Looking into living cells

Chemistry Nobel laureate Stefan Hell gives this year’s Leopoldina Christmas Lecture
Dear members and friends of the Leopoldina,

research requires and promotes international cooperation. Scientific exchange across borders not only encourages advances in individual scientific fields, it can also assist positive relations between the scientists’ home countries.

In recent months, researchers from Israel and Germany have been commemorating the official establishment of diplomatic relations between the two countries 50 years ago. Back then, science “set the stage” for those developments, as my colleague Prof. Ruth Arnon, President of the Israel Academy of Sciences and Humanities, so aptly put it. Years before the rapprochement between the two countries, the Max Planck Society and the Weizmann Institute of Science signed a cooperation agreement on the initiative of Amos De-Shalit, a physicist at Weizmann, and Otto Hahn, the Max Planck Society’s first president.

These kinds of cooperation initiatives remain important to this day — and existing relations require careful nurturing. That’s why the Israel Academy and the Leopoldina signed a cooperation agreement in 2013. This year, to mark 50 years of bilateral relations, we have held several joint events, including a symposium on neurodegenerative diseases in Halle this May, and a chemistry symposium in Jerusalem this November (see page 5).

I would like to express my heartfelt gratitude to the scientists of the Israel Academy and of the Leopoldina who made these symposia possible. Here’s to continuing our excellent collaboration in the future.

I wish you a thought-provoking read.

The past weeks have seen a rapid increase in the number of asylum seekers coming to Germany in search of refuge as a result of war and persecution in their home countries (primarily Syria, Iraq, Afghanistan, Eritrea, and countries in West Africa), and this number is set to rise even further. The top priority of the German healthcare system is to protect the health of every person living in the country, which includes those who are seeking humanitarian protection. This can only be achieved through barrier-free access to adequate medical care. It is particularly important to consider the special needs of vulnerable persons.

Significant challenges for public health structures

Taking in such an influx of people over a short period of time and providing them with healthcare is posing significant challenges for the public healthcare system in Germany and across Europe. In Germany in particular, these healthcare responsibilities fall under the jurisdiction of public health structures that are not prepared for the magnitude of the current situation. What makes it all the more difficult is that many health institutions have been forced to cut budgets and staff over the past few years.

The joint statement, published by the Leopoldina, acatech and the Union of German Academies in mid-October, highlights the existing problems in the provision of healthcare for asylum seekers, and provides potential solutions.

Academies recommend outpatient-clinics in reception centres

The academies have identified the following key areas for action with regard to healthcare provision for asylum seekers: medical examinations and care in reception centres; care and treatment of people suffering from mental illnesses and trauma; meeting the demand for qualified personnel; taking linguistic and cultural needs into consideration; and expanding the scope of available data and research, particularly regarding the patients’ actual state of health.

The academies also recommend that specialist outpatient clinics provide medical care in the reception centres. The clinics should provide medical expertise that is sensitive to cultural and religious needs, have specialist interpreters on hand, actively engage with the structure and organisation of reception centres, and be linked to hospitals, local doctors and social welfare organisations.

THE PAPER CAN BE FOUND HERE
Making the smallest details visible

An interview with Stefan Hell, who won the Nobel Prize in Chemistry for developing an optical microscopy method that has made resolutions in the nanometre range possible

Prof. Stefan W Hell, a physicist from Göttingen who has been a member of the Leopoldina since 2013, opened up a new dimension in optical microscopy and was rewarded for his work with the Nobel Prize in Chemistry in 2014. Prof. Hell will give the traditional Christmas Lecture at the Leopoldina in Halle on 2 December. On behalf of Leopoldina news, Caroline Wichmann asked Prof. Hell about how he arrived at STED microscopy and about life with a Nobel Prize.

Your microscopic method opened the door to nanoscopy. Could you perhaps try to explain in layman’s terms the method and its importance for research?

Stefan Hell: I showed that it is possible to see much finer details with an optical microscope than was considered possible throughout the whole of the 20th century. This is important because only with an optical microscope can we look into living cells without destroying them. We can also use optical microscopy to highlight specific proteins in cells. We do this by equipping them with fluorescent (i.e. glowing) marker molecules. But although it was possible to highlight the proteins using the marker molecules, the level of detail at which we could see their spatial arrangement in the cell was limited. If they were closer together than half the wavelength of light (about a fifth of a thousandth of a millimetre), it was impossible to differentiate between them; they just looked like an indistinct mass.

So how do you make the finer details visible?

Hell: The solution was to not let the marker molecules all glow at the same time, but to stop a few from glowing at each registration. If the molecules take turns at glowing, you can tell them apart. This meant that I could substantiate an optical microscope with a resolution that theoretically reaches as far down as the molecular range – i.e. that theoretically achieves a molecular resolution.

