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PUBLISHER

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Editorial



Dear Reader,

Food security is one of the great challenges facing the world today. Currently, the war in Ukraine, which threatens to bring hunger crises not only to the war zone but also to seemingly distant regions of the world in its wake, is making that very clear. And climate change – with its in part disastrous consequences for agriculture in the form of droughts or floods – is also endangering global food supplies. Science must play a part in developing solutions to this challenge.

At the University of Düsseldorf, the "Cluster of Excellence on Plant Sciences" (CEPLAS) is working with the University of Cologne on the "plants of tomorrow" and thus on how food security can be ensured here and all over the globe in the future. The goal of the Cluster is to develop crop plants which are better at adapting to changing environments, ultimately produce higher yields and are more resistant to diseases.

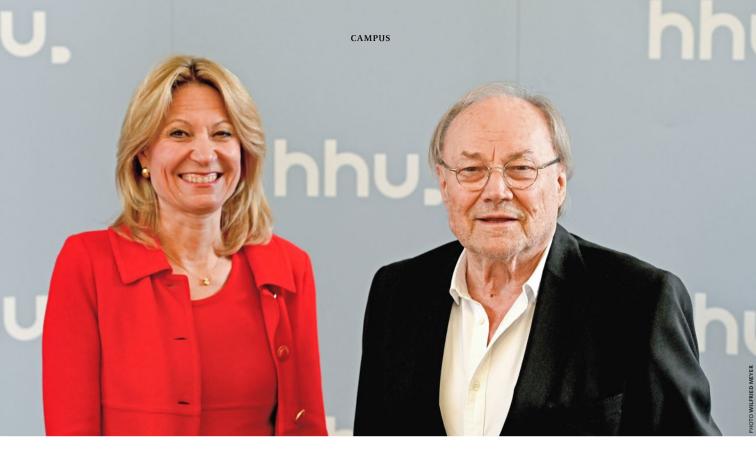
In their projects, the CEPLAS researchers are not staying in their ivory tower, but are instead seeking to share their results with society and advise the government. CEPLAS enters into dialogue with citizens and stakeholders, participates in parliamentary hearings and holds one-to-one discussions with political decision-makers. In many respects, CEPLAS has become a pacesetter for international, innovative and responsible research at HHU – beyond the boundaries of plant sciences.

This issue of the HHU Magazine focuses on this Cluster, its work and its impact on the university as a whole, and looks ahead to the participation of HHU in the next round of the Excellence Initiative. Excellent is also an appropriate word to describe the other projects from the various faculties reported on in this issue, all of which illustrate the depth and breadth of the outstanding research being conducted at HHU.

I wish you an enjoyable read! Kind regards,

Professor Dr Stefan Marschall

Vice President for International Relations and Science Communication



Klaus Maria Brandauer as the Heinrich Heine Guest Professor

Taking Heinrich Heine to heart

BY VICTORIA MEINSCHÄFER

The first event was full, the second even fuller:
As the Heinrich Heine Guest Professor, Klaus Maria
Brandauer attracted a large audience to the University
in April when he delivered two lectures entitled
"Heinrich Heine – Love, Revolution, Europe".
"A great role model for us all," is how Brandauer
referred to the poet, who he discovered at the age
of 14 and who has fascinated him ever since.
"I admire him and have taken him into my heart."

University President, Professor Dr Anja Steinbeck, on the Heinrich Heine Guest Professor, whose visit was originally scheduled for 2020 and had to be postponed due to the coronavirus: "Brandauer is an extraordinary actor with great charisma who can boost our courage and give us comfort through Heine's works, and he has a critical mind."

In his first lecture, Brandauer undertook a journey through Heine's life, talking of Düsseldorf and Paris, of years of study and travel. And he quoted poems in a way both accomplished and pointed, from the mocking "The young lady stood by the sea" to "I came from the

house of my mistress dear" from the Book of Songs and "Night Thoughts". With great professionalism and empathy for Heine's verses, Brandauer captivated the audience and transformed the lecture hall into a theatre. With regard to the war in Ukraine, he said: "Something has happened that we could no longer imagine in Europe. And now all of a sudden it is on our doorstep. We cannot be indifferent to it." But even in this situation, Heine – who experienced unbelievable suffering over the years in which he was bedridden – is again a role model, as "he was able to dream through and about other people. And he never gave up, even though his path through life was not easy."

