex organism. Some 50,000 individuals live cheek-by-jowl and yet still have room to move. Thanks to the ingenious division of labour, it's more a case of "busy as a hive" than "busy as a bee". Usually, what occurs in a beehive remains hidden from human view. Not so with HOBOS (HOneyBee Online Studies), the online research platform launched by our team. Specialised cameras operating at specific wavelengths of light enable us to look deep into the hive interior – without any risk that we might disturb the honeybees. Anyone can now view the natural behaviour of the bees in real time.

It's September 10th, 11:06 AM. The air temperature is 24.6 °C in the garden where the Würzburg Bee Station is sited and solar radiation is 668.10 watts/m². Precipitation is zero. Returning home, a forager bee lands on the hive's bottom board. The camera at the hive entrance films her while – simultaneously – a thermal imaging camera renders the bee's invisible thermal emissions visible to the human eye: the honeybee is shown in white, as the brightest and warmest area of the thermogram. She has flown from flower to flower, where she has sucked up energy in the form of sweet nectar into her honey sac, which she now wants to deliver within her hive. As she passes through the bidirectional photoelectric barrier and enters the hive she is counted automatically. She is one of 32 bees who enter the hive every minute. She has handled many different tasks in the hive before becoming a forager. In her first three days of life, for example, she worked on tasks in the central brood chamber. She was filmed here earlier, in fact – by the two endoscopic cameras that record events deep in the hive both day and night.

Long-term knowledge creation

With HOBOS, the honeybees are the stars, since they play a key role in the natural ecosystem and are an irreplaceable factor in terms of human food production. Following cattle and swine as our third most important domesticated animal, honeybees and their pollination underpin a quarter of plant-derived foodstuffs worldwide and yet are now under threat: disease, the introduction of insect pests such as the Varroa mite and habitat loss has made life very difficult for the honeybee. The HOBOS platform enables research scientists to perform observations on a real-life working honeybee colony. Live images and readings taken from the hive and its surroundings can be accessed and correlated with one another. Time frames can be chosen as required. The diagrams that result make the highly-complex life and times of the honeybee – and its natural context – plainly visible.

Accordingly, the project is making a contribution to cumulative honeybee research. This knowledge is needed today, since the future of our planet depends on the sound, sustainable handling of the biosphere by humankind. For these reasons, our bee research group has hooked up a real-life honeybee colony to the Internet. The platform has been in existence in preliminary form since 2009 and gives school pupils, teachers, students and beekeepers all over the world a completely new angle on the honeybee's world.

High-tech in the beehive

An array of cameras and sensors permit the highly-detailed study of a living bee colony and its environment. HOBOS provides live video streams via a camera at the hive entrance with infrared capabili-

ties, a thermal imaging camera, two endoscope cameras with microphones that film the hive box and bottom board (fig. 1) and an infrared-capable camera that logs environmental and weather conditions in the garden.

Data streams – both real-time and historical – are also offered on the bee colony, vegetation and weather conditions. Parameters relating to the hive weight, relative humidity and temperature, temperatures in the eleven gaps between the frames (fig. 2), the temperature at the front and back of the hive, and incoming and outgoing honeybees can also be reviewed. Supplementing the hive data are readings

Jürgen Tautz graduated in biology, geography and physics before receiving his doctorate from the University of Konstanz on an ecology-related subject. Work in insect, fish and frog bio-acoustics was followed by his foundation of the BEEgroup at the University of Würzburg, a group that focuses on basic research in honeybee biology. Alongside his scientific work (author of around 140 publications to date, including 30 cover articles in journals such as Science and Nature), Jürgen Tautz also pursues a successful career in public relations work, where he strives to interest the general public in life sciences research. In 2005, 2007 and 2008, his work in this field was recognised by EMBO, honouring him as one of Europe's leading science communicators. A further accolade Tautz received in 2012 was the Communicator Award from the DFG and the Donors' Association for the Promotion of Sciences and Humanities in Germany.

Kristina Vonend studied at the University of Würzburg, where she graduated with a master's in German Studies and Cultural Anthropology. Following her traineeship, she completed further training as a press liaison officer at the Academy of Journalism in Munich. From 2010, she has worked as a freelancer in the press and public relations sector and is responsible for press and online content in the HOBOS team.

taken from the hive's immediate vicinity. These include air pressure, temperature and humidity, the atmospheric electric field strength, precipitation, wind speed and direction, solar radiation, soil moisture and leaf wetness (fig. 3).

A new way to learn

Honeybees are appealing, highly motivational and quick to arouse interest. They offer an extremely rich biology, from simple facts to highly-complex phenomena. Today and in the future, the independent acquisition and dissemination of knowledge has been made easier by the Internet – the medium for kids and young people. The innovative project permits the online study of this important human-interest insect.

HOBOS assumes no prior knowledge whatsoever: basic information about the honeybee is offered online, as are teaching materials for inter-disciplinary classwork in schools. After all, the honeybee brings together a wide range of scientific disciplines: its nature is biology, its flight is physics, its behaviour is sociology, its honeycomb building ingenious architecture and, thanks to its signal importance for humankind, the bee has always inspired artistic expression. Accordingly, the project offers lesson plans for a wide range of faculties and types of schools. To date, teaching materials are available for mathematics, art and biology. The bilingual website also ensures that the platform can be used internationally. This facilitates global cooperation between schools, enabling pupils to discuss bee-related knowledge beyond their country's borders.

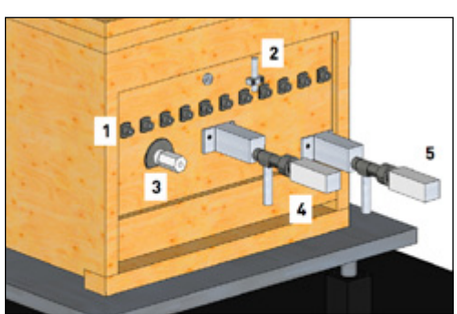
The power of observation

New discoveries result simply from the sheer volume of video and data files. After all, just by watching the recordings and looking at the data logs, questions quickly arise – and answers to match them:

- When do the first forager bees set off in the morning?
- How heavy is the beehive when food has been stored for the winter?
- What do honeybees do in winter?
- How are worker bees fed who are active in the central brood chamber?
- What sound does a young queen bee make just before she hatches?
- How hot is it in the centre of a beehive and how warm is it at the edges of the combs?
- Where do worker bees have their wax glands, which they use to secrete wax platelets for constructing a new honeycomb? (fig. 4)
- When a storm threatens, how fast do honeybees return to the bee colony?

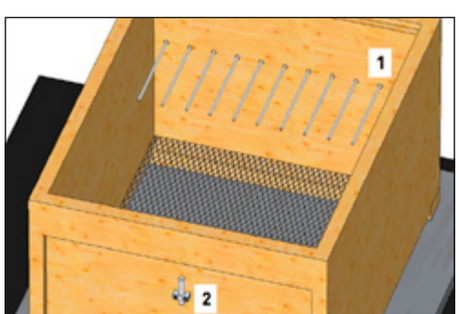
More complex investigations

HOBOS opens up new horizons for both researchers and non-scientists alike. Since all data is stored over a multi-year time frame, this permits not only high-resolution temporal observations, but also the discovery and tracking of long-term trends in the complex interplay between the hive super-



1 temperature sensor 1–11 in the frame gaps
2 temperature sensor back of the beehive
3 humidity sensor
4 endoscope camera frame
5 endoscope camera grid floor

Fig. 1 The two endoscope cameras that offer views of the colony interior are attached to the back of the beehive.



1 temperature sensor 1–11 in the frame gaps
2 temperature sensor front of the beehive

Fig. 2 The opened beehive, showing temperature sensors 1–11 in the frame gaps.

Bernhard Schneider joined the HOBOS team for his research in e-learning technologies. Before that he has worked for over eleven years in Computer Sciences. He received a M.Sc. and a diploma in business informatics at the University of Wuerzburg and the GSO University of Applied Sience in Nuernberg. He is a frequent speaker at academic events.

organism and its immediate environment. Any feasible analysis and correlation of the recorded events can be performed. Theories can be proposed and investigated, or the user can simply make use of sample project proposals and learning materials – just as Christoph Bauer, Biology and Chemistry tutor at Würzburg's Deutschhaus Grammar School has done.

As part of the nature and technology curriculum for year six, Christoph Bauer spent a double period with his pupils looking at the topic of thermoregulation in the honeybee hive – with HOBOS at the heart of the lesson. Bauer and his students compared temperature data recorded inside the beehive with temperature data recorded outside the colony on a warm and a cold summer's day. The basis for these investigations was the project proposal on the topic of temperature regulation in the hive and the readings provided by HOBOS. Bauer reports that the lesson was highly successful, with Internet-based learning being especially appealing to his pupils. In the future, HOBOS will become an integral part of the gifted child programme at the Deutschhaus Grammar School and an evolving e-learning project.

New scientific insights

The volume of data enables the acquisition of entirely new observations and measurements related to the hive. One example is the discovery of "heat peaks" in winter 2012. A heat peak is a key peak value that can be achieved by heating of the winter cluster. Temperature readings from HOBOS provided the first documentary evidence that, from 28 January 2012, specialised "heater bees" were deployed at multi-day intervals to heat the cluster from 28 °C to 30 °C over an entire day, before letting the cluster cool down again.

Outlook

There's still much to discover about the hive. A satellite station in Aura an der Saale is planned, which will be able to give the main site at the University of Würzburg a broad spectrum of reference values. The aim of our non-profit project is to be able to continue to provide important data about the honeybee into the future with the help of sponsors. This will enable us to keep tabs on our forager bee: she's just delivered her haul to a handler bee in the beehive and she's now leaving the colony again, to visit her flowers and forage for a new sacful of nectar.