How did you get into this area of research?

Hell: I did my PhD in physics in the offices of a Heidelberg University spin-off. The company, which was co-founded by my PhD supervisor Siegfried Hunklinger, developed so-called confocal optical microscopes that were used for inspecting computer chips. My PhD did not focus on resolution in itself, because of course it seemed to be fundamentally limited. However, confocal optical microscopes can produce 3D images, so it was about working out whether or not this 3D capability could be of any benefit in surveying fine chip structures. Ultimately, I found the topic too technical, and the physics didn’t offer enough scope for development. Optical microscopy and optics were physics subjects in the 19th century, after all.

And how did you get the idea to try and overcome the light-wave diffraction limit?

Hell: I started wondering if there was perhaps a really interesting problem still to be solved in optical microscopy. I
wanted to work on something more fundamental. At some point, I came to the conclusion that it might actually be possible to overcome the resolution limit. My intuition told me that since so many new discoveries had been made in physics in the 20th century, then at least one physical phenomenon must exist that could be used to overcome the diffraction limit. I also felt that physicists in general had turned away from the topic, which everyone seemed to think was done and dusted. They thought there was nothing left to be done. And that – looking at things that everyone else has turned away from – can open up opportunities.

When did you first sense that you might win a Nobel Prize for your work?

Hell: Right up until the end, I never really believed I would win the Nobel Prize. And once I had, it took a while for it to finally sink in emotionally. I thought that the Swedish Academy had many other topics and candidates, and that “my” topic wouldn’t come up until much later – if at all. However, to be completely honest, I have to say that I was invited to give talks in Uppsala, Stockholm and Lund back in May 2007 – at the request of the Nobel Committee for Physics. I received invitations almost every year after that, from both the physics and the chemistry Nobel committees. So in that sense, I did know that I was on the Swedish Academy’s radar. But others were, too. In my mind, I had brushed the Nobel Prize aside because I didn’t want the more or less real chance of winning it to affect my life in any way. But reality always catches up with you at some point...

How does winning the Nobel Prize change a researcher’s life? How has the Nobel Prize changed your life?

Hell: Basically, not a lot has changed. But one thing that has changed is that I get invited to numerous talks and events, and can only attend a small fraction of them. The public has become markedly more interested in my work and my career, as well as in the chemistry Nobel committees. So in that sense, I did know that I was on the Swedish Academy’s radar. But others were, too. In my mind, I had brushed the Nobel Prize aside because I didn’t want the more or less real chance of winning it to affect my life in any way. But reality always catches up with you at some point...

Stefan Hell in the laboratory

What are you researching at the moment? Are you inspired to overcome any other physical limits?

Hell: There is still a great deal to do in high-resolution optical microscopy – important stuff. This is especially true in terms of its use in the life sciences and medicine. Microscopy not only needs to become sharper, but also faster and more sensitive. We know that this is theoretically possible. There is also room for improvement in the way molecules and light interact. There are various approaches that one could take. But I can also imagine looking a bit to the left and the right, and moving away from microscopy. That won’t happen overnight, though. But who knows? When the right idea comes along, things can move faster than you think.

You’ve been a member of the Leopoldina since 2013. What role does that play for you as a researcher?

Hell: To be honest, it plays no role at all in my daily work. But as the national academy, the Leopoldina is an enormously important body. Good work in the Leopoldina can make life easier for all researchers in Germany, and it can multiply the benefits of science for society. It is also important for informing society's decision-makers. When it comes to simple members like me, the Leopoldina allows us to look beyond our own scientific horizons and become acquainted with outstanding colleagues from other disciplines and hear about their work. I have very clear pictures in my mind of some of the fascinating talks I’ve heard at the academy. I wouldn’t want to miss those kinds of opportunities.

Japanese pharmacologist and chemist Satoshi Ōmura ML has been awarded this year’s Nobel Prize in Physiology or Medicine. The researcher, who shared one half of the prize with William C. Campbell (USA), was presented the award for discovering a novel therapy against infections caused by roundworm parasites. The other half of the prize was awarded to Chinese pharmacologist Youyou Tu for her discovery of antimalarial drug artemisinin. Ōmura and Campbell discovered avermectins, an antiparasitic series of drugs whose derivatives reduce the risk of contracting infections transmitted by roundworms, including river blindness and elephantiasis. Ōmura, born in 1935, was president of the Kitasato Institute in Tokyo from 1990 to 2008. He studied at the Tokyo University of Science and subsequently obtained doctorates in pharmacy (1968) and chemistry (1970). Ōmura has been a member of the Leopoldina, in the Microbiology and Immunology Section, since 1992. (jk)
Microscopy in Seoul

German-Korean symposium during the visit of German Federal President Joachim Gauck

As part of the strategic partnership with the Korean Academy of Science and Technology (KAST), the Leopoldina organises a joint symposium every year to discuss scientific topics of relevance to society. Microscopy was at the heart of this year’s symposium, which was hosted within the special framework of the Joint Korean-German Conference – Science and Innovation. The conference, held in Seoul on 13 October on the occasion of the visit of Federal President Joachim Gauck, was organised by the German Embassy in collaboration with German and Korean partners from science and business.