Demonstrating the relevance of Heinrich Heine

In the second lecture of his Heinrich Heine Guest Professorship, Klaus Maria Brandauer explored Heine's works further and demonstrated how relevant the namesake of the university is today. Together with the pianist Arno Waschk at the grand piano, the Austrian actor enthralled the audience in the packed lecture theatre 3A. On this occasion, Klaus Maria Brandauer recited only a few well-known verses, concentrating primarily on Heine's text "French Affairs", which he wrote for the newspaper "Augsburger Allgemeine Zeitung", and his essay "Shakespeare's Maidens and Women". The report from Paris during the cholera epidemic in 1832 offered shocking parallels to our present time and Brandauer's reading of the almost 200-year-old text gave it a contemporary feel.

About the Heinrich Heine Guest Professorship

The Heinrich Heine Guest Professorship was a gift from the state of North Rhine-Westphalia to HHU on the occasion of its naming in 1988. Before Klaus Maria Brandauer, other Heinrich Heine Guest Professors have included Helmut Schmidt. Juli Zeh, Wolf Biermann, Siegfried Lenz, Joschka Fischer, Antje Vollmer, Cardinal Karl Lehmann, Ulrich Wickert and most recently Joachim Gauck. The first Heinrich Heine Guest Professor was Marcel Reich-Ranicki in 1991. The Guest Professorship is always selected by the University President and awarded to personalities who speak their mind and have an affinity with science.

"Heine fills me with wonder," said Brandauer, "and I wanted Heine, who I love, to speak wherever possible." He expressed his warmest thanks for the opportunity to read from Heine's works in Düsseldorf, while President

Enthralled and moved

Steinbeck thanked him on behalf of the audience for the two wonderful events, expressing her delight that so many people from Düsseldorf had accepted the invitation from HHU and made their way to the campus: "Thanks to you, we have enjoyed unforgettable evenings."





From

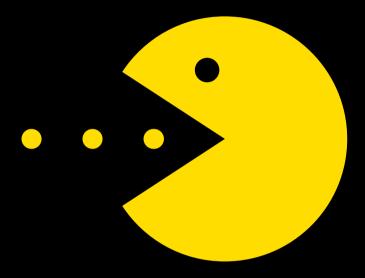


Pac-Man

to
Zagreus

Assistant Professor Dr Melanie Fritsch researches digital games





BY KATRIN KOSTER

There's a Pac-Man over by the window, a scarf with Nintendo figures on it lies on the cupboard, the tick of an Asteroids clock can be heard and next to the keyboard is a steaming cup of coffee with the logo from "The Legend of Zelda" on it. The cupboard is full of old computers, consoles and electronic toys. This is clearly the office of a game fan. Dr Melanie Fritsch has been Assistant Professor of Media and Cultural Studies, focusing on Game Studies and related areas, since October 2020. Playing games is part of her job.

ut not all of it. Above all, the 41-year-old listens very carefully because she researches sounds in games. Following her studies in Berlin and Rome, the theatre and performance studies graduate completed her doctorate on music performances in digital game culture at the University of Bayreuth.

Aren't the sounds in this medium just a decorative accessory, almost just background noise? Melanie Fritsch raises her eyebrows and elaborates: "The music in games has never been just that. Even in the eighties – on the early chips such as those in the C64, Amiga or NES – complex compositions were created that influenced the musical scene. Many people were introduced to the aesthetics of electronic music in this way." Several examples: "In the nineties, stars such as The Chemical Brothers or Leftfield supplied songs for game soundtracks. Last year at the Game Awards, none other than Sting – together with an orchestra – presented a song from the Netflix series Arcane, which is based on the game League of Legends."

Music as an opener of doors

Her area of expertise, game music research, has a melodious name: Ludomusicology. Nevertheless, some only consider classical music to be "proper culture". Yet, when game music helps bring a young audience into concert halls, it's clear that some doors are now opening. Almost two decades have passed since the first live orchestral concert outside Japan at the Gewandhaus venue in Leipzig – during the Games Convention in 2003. Game music can now fill large venues, is broadcast live on radio and influences musicians from all genres, from pop and techno to Neue Musik.