→ **tautz@biozentrum.uni-wuerzburg.de**
→ **bernhard.schneider@biozentrum.uni-wuerzburg.de**
→ **kontakt@vonend.com**

Photos: © Helga R. Heilmann

Creating connections – supporting honeybee research

The HOBOS (HOneyBee Online Studies) Würzburg honeybee project has been developed and directed since 2006 by Professor Jürgen Tautz. With the help of this interactive learning portal, anyone can keep tabs on the private life of a beehive equipped with the very latest technology. The platform also offers a wide range of environmental readings (weather, vegetation, soil), thus showing many aspects of ecology and sustainability that are of vital human interest. Conceived as a global endeavour, the portal has received many awards – from UNESCO among others. Since 2011, the official patron of HOBOS has been HRH Princess Basma bint Ali of Jordan. The non-profit project is supported by sponsors and partners, and welcomes new sources of funding that enable it to continue its work.

www.hobos.de

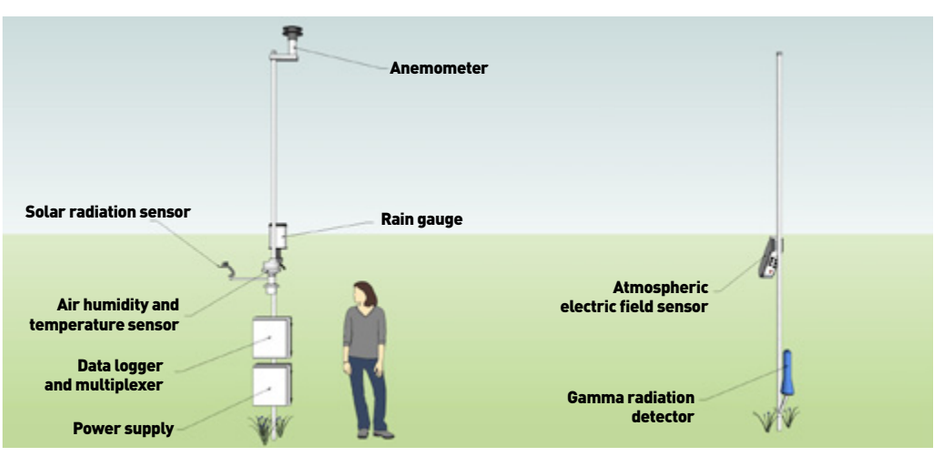


Fig. 3 The environmental sensor array in the bee project garden consists of weather instrumentation and a flash detector for the atmospheric electric field. The weather instrumentation measures soil moisture, air pressure, temperature, air humidity, solar radiation, precipitation, leaf wetness and wind parameters. Data is recorded using a data logger. The system is equipped with an autonomous power supply.

Fig. 4 To construct new honeycombs, wax platelets must be secreted. These are then handed to constructor bees who install them, working from top to bottom in the comb.

HOBOS' Prominent Patroness

The story of HOBOS started with a successful book entitled "The Buzz about Bees" written by Prof. Dr. Jürgen Tautz in 2008. This unique book about the superorganism (the honey bee colony) was translated into 15 languages within one year. One of these languages was Arabic. It was translated by Dr. Nizar Haddad, a scientist from the Hashemite Kingdom of Jordan. The Arabic translation of the book won a prestigious award in applied and basic sciences. The Arabic version of the book saw the light only due to the visionary leadership of Sheikh Mohammed bin Rashid Al Maktoum and his initiatives to develop the Arabic scientific library.

The deep conviction of Prof. Tautz, his team and Dr. Haddad that it is becoming more crucial to simplify basic sciences to make them more accessible and understandable to various levels of education and from different cultures and backgrounds, led to the development of HOBOS project. This project was honoured by Her Royal Highness Princess bint Ali who agreed to be its Patroness. She is a cousin of His Majesty King Abdullah II of Jordan. HRH is an environmentalist of international renown who plays an active role as founder and president in many non-profit projects and organizations that are related to sustainable development and the environment. By doing this, she raises the public's awareness for protecting the environment and has been granted many prizes for her deeds, e. g. the King Hussein Gold Medal for outstanding achievements.

HOBOS is not just a website, it is a project that works through three components

1. Online education: HOBOS is a real-time gateway to a real honeybee colony and its environment. It gives data from within the hive and its environment including climate, soil and vegetation. Storing all of the data over a period of several years allows long-term trends of complex inter-relationships to be followed. The HOBOS website is already receiving over 300,000 visits monthly, and thousands of schools from around the world are aware of HOBOS. Some have even integrated it into their curriculum.

2. HOBOS allows for a cross-cultural approach. The HOBOS team facilitates worldwide connections between school teachers and children providing them with questions to be answered using the HOBOS online database. This database gets visits from almost 100 nations.

3. Bee gardens and exhibitions: The HOBOS group has developed an exhibition which can be used for interactive discovery of a live beehive: learning about its outstanding contribution to the ecosystem through pollination and sustainable development through the various products the bees provide. Her Royal Highness Princess Basma bint Ali works closely with us in order to integrate a Royal Bee Garden inside the Royal Botanical Garden of Jordan (www.royalbotanicgarden.org). There is another exhibition in Luxembourg which has been seen by almost every pupil and a third one in Germany which has been visited by more than 10,000 children. What's more, we have printed thousands of posters that are distributed free of charge to schools in the Middle East region. These posters spotlight the value of honeybees for the ecosystem as pollinators of wild flora, agricultural crops and the value of beehive products.

Princess Basma bint Ali of Jordan supports the HOBOS bee project in Würzburg, Germany, in her capacity as patroness, and champions the project in public, especially at international level.

Nizar Haddad, Director of the Bee Research Department at the National Center for Agricultural Research and Extension, manages the use of HOBOS in the Near East and North Africa Region.

A group of guests visiting the Bee Research Station in northern Jordan.
The background depicts part of the exhibition made from HOBOS materials.
(photo: private)

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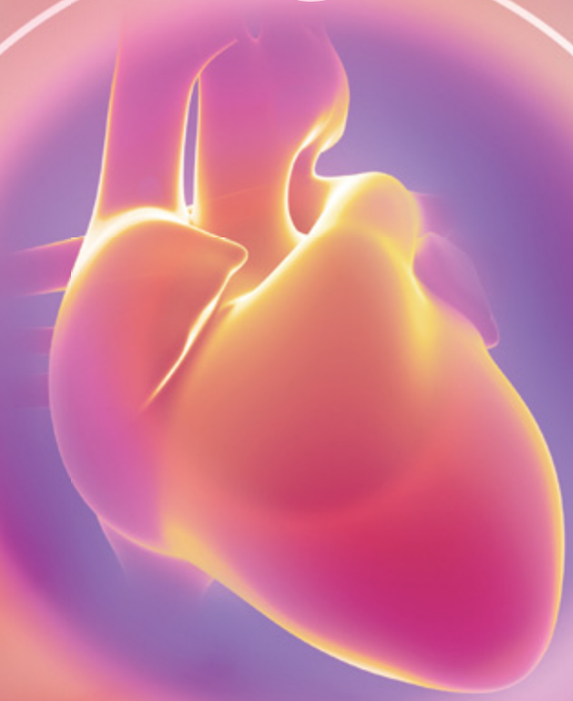


A Heart in a Petri Dish

Re-creating cardiac tissue

Prof. Dr Marko D. Mihovilovic
Institute for Applied Synthetic Chemistry, Vienna University of Technology

For medical research in the 21st century, regenerative medicine offers one of the most promising futures and prospects for further development. Revolutionary results have already been achieved by the efforts of genetic engineering, although ethical and regulatory aspects mean that such methods are unlikely to see widespread deployment. A complementary approach is now being pursued by the application of small-molecule compounds: a rapidly growing number of organic molecules are now available, which can influence the maturation processes by which precursor cells become specific types of tissue. This opens up the door to treatment techniques that are based on the basic principles of "normal" pharmaceuticals.

Depending on the type of tissue involved, the human body varies greatly in its ability to regenerate damaged organs. While skin and the liver possess highly advanced healing mechanisms, for example, at the other end of the spectrum we have neurons and cardiac muscle cells, which have very limited capabilities for self-repair. Such distinctions are increasingly playing a role due to a trend towards rising life expectancy, especially in developed countries: a fulfilling life in old age can only be ensured if as many bodily functions as possible are in good working order. As a consequence, particular attention is being made to research work that addresses the regeneration of organ function after suffering damage. For some disease conditions found in civilised societies (such as heart failure, neurodegenerative diseases and diabetes), there are currently no treatment options available that lead to a complete recovery of original organ function.

New insights into cell differentiation

Regenerative medicine concerns itself precisely with these research topics and objectives. During recent years, groundbreaking results have been achieved in this field. On the one hand, we have considerably improved our understanding of the processes by which precursor cells differentiate into mature tissue and organs (see sidebar: "Precursor cell types"). On the other hand, these insights have led to new pathways to treatment options that restore the original tissue function. Most of the approaches in this area to date have followed strategies based on "re-programming" cells by the targeted introduction of transcription factors. Thanks to these studies, our knowledge about cell differentiation has dramatically increased over the last few years. Genetic engineering of this kind is generally suitable only as a research tool, however: the likelihood of broad therapeutic application seems questionable, given the ethical aspects and regulatory conditions governing its use.

Yet, due to our growing knowledge of differentiation processes in cells at a molecular level and the related screening techniques that are now becoming available, recent years have witnessed the discovery of a steadily increasing number of small-molecule compounds capable of influencing cell maturation towards specific types of tissue. As these kinds of compounds resemble standard active pharmaceutical ingredients (APIs), they offer considerable advantages in terms of their broad application in medicine: (i) When developing an active ingredient of this type, one can draw on an established body of knowledge from pharmaceutical chemistry. (ii) Well-established approval processes exist for small-molecule drug substances, for the market launch of these APIs as products following an appropriate review of their benefit-risk profile. (iii) Treatment can be administered over a specific period without making genetic modifications to the organism being treated.

Precursor cell types

Omnipotent/totipotent stem cells:
can differentiate into any type of cell;
an entire organism can grow from just a single cell.

Pluripotent stem cells:
can differentiate into almost any type of cell found in the three germ layers;
often a synonym for embryonic stem cells.

Multipotent stem cells:
can differentiate into a range of cell types found in a specific kind of tissue.

Oligopotent cells:
are able to differentiate into a few types of cells found in a specific kind of tissue.

Unipotent cells:
can only produce cells of the same type.