Following the opening lecture by Gauck, Leopoldina President Prof. Jörg Hacker delivered a welcoming address and introduced Nobel laureate Prof. Christiane Nüsslein-Volhard ML, whom the Leopoldina had invited to give the keynote speech. She spoke about the “Development of Colour Patterns in Fishes – Towards an Understanding of the Evolution of Beauty” and demonstrated the importance of basic research for scientific development and innovation. Prof. Hacker then moderated the podium discussion on science and innovation with Korean and German participants from the worlds of science and business, including Prof. Helmut Schwarz ML and Prof. Matthias Kleiner ML.

The KAST-Leopoldina Bilateral Symposium on Bioimaging and its Application took place in the afternoon. The keynote speech was given by Prof. Patrick Cramer ML, director of the Max Planck Institute for Biophysical Chemistry in Göttingen. Prof. Matthias Rief ML, professor of molecular biophysics at Technische Universität München, and Prof. Vahid Sandoghdar, director of the Max Planck Institute for the Science of Light in Erlangen, were other speakers nominated by the Leopoldina. The event was open to the public. Some 80 participants from science and industry, including many young researchers, engaged in discussions with the speakers from Germany and Korea.

Chemistry – The Central Science

Symposium with Israeli academy to celebrate 50 years of bilateral relations

This year, Germany and Israel celebrate 50 years of diplomatic relations. To mark the occasion, the German National Academy of Sciences Leopoldina and the Israeli Academy of Sciences and Humanities (IASH) held a symposium entitled “Chemistry: The Central Science” from 9 to 10 November in Jerusalem. They wanted to honour the importance of science in diplomatic relations between the two countries and to strengthen scientific exchange in the field of chemistry. The Leopoldina works in close and friendly partnership with the IASH.

The event, organised by Prof. Helmut Schwarz ML (Berlin) and Prof. David Milstein ML (Rehovot), focused on the latest findings and advances in chemistry research. The diverse influences of chemistry on neighbouring scientific disciplines was also considered. The evening keynote lectures by Nobel laureates Prof. Dan Shechtman (Haifa) and Prof. Gerhard Errl ML (Berlin) were among the highlights of the symposium. The speakers discussed key developments in chemistry research, and talked about receiving Nobel Prizes for their achievements. Fifteen German and Israeli Leopoldina members took part in the event, along with other Israeli scientists.

The presidents of the Leopoldina and the IASH, Prof. Jörg Hacker ML and Prof. Nili Cohen, used the symposium as an opportunity to get to know one another and exchange ideas. Cohen has been president of the IASH since September 2015.
Research fellows at Stanford University

The Leopoldina regularly supports young German researchers through its Fellowship Programme, enabling them to conduct research at prestigious international locations. Currently, Dr Dominik Kölmel and Dr Thomas Wolf are working as postdocs at Leland Stanford Junior University in California, commonly known as Stanford University.

Since the spring of 2014, graduate chemist Kölmel has been working as a guest specialist in the field of organic chemistry at the Department of Chemistry with Prof. Eric T. Kool, who conducts interdisciplinary research involving organic chemistry, chemical biology and biophysics.

Kölmel is working on the synthesis of fluorogenic ODF markers for bioorthogonal protein labelling. This is based on working with oligo desoxyfluorides (ODF), a new class of DNA-based fluorescent dyes that have been developed in recent years in Eric T. Kool’s laboratory. The optical properties of these dyes can be adjusted according to requirements, and the fluorophores can be used for different purposes. In the current project, the ODFs will be used to label proteins and then visualise them by microscopy.

Until a few years ago, the targeted production of dyes by synthesising short DNA strands was unthinkable. This production method is much more cost-effective, enabling many more analyses. These make it possible to understand processes in the organism, correct faulty physiological processes, or render external influences harmless. Ultimately, these studies can help to combat diseases.

Thomas Wolf is also a chemist. He is interested in the physical properties of molecules, specifically the interaction between molecules and light. He is researching at the SLAC National Accelerator Laboratory in Menlo Park, a counterpart to the German accelerator research centre DESY. Since early 2014, he has been working in the research group of Dr Markus Gühr, who was recently awarded a Liebenberg Professorship by the Volkswagen Foundation.