So it's high time to review developments and speak to the trailblazers here. The committed researcher has an excellent network and has just completed applications for transnational projects. For example, she would like to research how game music (has) influenced Electronic Dance Music (EDM). Also at the top of her agenda is the history of digital games in Germanspeaking countries, another topic on which there has been virtually no research to date.

Even though almost everyone has something to say on the subject of games in practice, the topic largely represents uncharted waters in terms of research: "There are plenty of laurels to be won here as there are not yet even any definitive standards for quoting games and many terms have not been clearly defined. How can we describe games and a gaming experience?"

Fritsch talks to her students about this, as well as about gaming culture, technical details or the sound of the eighties, which has seen a resurgence in popularity thanks to the series "Stranger Things". "Isn't music itself also a form of play in practice?" asks the expert, reaching for a brightly coloured device from the year 1981, the Super Simon. While copying sound sequences on the device, she explains that every piece of hardware, every chip and every chip version sound different. "We are also looking at this because I would like to teach people at HHU who understand games and their culture, and can talk about them competently. To do this, they also need to know the history and what happens in the background: What chips can do, how production processes work or how game production is influenced by cultural contexts." Like in film and theatre studies, graduates should also be able to compose reviews.

Fritsch spends many hours in her office, writing expert reports, designing classes, tweeting busily and evaluating games. She reaches for her coffee. "When I'm not asleep, I'm usually sitting in front of a screen."

Fritsch recently spent several days in the underworld: In the rogue-like "Hades" – currently her favourite game – she took on the role of Zagreus, son of Hades.



He wants to flee the underworld and faces many obstacles along the way. When playing the game, you learn a lot about (Greek) myths; this knowledge inspired a seminar on the figure of Orpheus in audiovisual media, amongst other things. Zagreus frequently dies, but this doesn't bother Fritsch. "It takes a lot to frustrate me. Anyone who learned about games through Super Mario or Donkey Kong just carries on regardless."

Digital games – a recognised cultural asset

Digital games now count as a cultural asset: Fascinating video and music artworks from the scene, so-called demos, which have been created with minimal storage volume since the eighties, have just been granted intangible cultural heritage status by UNESCO. "Hopefully that will finally put an end to the criticism that game players are only consumers. They produce so many new things." And strengthen the economy: With sales totalling around 180 billion US dollars worldwide, games are now the fifth largest sales market. That makes a sound all of its own – in the tills.





Games researcher Assistant Professor Dr Melanie Fritsch with the Super Simon (left): "Like millions of others, as a child of the eighties I grew up with Super Mario." A vibration feedback gamepad for the Nintendo GameCube (right).



Germany, 1923: Children playing with banknotes. Can we expect inflation like in the 1920s or are the currently rising inflation rates just temporary?

Fear of inflation?

BY CAROLIN GRAPE

At the moment, anyone who receives post from their energy provider or even just goes shopping at the supermarket can see at first hand that prices are rising sharply. Many everyday items, in particular energy (gas, heating oil, diesel or petrol) and food – and here in particular vegetables – have become more expensive. Price shocks everywhere: Will inflation rates rise further or are the increases just temporary?

nflation risks are not only a topic of discussion in the economy consumers are also concerned. If the price of goods continuously increases but wages and salaries rise more slowly than consumer prices, purchasing power is reduced. "When prices rise as a result of inflation, you get less than you did in the past for the same amount of money," says economist Dr Ulrike Neyer, Professor of Monetary Economics. Her research interests lie in the areas of euro system monetary policy, the implementation of monetary policy and financial stability. She regularly writes guest commentaries on these topics. "Following the slump during the coronavirus crisis, the economy is experiencing a

Calculating the inflation rate

recovery and growing. At the same time, we are observing – also as a consequence of the war in Ukraine – disrupted supply chains and supply bottlenecks, resulting in significant price rises for raw materials, which are increasingly spreading through the product chain. Many goods are becoming more expensive and the inflation rate is rising at the same time. In April it

was 7.4%, which is higher than it has been for a long time," explains the expert.