Tissue from the test tube. The treatment of the patient's own cellular material with small-molecule APIs could lead to the functional repair of damaged organs in the foreseeable future. *Photo: VUT*

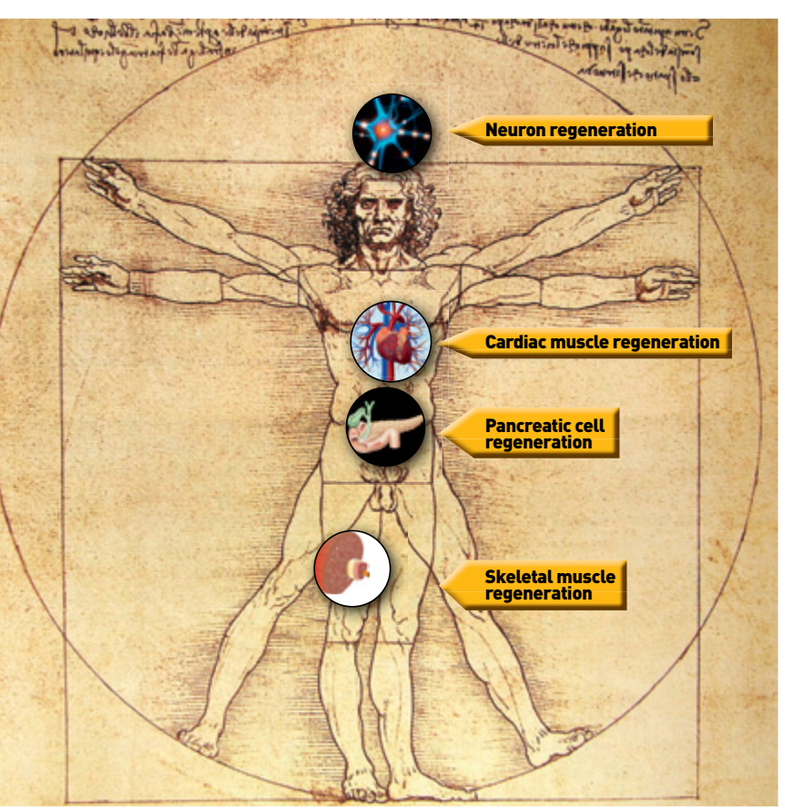
Marko D. Mihovilovic graduated in technical chemistry at the Vienna University of Technology in 1993, also receiving his doctorate from the same university in 1996, in the field of organic synthetic chemistry. Post-doc placements as an Erwin Schrödinger scholarship holder then followed at the University of New Brunswick (Canada) and the University of Florida (USA), in the fields of biocatalysis and molecular biology. Returning to VUT, he set up his own research group in 1999. He completed his habilitation in 2003 in bio-organic chemistry and was appointed Associate Professor in 2004. Marko Mihovilovic has been Head of the Institute for Applied Synthetic Chemistry at VUT since 2003 and was recently appointed as Full Professor for Bioorganic Synthetic Chemistry (February 2014).

Lead substances for cardiac muscle cells

The regeneration of damaged cardiac muscle tissue is of particular significance for industrialised nations, since heart failure and its consequential effects make up one of the three leading causes of death in such countries. In this context, the discovery of Cardiogenol C [1] as a hit compound by a team of researchers in the USA truly catalysed work in this area (see sidebar: "Small molecules for tissue regeneration"). This compound is capable of inducing embryonic stem cells to differentiate into cardiac muscle cells. While this effect had already been discovered for naturally-occurring substances such as retinoic acids, the latter compounds often trigger non-selective differentiation into a range of tissue types.

Basing our work on these results with Cardiogenol C, we have spent the last few years conducting a systematic investigation of this class of compounds. Medicinal chemistry techniques such as "bioisostery" featured strongly in such work. This method replaces structural aspects of the lead substance with functional groups possessing certain similarities but also slight variations in terms of their physical chemical properties: the goal is thus to fine-tune the compound's pharmacological effect. Synthesis procedures driven by automation were also used extensively (microwave chemistry, continuous-flow chemical synthesis): these enable rapid access to highly-focused substance libraries.

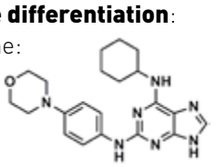
In the course of such work to date, we have succeeded in significantly increasing hit compound activity in a mouse model. In addition, the substance VUT-MK142 establishes a new lead compound that is capable of inducing differentiation into cardiac muscle cells not only from embryonic stem cells (P19) but, beyond this, to achieve the same by "re-programming" pre-existing, pre-differentiated precursor cells for skeletal muscle (C2C12). This constitutes a key step towards future use as a treatment method, since it obviates the direct dependency on embryonic stem cells, which are not only difficult to obtain but are also potentially subject to ethical restrictions. In a second generation of modifications, more radical changes were then made to the lead substance (including alterations to its underlying heterocyclic ring system), which culminated in triazines [2] as a new structural class featuring an altered activity profile. With the VUT-MK142 compound, it ultimately proved



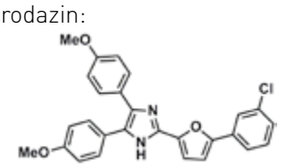
Interventional goals for tissue regeneration using small-molecule APIs of primary interest for their relevance in the treatment of lifestile diseases.

Small molecules for tissue generation

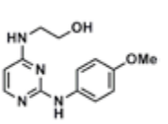
Reverse differentiation:
Reversine:



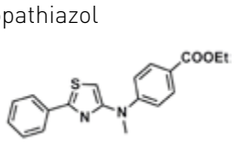
Neuron regeneration:
Neurodazin:



Cardiogenesis:
Cardiogenol C:



Neuropathiazol



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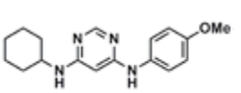
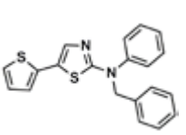
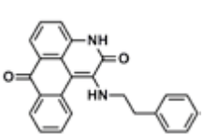


Skeletal muscle regeneration:
VUT-BW37



Pancreatic ß-cell regeneration:
BRD-7389



possible to produce autonomously beating cell clusters of functional cardiomyocytes [3].

Another interesting "side effect" of this research work was the discovery of a class of compounds that had the effect of speeding up the differentiation of precursor cells into skeletal muscle tissue [4]. In the long term, this might offer the possibility of accelerating the treatment of muscle fibre injuries. This discovery is all the more important for showcasing the extraordinary diversity that can be seen in the influence of small molecule compounds on cellular development processes. In this context, the availability of sensitive, high-throughput procedures for substance testing is of central importance, as they facilitate the identification of potent new lead compounds.

Notwithstanding these achievements, differentiation into target cells via induction by small-molecule APIs is only half the story in terms of a potential future therapy, since this technique is always dependent on the availability of a sufficient quantity of precursor cells. In this context, it is interesting that discovery of the compound reversine also identified a lead substance that permits the inversion of cell differentiation for mature tissue cell lines into more "pliable" developmental stages (progenitor cells). This inversion has been successfully demonstrated by "reverse differentiation" of skeletal muscle cells, followed by their subsequent differentiation into osteoblasts or, alternatively, adipocytes [5].

Taken together, these API candidates offer the prospect of actually being able to set our sights on regenerative tissue treatments that are based on easily-extractable cell types that are available in sufficient quantities. It is of course true that the majority of results achieved to date must be duly transferred from the animal cell model to human cell lines, which will require particular efforts in basic research. The regeneration of organ function also presents potential obstacles in the form of constructing complex three-dimensional structures from a range of tissue types (perhaps aided by bio-compatible polymers), followed by successful re-implantation into the patient. While solutions to such obstacles will be needed, the potential diversity shown in the restoration of damaged tissue is nonetheless reflected in the fact that, alongside the regeneration of cardiomyocetes, other synthetic compounds have been identified. These can stimulate differentiation into neurons, for example [6], or can positively influence the functionality of pancreatic β cells in terms of their insulin production.

In summary, the rapid progress made over the last few years in research into the induction of regenerative processes by small-molecule substances has thrown open the door to potential applications in medicine. On the basis of the scientific evidence it provides, we can contemplate novel forms of therapy that, mere decades ago, would have been dismissed as science fiction.

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Portions of the research work presented here were completed in close collaboration with colleagues from the Medical University of Vienna.