The aim of the project is to conduct ultrafast time-resolved photoelectron spectroscopy of nucleobases, primarily thymine and uracil. These nucleobases, basic building blocks of DNA and RNA, can absorb radiation well in the ultraviolet range, extremely efficiently convert it to heat, and release it into the environment. The conversion is so effective because the process in the molecule occurs within a few hundred femtoseconds or picoseconds. This is faster than any other potentially reactive process, which could cause damage. The first experimental results have significantly broadened our perspective on the relaxation dynamics of thymine.

Both research fellows report that they feel very comfortable in the stimulating Californian environment. The outstanding working conditions also provide a solid foundation for building their own research teams in the future.

15TH GAIN CONFERENCE IN SAN FRANCISCO

This year’s German Academic International Network (GAIN) Conference took place from 28 to 30 September, again with an extensive programme and the involvement of many German organisations. Leopoldina research fellows based in the local area were among the more than 400 participants. They took part in the workshops and provided information on career opportunities in Germany. Previous participants had assessed this as a useful aid in their career development. As the keynote speaker, Leopoldina President Prof. Jörg Hacker provided an overview of current career prospects in science, business and administration, and applied his expertise to two working groups.
People

Deceased Members

- **Roberto G. Burgio ML**
  30 April 1919 – 8 March 2014 | Pavia, Italy
  **Gynaecology and Paediatrics**
  Roberto G. Burgio, elected to the Leopoldina in 1976, focused on paediatric haematology and immunology. He mainly dealt with clinical nutrition issues and the impact of malnutrition on children, with a particular focus on the damage caused by protein and vitamin B12 deficiencies. Burgio was a member of the European Society for Paediatric Research and the European Society for Paediatric Haematology and Immunology.

- **Daniel Kastler ML**
  4 March 1926 – 8 July 2015 | Bandol, France
  **Mathematics**
  Mathematician Daniel Kastler researched mathematical problems associated with supersymmetry. He also conducted research into the Dirac operator and gravitation. Kastler was appointed a member of the Leopoldina in 1995.

- **Eberhard Sander ML**
  21 December 1922 – 3 August 2015 | Halle (Saale), Germany
  **Surgery, Orthopaedics, Anesthesiology**
  Eberhard Sander focused on surgery in the course of his scientific career, in particular bone and pancreatic surgery. He was elected to the board of the German Democratic Republic’s Surgery Society, and later taught classes in the field of trauma surgery at Martin Luther University Halle-Wittenberg. Sander became a member of the Leopoldina in 1976.

- **Gottfried Schatz ML**
  18 August 1936 – 1 October 2015 | Basel, Switzerland
  **Genetics / Molecular Biology and Cell Biology**
  Biochemist Gottfried Schatz was one of the scientists who discovered mitochondrial DNA. He also conducted research into cellular transport systems that supply the mitochondria. Alongside his academic career, Schatz worked as a scientific advisor to the Swiss Federal Council, and was President of the Swiss Science and Technology Council from 2000 to 2004. He was awarded the Leopoldina Schleiden Medal in 1993. He had been a member of the Academy since 1985.

- **Peter Sitte ML**
  8 December 1929 – 13 September 2015 | Merzhausen, Germany
  **Genetics / Molecular Biology and Cell Biology**
  Peter Sitte conducted research into the cellular structures of plants. He was the founding president of the German Society for Cell Biology. Sitte was elected a member of the Leopoldina in 1969 and held various positions within the academy, including as a member of the Senate and representative of the General Biology Section from 1974 to 1984, and representative of the Cell Biology Section from 1989 to 1998. Sitte was awarded the Leopoldina Schleiden Medal in 1991.
Imprint

Deutsche Akademie der Naturforscher Leopoldina – Nationale Akademie der Wissenschaften
Jägerberg 1
D-06108 Halle (Saale)
Telefon: +49-345/4 72 39 – 800
Telefax: +49-345/4 72 39 – 809
presse@leopoldina.org

Editing:
Caroline Wichmann (cw)
Julia Klabuhn (jk)
Daniela Weber (dw)

Other Editors:
Prof. Jutta Schnitzer-Ungefug (jsu) (responsible according to the German press law)
Prof. Gunnar Berg ML (gb)
Anna Baltrusch (ab)
Hannes Junker (ju)

Other authors in this issue:
PD Dr. Andreas Clausing, Coordinator of the Fellowship Programme (ac)
Dr. Kathrin Happe, Scientific officer, Deputy Head of Department Science - Policy - Society (kh)
Dr. Ruth Narmann, Deputy Head International Relations Department (rn)
Dr. Jan Nissen, Senior Officer, International Relations Department (jn)

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Design:
Agentur unicom, Berlin

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Abbreviations:
ML = Member of the Leopoldina