In Germany, the Federal Statistical Office - like other national statistical offices in the European Union - calculates the consumer price index: It measures the average price development of an imaginary market basket on a monthly basis. Ulrike Neyer: "This basket contains various goods and services which are representative of consumption in Germany. In addition to food, clothing and consumer goods such as cars, it also includes rent and insurances. The inflation rate is calculated by comparing how much the basket costs each time. The prices of products we spend more money on (e.g. electricity) are given a greater weighting than products we spend less money on (e.g. sugar or postage stamps). The weightings reflect the consumer behaviour of a typical household. The change in the consumer price index compared with the prior-year month or the prior year is known as the inflation rate." Not everyone notices the price increases to the same degree - it ultimately depends on what people choose to spend their money on as some things have become significantly more expensive while the prices of other things have barely risen at all. "Some people have a car and

like to eat meat, while others always use public transport and are vegetarian. If a person's consumption behaviour differs from that of a typical household, they may be impacted to a greater or lesser degree than indicated by the official inflation rate. You can calculate a personal rate using the inflation calculator provided by the Federal Statistical Office," says the economist.

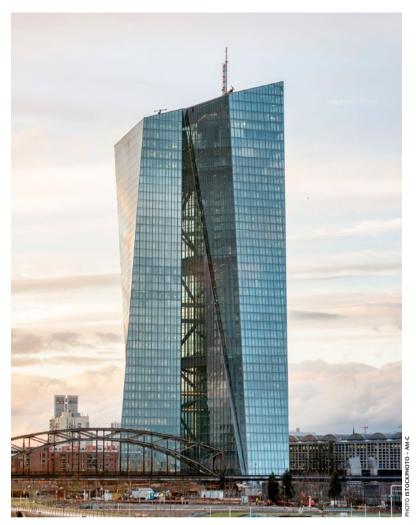
Fluctuations are not rare

Fluctuations in the inflation rate are in principle not unusual: "At the beginning of the nineties, the inflation rate was at a similar level at 4 - 5%. So we need to look at where the high rate comes from - in March 2022 for example, the prices for heating oil were 107% higher and for petrol 47% higher than in the previous March. And it is not only Germany that is affected by this. Prices in Europe have also risen by 7.4% on average in this period," says Neyer. In the meantime, the increase in consumer prices is no longer limited to energy and food. Core inflation, which does not include these things, has also increased significantly, reaching 3.5% at the end of the first quarter of 2022.

"Monetary policy is focused on the medium term and cannot take account of short-term fluctuations. Sometimes it can take more than a year for a monetary measure aimed at stabilising prices to take effect."

Professor Dr Ulrike Neyer - economist

The European Central Bank, based in Frankfurt, is responsible for ensuring price stability in the eurozone. To this end, it prepares regular inflation forecasts.



In the eurozone, the European Central Bank (ECB) holds the key to fighting inflation. It has a clear mandate to ensure price stability through its monetary policy. To this end, it prepares regular inflation forecasts. In addition to modifying interest rates, its instruments also include bond purchases. However, as Neyer says, "monetary policy is focused on the medium term and cannot take account of short-term fluctuations. Sometimes it can take more than a year for a monetary measure aimed at stabilising prices to take effect. This means that there should have been a reaction in monetary policy a year ago - at the height of the pandemic - which would not have made sense and would have choked economic growth. The extensive special measures aimed at tackling the pandemic and its

impact had a stabilising effect and were in principle the right thing to do." In its regular forecasts, the ECB has assumed a relatively moderate inflation rate of 2.4% for 2023, expecting the prevailing high level of inflation to be only temporary. Since the spring – also due to the war in Ukraine – there has been a risk that inflation will become entrenched and thus lead to second-round effects and a wage-price spiral.

The ECB controls monetary policy

What is the ECB doing to counter an entrenchment of inflation? Over the spring

it adopted a "wait and see" attitude, maintaining its expansive course, even though many experts are calling for a drastic turnaround with interest rate rises and an end to net bond purchases in the current situation. Ulrike Neyer: "Monetary and fiscal policy needed to be expansive during the pandemic. However, I am critical of the fact that these extremes are not being reversed under the current conditions. I also find the insistence of the ECB on sticking to the excessively low interest rates over such a long time problematic. With its policy indecision, the ECB is contradicting its own findings."

It remains to be seen when and whether the European currency watchdogs will alter their monetary policy course.