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Code Identified

Extending the genetic system

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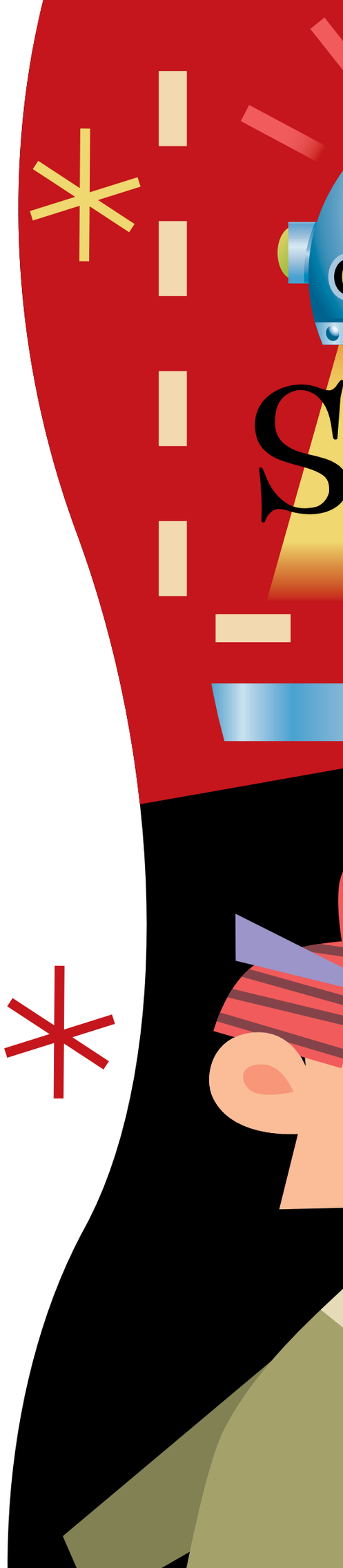
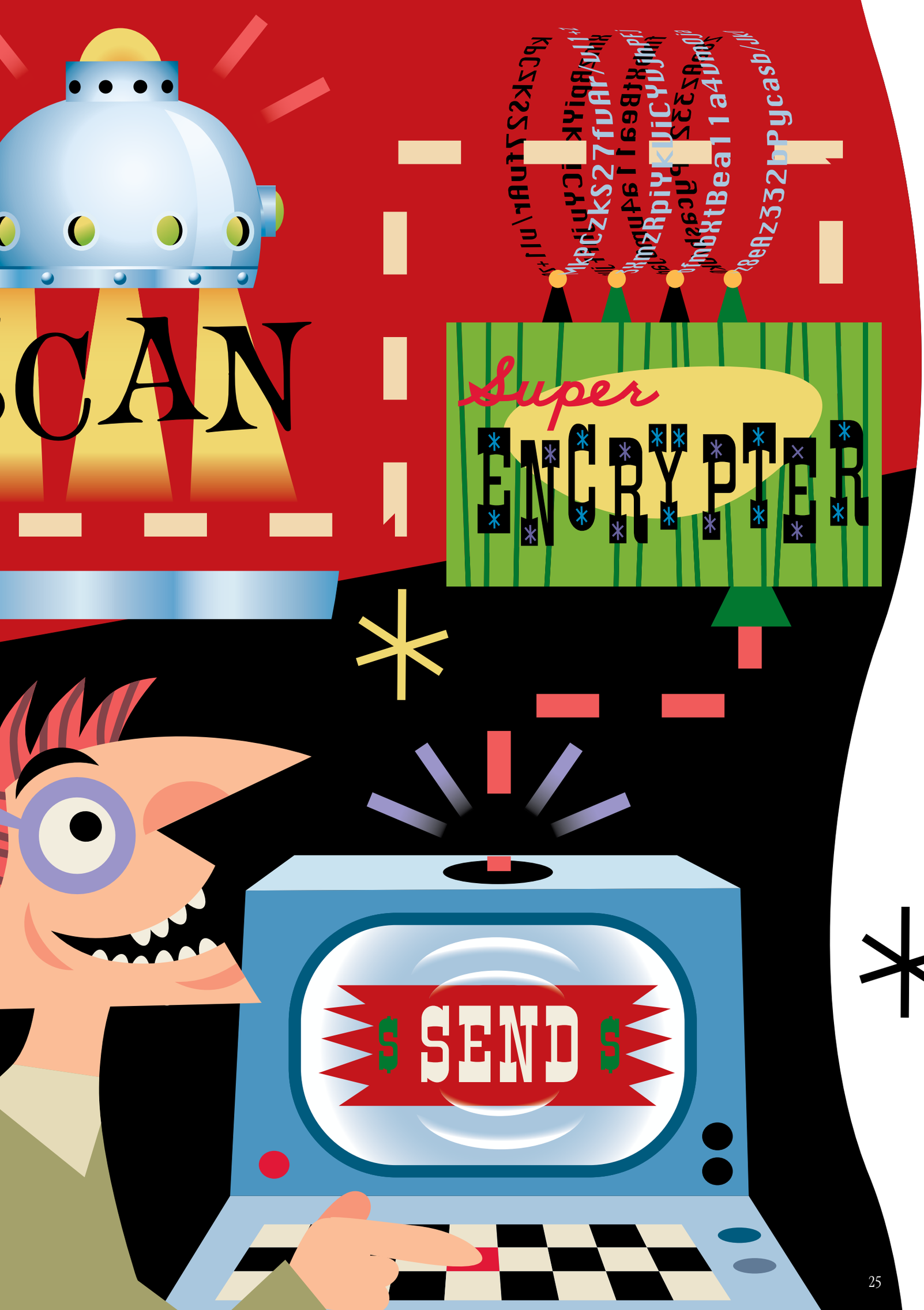


The genetic code encodes all of the information that each cell requires to function and interact correctly with its environment. The code is constructed from four separate molecules, known as the "canonical" Watson-Crick bases, namely: adenine, cytosine, guanine and thymine. The genetic code arises from the sequence of these four bases – given as A, C, G and T – in the DNA double helix.

Since the discovery of this DNA double helix structure by Watson and Crick in 1953, we know how these four bases are arranged in the DNA molecule. From this point in time, a large part of the international scientific community has been addressing the question of how reader proteins recognise this four-base sequence and translate it into proteins, i.e. the cell's functional units. For a long time, it has been known that a fifth base – 5-methylcytosine – exists alongside the four standard bases (Fig. 1). This base is used to switch genes on and off. While all cells possess the same DNA molecule and thus the same sequence data as their "hardware", the various types of cell differ significantly in terms of their functionality (we need only compare a neuron with a skin cell). As a result, there must be a higher-order informational domain external to this sequence data. At this level, decisions are made about which genes to activate for a specific cell type – and which genes this type switches off. This is the domain studied by the field of research known as epigenetics. Until 2009, the construction of our genetic system from this 4 + 1 base model was assumed to have been proven.

5-hydroxymethylcytosine

In 2009, the discovery was made that a further base could play a major role in our genome and is therefore now referred to as the genome's sixth base. The base in question is 5-hydroxymethylcytosine (5-hmC, Fig. 1) [1]. Previously, this base was classified as "oxidative damage", i.e. it was assumed that 5-hydroxymethylcytosine is


CAN
Super
ENCRYPTER
SEND

epigenetics

Thomas Carell graduated in chemistry, completing his doctorate at the Max Planck Institute for Medical Research under the tutelage of Prof. Dr Dr H. A. Staab. Following a research position in the USA, he accepted a position at ETH Zurich, setting up his own research group in the Laboratory for Organic Chemistry. After completing his habilitation in 1999, he moved to Philipps University Marburg, followed by LMU Munich in 2004. Prof. Carell is the director of Collaborative Research Centre 749 (Dynamic and Intermediate Molecular Transformations) and the CiPSM (Centre for Integrative Protein Science) excellence cluster. He is the holder of the Otto Bayer Prize, the German Research Foundation's Leibniz Prize and the Cross of the Order of Merit of the Federal Republic of Germany.

a degradation product that, on its occurrence in the genome, is rapidly removed by repair processes. There are numerous such DNA degradation products. They occur as a result of reactive oxygen species, released within our mitochondria during the process of cell respiration. These oxygen species attack the DNA bases, leading to their modification into oxidative damage. These "damage products" – a term also including 5-hydroxymethylcytosine to date – are efficiently tracked down and cleared up by repair enzymes in the genome.

In 2009, it was discovered that hydroxymethylcytosine is not merely the result of oxidative stress but is actively produced within our genome. Specialised enzymes are responsible for its production. Known as "TET" enzymes, three (Tet1 to Tet3) have been discovered to date [2]. These Tet enzymes are oxidation enzymes, which trigger oxidation processes with the aid of the cofactor ketoglutarate and with an iron atom bound at the active site. In an initial step, these enzymes oxidise the genome's fifth base 5-methylcytosine to 5-hydroxymethylcytosine. This discovery has fundamentally changed the work conducted in the field of epigenetics, i.e. the area of scientific research concerned with gene activation and deactivation. Recalling that regulated gene activation and deactivation forms the basis for cell differentiation, we can grasp how the discovery of hydroxymethylcytosine is also hugely influential on contemporary stem cell research. Pluripotent stem cells, created following the fertilisation of the egg cell by the sperm cell, are the basis for the development of all forms of tissue. During this development process, the DNA sequences responsible for the creation of specialised tissue must be selectively activated and others selectively deactivated. Gene activation and deactivation, plus the processes underlying these switching activities, form the basis for the development of a complex organism from a fertilised egg cell, known as a "zygote". The targeted oxidation of methylcytosine into hydroxymethylcytosine – i.e. from the genome's fifth base to its sixth – is now suspected to play a major role in these activation and deactivation processes. Indeed, recent research data now underpins this theory, showing that embryonic stem cells in particular exhibit surprisingly high concentrations of hydroxymethylcytosine [2].

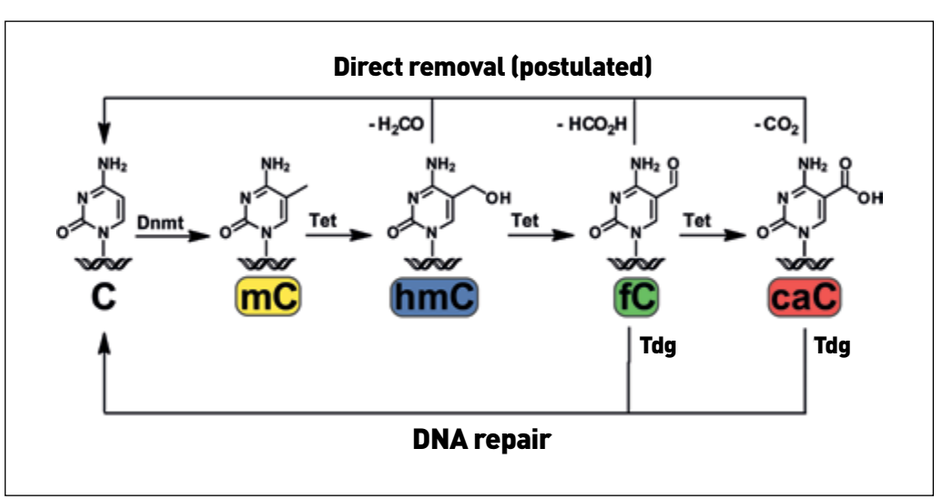


Fig. 1 Depiction of the new DNA bases hmC, fC and caC, including the repair/removal processes as currently postulated.

Complex oxidation processes

Other research hints at significantly greater complexity in the oxidation processes from methylcytosine to hydroxymethylcytosine. In 2011, for example, two further cytosine-derived bases were found, which can today be classified as the genome's seventh and eighth bases [3–5]. The bases in question, formylcytosine and carboxycytosine (fC and caC, Fig. 1), are higher-order oxidation products of hydroxymethylcytosine. Research has shown that the TET enzymes not only oxidise methylcytosine to hydroxymethylcytosine, but also perform further oxidation steps – ultimately yielding both formylcytosine and carboxycytosine (Fig. 1). To date, nothing is known about the agent controlling these oxidation processes, nor the significance of their successive nature. We are also unaware of the extent to which these new bases – hydroxymethyl-, formyl- and carboxycytosine – possess their own biochemical functions, i.e. how they recruit specific proteins that then participate in the processes of gene activation and deactivation. All over the world, mass spectrometric methods are being applied to search for proteins exhibiting high-affinity binding to these new bases, so as to gain insights into the biochemical processes that are regulated by these new DNA bases [6]. One aspect of the overall picture is now becoming clearer: these oxidation processes targeting DNA – and cytosine bases in particular – are crucial for controlled gene (de-)activation. One paper has shown that

hydroxymethylcytosine is not recognised by human DNA repair machinery, for example. Accordingly, it stays in the genome, even while repair processes identify and excise the majority of modified bases created in each and every cell on a daily basis. This fact alone – that hydroxymethylcytosine remains in the genome – suggests that we have yet to fully appreciate the importance of the role played by this base. Unlike hydroxymethylcytosine, formylcytosine and carboxyl compounds are readily excised from the genome by repair processes: we may therefore conclude that these bases are created as Nature's way of achieving the targeted removal of mC from the genome. Alongside the repair of hmC, fC and caC, straightforward direct "removals" – i.e. conversion to C – can also be considered here, based on a dehydroxymethylation of hmC, deformylation of fC or decarboxylation of caC. Today, we still have yet to understand whether repair processes or these direct conversions are actually involved in the reactivation of genes – or whether they merely remove the bases that are the result of undesired overoxidation within the genome. Are formyl- and carboxycytosine damage products, formed by excessive and deleterious activity of the TET oxidases? Or is the formation of formyl- and carboxycytosine a deliberate and biochemically necessary step, which triggers processes that we have yet to fully comprehend?

Recent research has also shown that the TET enzymes are also able to oxidise small quantities of the canonical base thymine to hydroxymethyluracil. Hydroxymethyluracil is also a base that is efficiently detected and repaired by the human DNA repair system. In this scenario, too, we also have to ask ourselves whether hydroxymethyluracil is a base possibly created by oxidative stress – or whether the oxidation and subsequent repair actually act as triggers for unknown biochemical processes? All of these observations suggest that gene activation and deactivation is an activity closely interwoven with the various DNA repair processes. DNA sequences are methylated and thus deactivated. Oxidation processes acting on methylcytosine create hydroxymethylcytosine, formylcytosine and carboxycytosine, with hydroxymethylcytosine itself remaining stable in the genome. In the case of formylcytosine and carboxycytosine, on the other hand, DNA repair processes or direct conversions to C are triggered. A similar picture results for thymine, which is oxidised by the same TET enzymes to hydroxymethyluracil, which also triggers repair processes. In all cases, these repair/conversion processes cause the replacement of the highly-oxidised bases hmC, fC, caC and also hmU by the canonical bases cytosine (C) and thymine (T), whereby the process can then reiterate. This generates a cycle of methylation (for C-bases only), oxidation and removal of the oxidised bases, followed by their replacement with "fresh" cytosine or thymine. The resulting picture is one of a dynamic genome, in which the sequence information may be static, but where gene activity is regulated by oxidation and repair. We have yet to unmask the precise biochemical processes that trigger the oxidised bases. Yet while the biochemical regulator of the four bases remains a mystery, one fact is already clear: our genetic system is much more complex than previously assumed.

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Meat as a Doping Trap

Clenbuterol testing in doping control samples: drug abuse or food contamination?

Prof. Dr Mario Thevis &
Prof. Dr Wilhelm Schänzer
Centre for Preventive Doping Research and European Monitoring Centre for Emerging Doping Agents, German Sport University Cologne

Clenbuterol, a β_2-sympathomimetic drug, has been on the list of substances prohibited in sport for over 2 decades. Due to its putative performance-enhancing properties, urine samples are routinely tested for its presence during doping control: by using modern liquid chromatography-mass spectrometry instruments, detection limits at the level of just a few picograms per millilitre are possible. This sensitivity not only makes detection possible long after use of the illegal substance has been discontinued but, for a number of regions outside Europe, has also uncovered a food contamination problem that could make life very difficult for professional athletes.

Clenbuterol is a racemic mixture of two enantiomers (Fig. 1). Banned in sport since 1992, its presence is usually tested for in doping control with the aid of liquid chromatography/(tandem)-mass spectrometry. On account of its anabolic properties, clenbuterol is not listed in sport as a β_2 agonist, but in the category S1.2 ("Other Anabolic Agents") and is thus prohibited at all times, i.e. both during the sporting event itself and at any other time [1]. There is no threshold limit for clenbuterol: the detection of the analyte in doping control samples immediately results in an "adverse analytical finding" (AAF). To maximise the potential time frame for detection following discontinuation of a (presumably illegally) consumed substance, instrumental analysis has been pursuing significant improvements over the last few years. This has resulted in very low detection limits and, as a consequence, athletes' consumption of clenbuterol has been proven in a great many cases. Figure 2 gives a typical example of analytical clenbuterol testing, on a urine sample containing approx. 3 pg/ml clenbuterol. The method used here consists of a liquid-liquid extraction from urine into methyl tert-butyl ether with subsequent re-extraction into aqueous hydrochloric acid (0.06 M) and LC-MS/MS analysis.

Clenbuterol in foodstuffs

The fact that clenbuterol exhibits anabolic effects – especially at high doses of the drug – has also led to abuses of the substance in the area of meat production. As a result, this industry has banned its use in food production at an international level [2]. Yet in 2010 and 2011, athletes tested positive for clenbuterol after participating in overseas sporting events outside the European Union (in China and Mexico). The results are traceable back to contaminated foodstuffs. In 2010, routine doping control of a German team returning from a tournament in China found low – yet clearly detectable – concentrations of clenbuterol in the urine of every single member of the squad [3]. A follow-up study, conducted with people residential in China and with tourists staying in China for various lengths of time and in various locations, further illustrated the problem of illegal use of clenbuterol in animal feed: based on current anti-doping regulations,

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Wilhelm Schänzer followed a first degree in sports and chemistry with a doctorate from the Institute of Biochemistry at German Sport University Cologne, completing his habilitation there in 1995. He was appointed Professor of Biochemistry and Head of the Institute of Biochemistry and its WADA-accredited doping control lab at German Sport University Cologne in 1997. His key areas of research focus involve the clarification of steroid metabolism and the identification of new long-term metabolites; improving analytical techniques for autologous doping-relevant substances such as erythropoietin (EPO), testosterone and related prohormones; and clarifying the structural properties of new designer substances.

no fewer than 22 of the 28 volunteers tested would have returned "positive" test results. As a number of anti-doping organisations were aware of this problem in advance of the Olympic Games in 2008, advisory notices warning against eating meat in China were circulated to athletes, so as to guard against inadvertent consumption of clenbuterol and falling into this "doping trap". After all: differentiating between a drug abuse incident sometime in the past – and thus relevant for doping control – and a low dose as consumed in contaminated food is, in analytical terms, a highly sophisticated task.

In Mexico, a similar situation can be found: here, too, a series of results from food testing have uncovered the unlawful use of clenbuterol in animal feed over the last few years [4, 5]. The potential repercussions for professional athletes were highlighted first in May 2011, when five players of the Mexican national squad (men's football) tested positive for the β_2 agonist [6]. This finding proved to be especially problematic, since the U-17 World Cup for junior football teams was scheduled to take place the following month. As a result, soccer governing body FIFA organised a comprehensive programme of food quality testing alongside routine doping controls during the tournament. All in all, athletes submitted 208 urine samples for doping control testing. The analytical findings revealed the presence of clenbuterol in 109 cases, with concentrations of up to 1500 pg/ml urine [7]. The food samples taken in parallel were tested in a suitably-equipped laboratory in the Netherlands, with 14 of the 47 samples containing – in some cases considerable – quantities of clenbuterol. Viewed as sufficient to account for the drug's presence in the doping control samples, no player was sanctioned for breaching the anti-doping rules. A breakdown of the samples by tournament location revealed no clear trend: the matches had been played in Guadalajara, Mexico City, Monterrey, Morelia, Pachuca, Querétaro and Torréon, with 8 to 36 players being tested at each location. Since some teams played matches at several locations, no conclusions can be drawn from urine samples about the place where contaminated food was eaten. One inter-

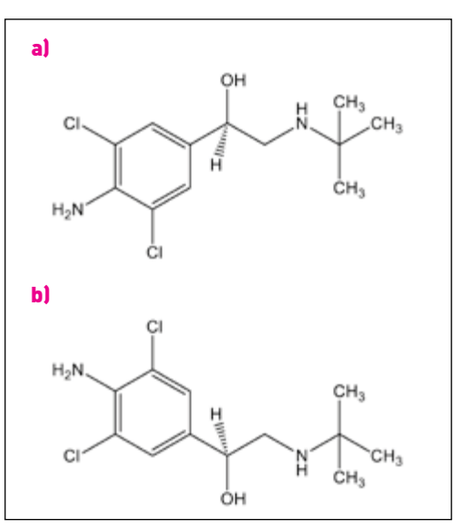

Fig. 1 Clenbuterol enantiomer structures: a) (-) clenbuterol (active isomer) and b) (+) clenbuterol (inactive isomer)

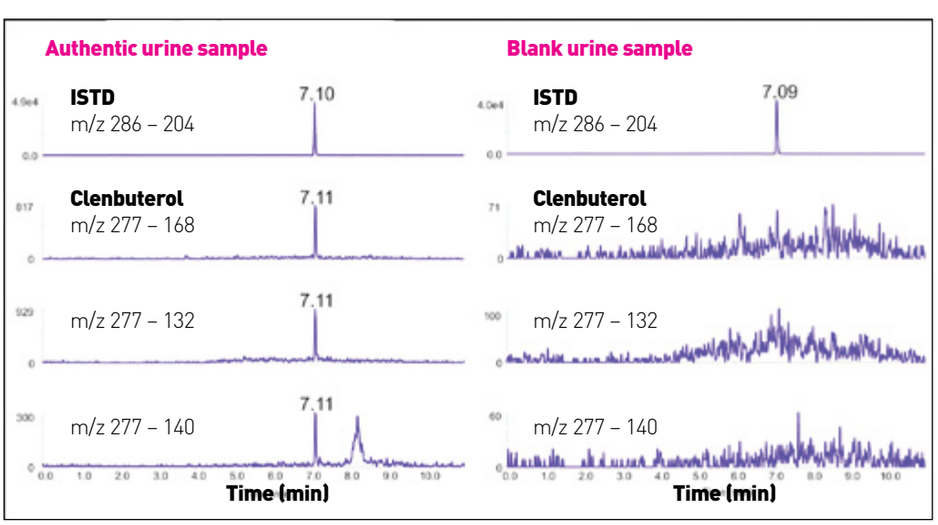

Fig. 2 Extracted-ion chromatograms of a urine sample with approx. 3 pg/ml clenbuterol (left), compared to a blank urine sample. The enantiomers remain unseparated by conventional liquid chromatography.

esting aspect may be noted, however: of the 24 teams taking part, five teams returned consistently negative sets of doping control results. Of these, at least one had heeded the advisory notice and refrained from consuming meat for the entire competition.