Professor Dr Andreas Weber Biologist

MAGAZINE In 2005/2006, the Federal Government and states launched the "Excellence Initiative", in which HHU has been involved for more than ten years through the Cluster of Excellence on Plant Sciences (CEPLAS). The second funding period began in 2019 within the framework of the new "Excellence Strategy". We would now like to take stock. Professor Steinbeck: How has the "Excellence" concept changed German universities and their relationships with each other?

Anja Steinbeck In my opinion, the Excellence Initiative has resulted in a vertical differentiation of universities. They have grown apart in the sense that there are Excellence Universities – a level that HHU has not (vet) achieved - then universities with Clusters of Excellence and finally universities that are not involved in the initiative. In the participating universities, we are seeing a centring and concentration on the areas funded by the Federal Government and states, with the universities themselves then also providing internal funding for these areas. This strengthens such areas further, but not others; we unfortunately only have limited funds. And it must also be noted that the Excellence Initiative has only been having an impact on research. With the exception of those study programmes established within the framework of the funded clusters, for example quantitative biology at HHU, it has had little effect on the area of teaching.

Andreas Weber In my subject – biology – there has been a shift in weighting towards plant biology. We have become greener.

Anja Steinbeck Which is no bad thing in the current times. Plant biology addresses questions that are extremely important for mankind in view of climate change and a growing global population.

Andreas Weber Exactly: Thanks to CEPLAS, we can now tackle fundamental biology questions together in a much better way because we have gained more expertise in our subject. But fundamental plant biology findings, above all in genetics, also have an effect on other areas of biology.

Anja Steinbeck CEPLAS is also a real pacesetter in many areas. For example in supporting early career researchers – they led the way with tenure-track professorships. Other subjects often look at how CEPLAS has done something and orient their activities to that. CEPLAS acts like a pilot project and trials things, which are then taken up by other disciplines if they are successful.

CEPLAS is raising the international profile of HHU

MAGAZINE Has CEPLAS helped raise the international profile of HHU?

Andreas Weber Definitely, yes. The partnerships we have and the international researchers who work with us clearly show that Düsseldorf has gained a reputation internationally in the plant sciences sector. We can attract better talent on an international level and postdocs from Anglo-American countries are now also coming to us. That wasn't the case in the past.

Anja Steinbeck We are attracting good people. The Humboldt professorship held by Wolf Frommer, who came to HHU in 2017, is certainly the most prominent example.

"Thanks to CEPLAS, we can now tackle fundamental biology questions together in a much better way because we have gained more expertise in our subject."

Professor Dr Andreas Weber – biologist







CEPLAS I

From complex traits towards synthetic modules (2012 - 2018)

Total funding: 34 million euros

CEPLAS II

SMART Plants for Tomorrow's Needs (2019 - 2025)

Total funding: 42 million euros

MAGAZINE Such a large cluster requires organisation. How is the research planned and how do you fit all the individual pieces together?

Anja Steinbeck When a cluster is established, you start with a rough framework and high-level objectives. These objectives must present a coherent image and form a convincing whole. At the same time, however, a "critical mass" of questions must be brought together to enable major issues such as food security to be tackled comprehensively. If a research application does not present these two aspects credibly and simply appears to be a collection of individual projects, it won't be eligible for funding.

Andreas Weber These overarching objectives formulated in the application are the view from outside - looking down from a satellite, so to speak – while the research projects themselves are initiated from the bottom up. No-one tells the working groups what to do. We review the projects to ensure they contribute to the mission, but the ideas and initiatives come from them. In the first round of CEPLAS, we concentrated on the genetic architecture of selected plant properties. In the second round, we have expanded the focus and are now also targeting the predictability of properties from the genome sequence. In the course of our development, we have moved from selected examples towards generalisability. The research areas of synthetic biology, theory construction and data sciences have been added. For the next round of the Excellence Strategy and thus also "CEPLAS 3", we are in discussions with further potential partners about heading more in the direction of translational biodiversity research.

MAGAZINE What does that mean?

Andreas Weber Biodiversity means the genetic variety within a species and beyond species boundaries. The

four of us sitting at this table all look different – we are diverse. How does that come about? What is the relationship between our DNA – the programme that defines the formation of an organism – and its expression, the so-called phenotype? Environmental conditions play a central role here.