Challenges for analytical testing

These examples clarify the analytical difficulties surrounding clenbuterol in the context of doping control testing. Accordingly, a number of approaches have been taken to generating analytical methods capable of differentiating between foodstuff contamination and previous (non-recent) deliberate consumption of the drug. One of the more recent strategies adopted relies on the fact – as mentioned above – that clenbuterol is a racemate (see Fig. 1) in its drug formulation. After administering clenbuterol, a pig study has shown that enrichment in edible tissue (e.g. muscle) is considerably higher for the therapeutically inactive (+) stereoisomer than for the (-) stereoisomer. Accordingly, once clenbuterol treatment is discontinued, a significant disparity in concentration between the two components will develop over time [8].

Enantiomer analysis offers new potential

This would mean that there is a functional difference between a drug product dose and food contamination: a difference that is detectable insofar as the (-) stereoisomer complement of clenbuterol has undergone sufficient depletion. To test this hypothesis, a method for enantiomer separation with subsequent isotope dilution analysis using LC-MS/MS was developed, with the aim of determining the enantiomeric ratio and thus potentially identifying either a case of therapeutic drug dosage or a case of contamination. Figure 3 presents a chromatogram of a urine sample with clenbuterol following enantiomer separation: baseline separation is clearly visible here. Two excretory studies with simple therapeutic doses of clenbuterol were conducted. Results were as expected: the (-)/(+) enantiomer ratio in urine never fell below 1 at any point during the 160 hours of testing. This is due to the fact that the (+) stereoisomer also exhibits elevated tissue retention in such cases, meaning that the (-) stereoisomer is excreted to a significantly greater degree [9]. Following the oral intake of a clenbuterol enantiomer mixture with the (-) stereoisomer component already depleted (as might occur in cases where contaminated meat is consumed), the ratio may show a decremented value that cannot be successfully reconciled with therapeutic administration of the substance. While the authors are not aware of clearance studies involving enantiomer-depleted clenbuterol mixtures, results from athletes' urine samples have nonetheless shown that (-)/(+) ratios significantly lower than 1 have been determined in a number of cases. In consideration of the fact that a value greater than 1 cannot prove doping took place, yet a value less than 1 is, on the basis of current scientific knowledge, inconsistent with the therapeutic administration of clenbuterol as a drug in humans, the determination of the enantiomer ratio for clenbuterol findings is certain to contribute some useful data. While other – potentially wide-ranging – studies are required to evaluate the potency of enantiomer analysis, one possible approach seems nonetheless practicable.

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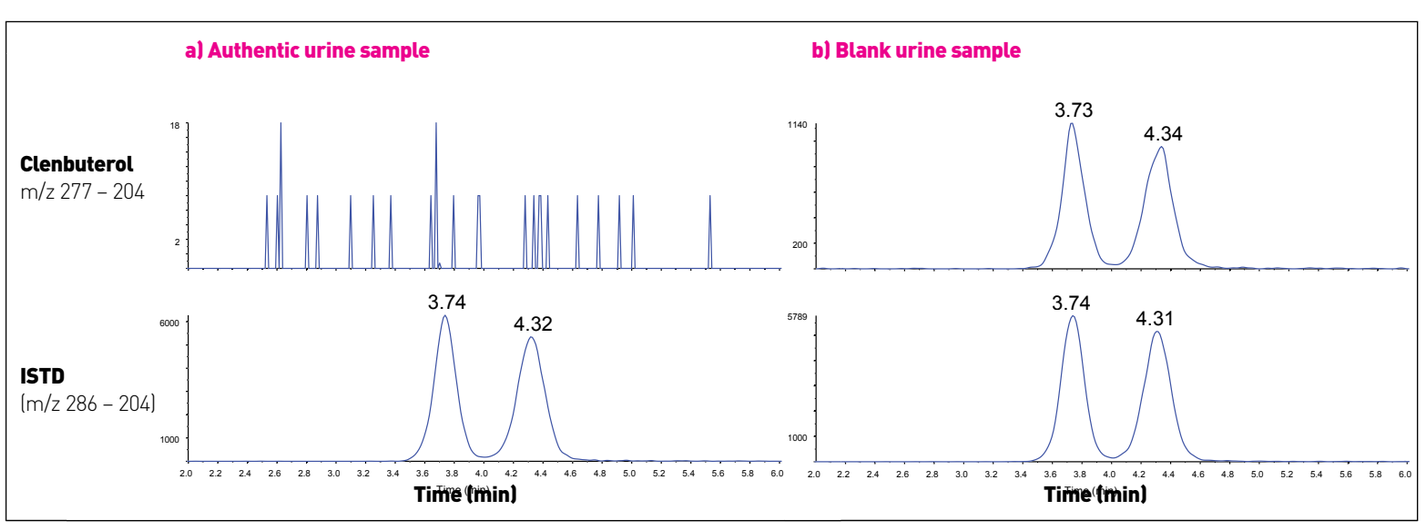

Fig. 3 Extracted-ion chromatogram of a urine sample with approx. 200 pg/ml clenbuterol (A) with separation of the (-) and (+) enantiomers at 3.7 and 4.3 min. The upper patterns represent clenbuterol, while the lower patterns depict the 9x(2)H-labelled internal standard, also present as a racemate. As a comparison, (B) shows a blank urine sample.

from the industry

Non-Invasive Cancer Diagnosis

A new application for microscopy

Cancer has been a part of human life from our earliest days. In research conducted by Aachen-based oncologist Dr Leo Habets, a non-invasive, microscope-based diagnostic procedure has the potential to revolutionise research and progress in understanding the circumstances of the disease, so as to develop new therapeutic approaches. Microscope-based high-content screening systems in basic clinical research: can a non-invasive procedure replace the biopsy?

A 2,000-year quest

Hippocrates, the founding father of modern medicine, described growths whose blood vessels spread in all directions and were arranged like the legs of a crab. Once translated to the Latin word for crab, "cancer", the disease now had its modern name. Yet progress was slow for both diagnosis and treatment. For two long millennia, cancer was believed to result from a surfeit of "black bile" (from the Greek "melancholia"). In the absence of any empirical data, metaphysics long reigned supreme. Today, while "black bile" won't be found in any diagnosis, many of the mechanisms by which cancer cells develop and propagate still remain shrouded in mystery. As one example, researchers have seen how cancer patients will initially respond well to modern monoclonal antibody treatments, yet some patients then suffer recurrences, relapses with new metastases, even though the disease appeared to be already beaten. Why – and how – do these new metastases occur? Are there warning signs or early indicators that hint at the danger?

Empirical basic clinical research

Aachen-based oncologist Dr Leo Habets has been studying these questions, examining samples from cancer patients on a day-to-day basis in his lab in Aachen, supported by funding from METARES – the "Society for the Promotion of Cancer Diagnosis and Treatment at the Micrometastasis Stage". His work focuses on monitoring the success of treatment regimens for breast cancer patients. The approach he follows is empirical basic clinical research, which identifies indicators for metastases, as well as their propagation routes and mechanisms. "Our lab has studied samples from around 16,000 cancer patients," explains Dr Habets. "And we add 16 new datasets every day, on average." Even to the untrained eye, Habets' workplace would seem rather unusual, since refrigerators full of tissue samples – the predominant

feature of this kind of lab – are entirely absent. Apart from blood analyser units, only a few optical microscopes meet the eye. "What you see here," he says, pointing to a microwell plate on a microscope's specimen stage, "is the modern approach to tissue sampling: 20 millilitres of patient blood."

Biopsy as standard – "liquid biopsy" as the alternative

Previously, cancer diagnosticians were reliant on the biopsy, i.e. the surgical removal and analysis of tissue from a patient. Nor is it merely the case that the operation is complex, expensive and fairly unpleasant for the patient concerned. The biopsy itself is now suspected of propagating tumour cells in the body. Blood tests certainly seem to indicate that the blood tumour cell count rises after tissue piercing for biopsies. A less drastic method therefore seems to be called for. "With our procedure, we can largely eliminate patient stress," states Dr Habets. "Instead of surgery, patients merely need to have blood drawn – and we need just 20 millilitres."

"Liquid biopsy" is what researchers are calling this new diagnostic method, which has the potential to revolutionise cancer diagnosis. "The procedure offers advantages at all stages of cancer diagnosis and treatment monitoring," says Dr Habets. "We only have to look in the microscope to see whether or not a treatment is working. Non-invasive diagnosis even makes it possible to test drugs against patient blood before administering them. This enables the identification of potentially effective substances without inconveniencing the patient."

The dangers of circulating epithelial tumour cells

"The method we use was first developed by Professor Katarina Pachmann at the University of Jena," explains Dr Habets. "Her Maintrac procedure is extremely effective at identifying circulating epithelial tumour cells (CETCs) in blood. Their proliferation in blood is a clear warning sign. The underlying hardware is a Scan^R screening station from Olympus, running Scan^R software for data acquisition and analysis, which was specially developed by Olympus for this procedure. We use fluorescent dyes to label the cell types and cells of interest to us with antibodies."

Dr Habets, oncologist, Aachen, Germany.

The differentiated display of the fluorescent dyes is a major advantage offered by the system. Cells that display all dyes as spots of colour are of particular interest. As one example, Figure 1 shows CETCs that exhibit specific oncogene characteristics due to the HER2 and EpCAM markers. Habets explains: "As you can see, some cells take up the fluorescent dye and show saturation over a wide area, while some have only spots of colour. Others have diffuse colouring or lack colours. As our data repository grows, we constantly improve the precision of our statements about the correlation between the occurrence of certain cell types and antibodies with cancer treatments and disease progression. All of the data are analysed in software, stored as image files and accessible from the database for later comparative studies."

Scan^R: a modular high-content screening solution

The Scan^R system as deployed by Dr Habets combines the modular and flexible approach of a microscope-based system with ability to meet the requirements of screening applications in terms of automation, speed, throughput, reliability and reproducibility (Fig. 2). The system is equally capable of handling both fixed and living cells. This makes the system – developed by Olympus in close collaboration with the European Molecular Biology Laboratory (EMBL) – suitable for use in a wide range of high-content screening applications. Results achieved include multiparameters and functional data about the interaction of a substance with the target or other cell components – such as absorption, permeability, selectivity, specificity or substance metabolism. Dr Habets: "The entire system is managed via a user interface which is for the most part self-explanatory. Users have access to all of the image acquisition and image analysis parameters." The images are acquired with multiple dimensions (X, Y, Z, t, λ), which can be evaluated subsequently with the aid of the integrated analysis system. "The options available to users in terms of image and data analysis are effec-

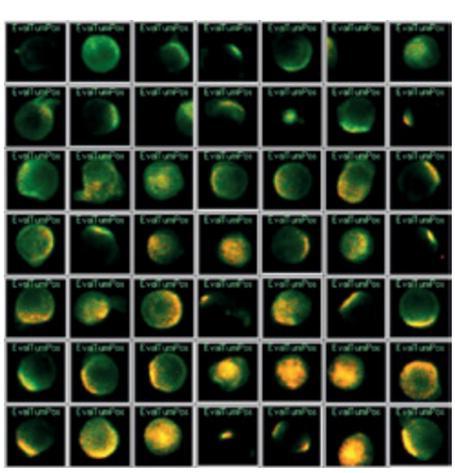

Fig. 1 Maintrac procedure for cancer cell profiling with the Olympus Scan^R system. Detection of oncogenic molecular labels HER2 (orange) on EpCAM-positive cells (green).

tively unlimited," says Habets. The procedural approach taken by the Scan^R system's analysis module is oriented on cytometry, which enables the analysis of a large volume of multidimensional datasets. This sort of analysis is applied in infection biology, for example, to gain new insights in relation to infectious diseases. As two examples, the Scan^R system has previously been used in work studying Chlamydia bacteria and gastrointestinal viruses. While Chlamydia bacteria predominantly affect Africa – where they can cause blindness in many cases – gastrointestinal viruses are also widespread in Europe. Across Europe, 50% of its inhabitants are host to such viruses, which are suspected of causing cancer. Other fields of application for the system include diabetes research and the investigation of disorders such as coronary heart disease or atherosclerosis – each at the molecular level. Or – as in the case of Dr Habets' work – cancer.

Fig. 2 Olympus Scan^R high-content screening system. The modular all-in-one solution forms the basis for the Maintrac procedure deployed.

Extraction guaranteed

The Olympus system currently records up to five fluorescent tumour markers in parallel per scan. For each patient, this means some 10,000 blood cells are recorded at maximum resolution using specialised auto-focus routines. Such a precise quantitative analysis is ultimately dependent on the use of a highly stabilised fluorescent light source. The analysis software setup is based on the scatter plot approach used in flow cytometry, and enables the extraction of cell populations on the basis of parameters related to both intensity and morphological features. From those 10,000 blood cells, this enables the detection of a tumour-relevant population of as few as 1–50 cells, which can be displayed directly as an image gallery. Importantly, the Scan^R software offers bidirectional linking between the data point and the individual image of the cell in question, which enables interactive assessment and manipulation of the analysis.

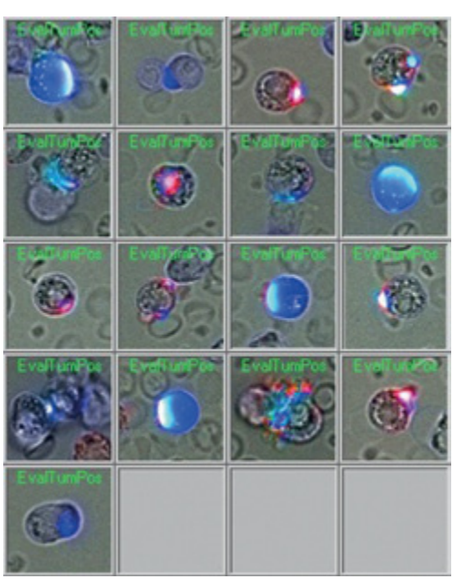

Fig. 3 Visualisation of metastasis risk indicators with the aid of the Maintrac procedure. Detection of CD44 antigen markets (blue) on CETC with the aid of fluorescently labelled antibodies.

Vast volumes of data

The datasets involved are tremendous: every month, the research lab fills a terabyte-sized hard drive with its data. "We'd be lost without software-driven data management," confesses Dr Habets. The fees charged for testing are moderate, however: "Our going rate for the identification of three antigens per patient is about 10 euros. That's incomparably cheaper than similar procedures." For the moment, analysis work with the Scan^R system is confined exclusively to basic research: in the future, it could help to develop or establish diagnostic procedures.

New insights, new questions

Within oncology, there is growing demand for affordable methods in basic clinical research. For every new insight, new questions arise. Tumour cells are usually epithelial cells, i.e. cells from the surface layers of tissue complexes. If cells taken from a breast cancer patient after "successful" treatment for cancer can be shown to be circulating epithelial tumour cells (CETCs), for example, this indicates the cells have survived the therapeutic bombardment unharmed in a kind of "hibernation". Alongside this survival, it's also a mystery why they are in the blood system in the first place. As epithelial cells, their path into this system should technically be blocked. "In a sense, they change their 'identity'," explains Dr Habets. "They undergo epithelial–mesenchymal transition (EMT), penetrate the blood vessels, roam about the body and can then metastasise. The Maintrac procedure gives us a reliable technique for identifying them in blood (fig. 3). Our next task is to explore the treatment options that are most effective in hampering EMT."

→ **Hagen Lang, Heinz-Jürgen Zamzow**
→ **microscopy@olympus-europa.com**

Figs. 1 and 3 with kind permission of Dr Leo Habets.
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Requirements for the Technical Equipment

Safe operation of laboratories

Safety and energy efficiency are today principal requirements for the technical equipment of labs. The safety of people in the workplace is of paramount importance and must be ensured at all times. This is particularly true for workplaces which are exposed to increased risks. This article describes the role of the ventilation and air conditioning technology in such an environment.

A chemical accident in a laboratory can quickly lead to a harmful or even life-threatening concentration of hazardous substances in the room air. This is why the ventilation and air conditioning system plays a key role in maintaining safe working conditions for the staff in a lab. In case of an incident it does not suffice to just open a window in order to let fresh air in. The air change rate is just one factor; other factors that need to be considered include turbulences, heat sources, face velocities, noise levels, and most of all the ever changing volume flows of fume cupboards and safety cabinets.

Air management system

The highest levels of safety can be achieved with an air management system. Such an air management system includes VAV terminal units with volume flow controllers that increase or reduce the extract air for each fume cupboard individually and depending on the overall situation. Based on the room pressure, volume flow controllers balance the supply air and extract air ratio without restricting the function of each fume cupboard. This results not only in a safe working environment but also in a reduction of the operating costs for the air conditioning system.

Removing hazardous substances from the air is the most important goal. At the same time, neighbouring compartments must also be protected from those hazardous substances.

David Miller, Sales Manager, TROX Middle East (LLC)

Fume cupboards

Fume cupboards have a special function when it comes to protecting the staff in a lab. Three prime objectives are obvious:

1. Retention: Fume cupboards must prevent dangerous concentrations of gases, fumes or dusts from escaping the fume cupboard and being released into the lab.

2. Increased air change: Fume cupboards must prevent the development of an atmosphere that can ignite or even explode.

3. Splash and shatter protection: Fume cupboards must prevent spray or flying fragments from injuring people.

While splash and shatter protection is obviously ensured by the construction of a fume cupboard, the first two points require volume flow control. Even though there is a multitude of different applications and requirements for laboratories, today's control systems cover all common control strategies.

Control strategies

Air management systems can support various strategies regarding the control of supply air and extract air in rooms, of fume cupboards, and of room and duct pressure. An air management system combines control functions with energy management and monitoring functions and individual room operating modes.

▶ Room control

An air management system controls and balances the volume flows for various room scenarios and fume cupboards. Stable control requires that the actual volume flow rates are precisely measured and the setpoint values quickly be achieved or maintained.

▶ Differential pressure control

Differential pressure control for rooms or ducts can be included in individual control strategies. Cascade control rather than differential pressure control with a damper blade – without considering any special volume flow limits – allows for much more stable room situations even with quick-response volume flow control loops.

▶ Control for areas with potentially explosive atmospheres (ATEX)

For areas with potentially explosive atmospheres special components are available that fulfil the requirements of rapid response volume flow controllers, room pressure controllers, and fume cupboard controllers, including monitoring.

▶ Interface with the central BMS

Safety systems must be connected to higher-level building management systems.

Such connections require flexible interfaces. In addition to analog inputs and outputs and switch contacts as a means of changing the operating mode and transmitting information, digital network communication can provide transparency yet requires very little wiring effort.

The central BMS can request the following information:

- Volume flow rate and room pressure setpoint and actual values
- Local faults
- Consolidated fault messages with configurable content
- Damper blade positions (optimised air management)
- Operating modes
- Sash position (for fume cupboard control)
- Face velocity (for fume cupboard control)
- Set fume extract level (for fume cupboard control)

The central BMS can preset the following parameters as defaults for the room or a fume cupboard controller:

- Operating mode
- Change of priority for operating mode default setting between the control panel and the central BMS
- Switching between two room pressure setpoint values
- Volume flow rate setpoint change signals (external temperature and pressure control)

Reducing costs by saving energy

Supply air and extract air volume flows must comply with national and international standards regarding safety in the workplace and protection of the environment. As a consequence, air management is of central importance when energy consumption and operating costs shall be reduced. An air management system ensures a high level of energy efficiency due to the demand-based volume flow control.

Fume cupboard control – quick-response control

While the common variable air volume controllers react within approximately 120 s, controllers developed for the ventilation of laboratories react within only 3 s. These rapid response times ensure that no outbreak of hazardous substances can occur, e.g. in fume cupboards with variable, demand-based extract air. For slave control loops, these rapid response times enable stable room situations that ensure room pressure conditions according to DIN 1946, part 7. Dedicated actuators move the damper blades such that the setpoint value is reached quickly and precisely.

→ d.miller@trox.ae
→ www.trox.ae

Areas of application for air management systems

- Research facilities, laboratories with fume cupboards, livestock facilities
- Operating theatres and sterile areas in hospitals and health facilities
- Clean rooms in pharmaceutical and semiconductor production
- Volume flow rate control in rooms with special requirements (offices, meeting rooms)

Fume cupboard control – quick-response control

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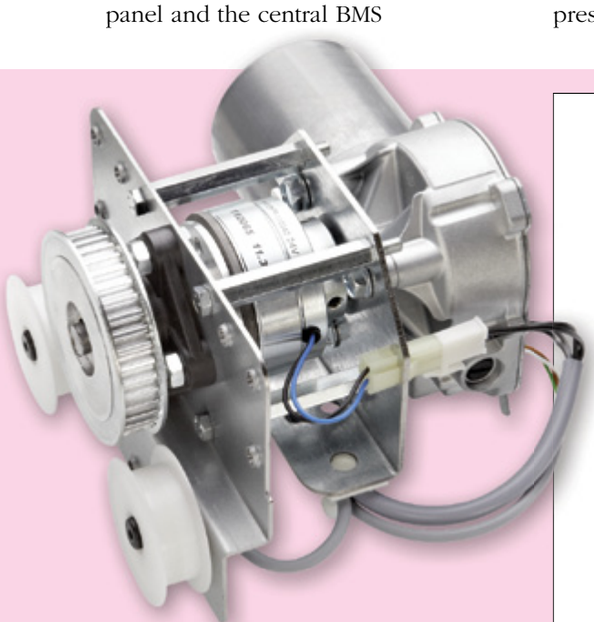
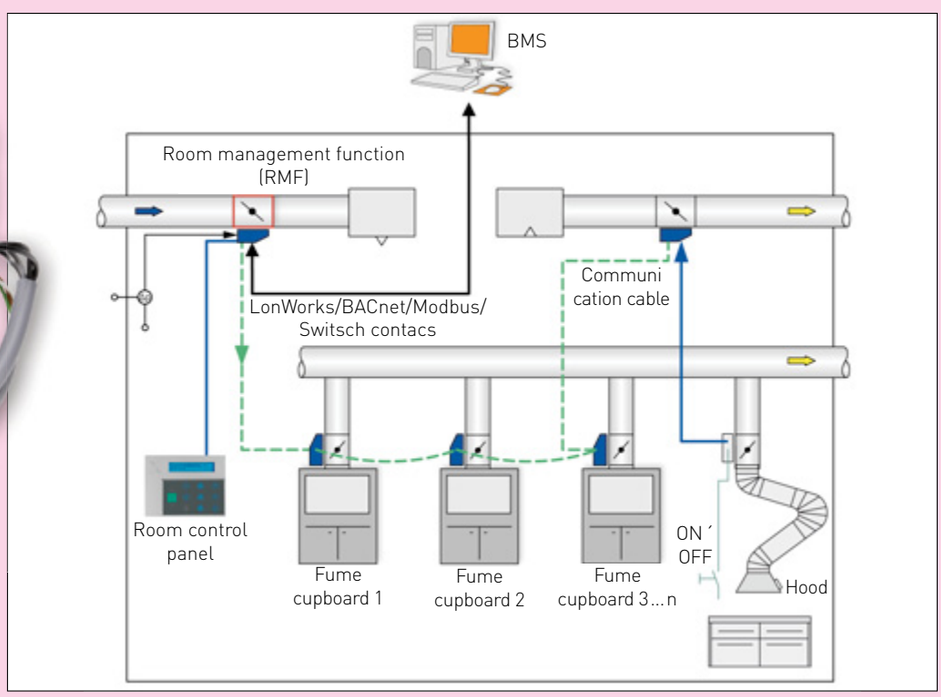


The new FSE automatic sash device for fume cupboards ensures that sashes that have been left open unintentionally will be automatically closed after a certain time. Users can comfortably open or close the sash by just pushing it lightly or else by pressing a button or actuating a pedal switch. The volume flow will be adapted to the sash opening, which results in less energy being consumed and at the same time perfect safety of the surroundings. The device can be retrofitted.



A bus connects the individual controllers. All fume cupboards in a room can be controlled using just one room control panel, and just one interface is required to integrate the system with the central BMS and to transmit the consolidated room data. Additional controllers and measuring points can be included in the room balance via a 0 V to 10 V signal. (All figures by TROX GmbH)

market

Amgen and Illumina Enter Agreement to Develop Oncology Companion Diagnostic Test

Illumina, Inc. (NASDAQ:ILMN) announced it has entered into an agreement with Amgen Inc. to develop and commercialize a multigene, NGS-based test as a companion diagnostic for Vectibix (panitumumab), a fully human anti-EGFR monoclonal antibody therapeutic for the treatment of metastatic colorectal cancer approved in the US and EU. Under the terms of the collaboration, premarket approval of the test by the US Food and Drug Administration (FDA) and other regulatory bodies will be sought. The test will be developed for use with Illumina's MiSeqDx™ instrument, which received premarket clearance from the FDA on November 19, 2013 and was CE-marked for the European Union on July 16, 2013.

→ **investor.illumina.com**

Merck Announces Increased Acceptances and Extends Offer Period for AZ Electronic Materials

Merck, a global pharmaceuticals and chemicals company, announced that as of 1 p.m. (GMT) on February 5, 2014 shareholders representing 56,48% of the share capital of AZ Electronic Materials (AZ) had accepted Merck's recommended cash offer for the company. Merck on December 5, 2013, announced that it was offering GBpence 403,5 per share of AZ in cash, with the successful completion of the transaction being conditional among others upon antitrust clearances as well as a minimum acceptance level of 95% of the share capital. Merck today extended the offer period to February 18, 2014. Merck also announced that in addition to the US antitrust clearance announced on January 23, 2014, in the meantime the German Federal Cartel Office has granted early clearance with effect from February 5, 2014 and the Taiwan Fair Trade Commission has granted early clearance with effect from January 24, 2014.

→ **www.merckgroup.com**

Wyatt Launches First MALS Detector for UHPLC

At the forthcoming Pittcon in March, Wyatt Technology will launch the first multi-angle light scattering (MALS) detector that can be coupled to any ultra-high performance liquid chromatography (UHPLC) system. This combination of UHPLC and the new MALS detector, known as µDAWN, will be able to determine the absolute molecular weights and sizes of polymers, peptides, and proteins or other biopolymers directly, without resorting to column calibration or reference standards. By taking advantage of novel detection optics and mechano-optical technology, Wyatt has been able to reduce µDAWN's light scattering flow cell volume to just 10µL, allowing it to accommodate the narrow peaks produced by UHPLC separations.

→ **www.wyatt.com**

Sartorius Appoints Internationally Experienced Lab Manager to Join Its Top Management Team

Michael Melingo, Member of the Group Executive Committee
Photo: Sartorius

Michael Melingo will head marketing, sales and services of the Lab Products & Services Division at Sartorius. He will therefore succeed Dominique Baly, who will retire from the company as planned after reaching retirement age. Michael Melingo will be a member of the Group Executive Committee, the highest operational management level of the Sartorius Group. Michael Melingo, who brings more than 30 years of experience in the industry as a sales and marketing executive, will be joining Sartorius from Metrohm, the Swiss manufacturer of analytical instruments, where he was CEO of its U.S. subsidiary. Before that, he had worked for Baxter, Bio-Rad, Millipore and Waters in Europe and Asia. Michael Melingo is of Austrian nationality and a bioengineer who specializes in biochemistry and food technology.

→ **www.sartorius.com**

Tosoh Bioscience Announces NEW TSKgel® High Temperature Gel Permeation Chromatography Columns

Tosoh Bioscience LLC announced the introduction of its newest gel permeation chromatography/size exclusion chromatography (GPC/SEC) columns, the TSKgel High Temperature (HT) and Ultra-High Temperature (HT2) GPC Columns. The release of these columns is accompanied by the new EcoSEC High Temperature GPC System for polymer analysis up to 220°C. The TSKgel HT and HT2 columns are recommended for the analysis of organic-soluble polymers and are packed with spherical particles composed of polystyrene cross-linked with divinylbenzene (PS-DVB). The TSKgel HT columns are for high temperature applications up to 140 °C, while the TSKgel HT2 columns are used in ultra-high temperature applications up to 220 °C.

→ **www.separations.us.tosohbioscience.com**

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Updated Product Guide for 2014/2015

Phenomenex Inc., a global leader in the research and manufacture of advanced technologies for the separation sciences, announces the publication of its updated product and services guide for 2014/2015. Covering the company's comprehensive lines of HPLC/UHPLC Columns, GC Columns, and SFC columns and sample preparation products, this year's catalog includes many new offerings, including a new Yarra™ analytical dimension and prep column and a new Aeris™ Peptide 2.6µ column. The 412-page guide incorporates a Kinetex® column selection guide, new excipient applications on Phenogel™ GPC

columns and new chiral column comparisons. Also new this year is a sample request tool for solid phase extraction tubes, Verex™ certified vials, and Phenex™ syringe filters.

→ **www.phenomenex.com**

Sartorius Extends arium® Lab Water Family by Three New Product Lines

The Sartorius technology group extended its successful arium® lab water family by three new product lines: the arium® pro ultrapure water system, the arium® advance pure water system and the arium® comfort combination system. These new product lines generate Type 1 to Type 3 ultrapure and pure water, delivering the right water quality for any laboratory application. The highlight of these new lines is the arium® comfort series. In addition to providing ASTM Type 1 ultrapure water, this space-saving combination unit also produces Type 2 and Type 3 pure water.

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