Anja Steinbeck If you understand that for one plant, can you also transfer it to other plants or organisms? Andreas Weber You could predict which genetic variants would be particularly beneficial in a specific environment. So you could significantly shorten the breeding process for plants: You would not have to rely on conducting trials involving many random new gene variations created via crossbreeding or mutagenesis. Instead you could predict which combination of genes is particularly well suited to a specific environment on the basis of existing knowledge of fundamental principles and specific genetic information.

Drastically reducing the duration of breeding processes

MAGAZINE In a way that sounds like a paradigm shift in biology.

Andreas Weber Biology is in fact following the path already taken by physics at the beginning of the 20th century. On the basis of fundamental laws and a large data basis of genes – and the phenotypes manifesting from them under specific conditions – we want to systematically generate new plant species. So not through coincidental trial and error, but rather in a targeted process. If that succeeds, it would be a breakthrough innovation! The breeding process – and thus also adaptations to various environmental conditions – could be radically shortened as we would know exactly what we are doing.

Number of publications arising from CEPLAS

>800

Since 2012 (CEPLAS I and II)

Number of PhDs

30

completed (in CEPLAS I), since 2012

38

PhD students in CEPLAS II











President Steinbeck: "Plant biology addresses questions that are extremely important for mankind in view of climate change and a growing global population."

MAGAZINE How far from or close to understanding these interrelationships are you?

Andreas Weber We can already do this for individual properties. For example, with knowledge of the genome we can predict the shape of a leaf: Does it have a jagged or straight edge? But we can't make genome-wide predictions, i.e. for a large number of different properties.

MAGAZINE What needs to happen to make that possible? Andreas Weber We need to be able to apply genome editing in more plant species more quickly. We can do this in model plants like *Arabidopsis thaliana*, but it is significantly more difficult e.g. for wheat. What is really holding us up is our inability to transform plants. In the area of plant research we do not have cell cultures – for example from leaf or pollen cells – that we can work with. By contrast, medical scientists can for example work with liver cells in petri dishes, which makes many things easier.

MAGAZINE So your goal is to develop crop plants which are better adapted to the changing environment, offer higher yields and are more resistant to diseases. How does that work?

Andreas Weber Take barley for example, a research area of Professor Maria von Korff Schmising. She has found out why spring barley is no longer well pollinated above a certain temperature. There is a temperature threshold that limits the fertility of pollen. If you influence this factor, reliable yields can still be achieved above that threshold. This is of concrete relevance in the context of climate change: Spring and thus also higher temperatures are occurring ever earlier, meaning that it may already be too warm for pollination when the barley is in the fields.

MAGAZINE How does this research translate into marketable seeds and thus reach the fields?

Andreas Weber Getting such adaptations into plants via conventional breeding takes a very long time: The entire process, including approval of a new seed, takes at least ten years. If you know where and how the temperature threshold is coded in the genome and use state-of-the-art methods – which we can of course do in research – it would be possible to create climate-adapted barley seeds within a few years.

MAGAZINE Are you referring to the CRISPR/Cas genetic scissors?





New crop plants are growing in the greenhouses in the Botanical Garden.

Andreas Weber Yes. The genetic scissors have revolutionised our work in a very short space of time and are now essential in all areas of CEPLAS. The precision and speed with which we can now realise sequence changes were inconceivable even just ten years ago when CEPLAS I began. CRISPR/Cas was a real breakthrough innovation. The genetic scissors are already being used internationally in plant breeding and plants developed using them will soon be growing in fields outside Europe. Even in Switzerland, the food industry is pushing for approval of the use of the genetic scissors in plant breeding. By contrast, the European Union is at risk of getting left behind and jeopardising the future of plant breeding in Europe.

MAGAZINE By contrast, CRISPR/Cas has gained full acceptance in medical research.

Andreas Weber At least significantly more than in our area. The argument against genetic engineering in plants is that genetic changes to plants in the field may spread through the environment, but this argument misunderstands CRISPR/Cas: As a rule it involves simply

activating genetic variations which already exist in nature and which could also be brought into the plant through crossbreeding. The new process is just much quicker and above all more precise.

Anja Steinbeck It's nonsense to only consider the process. The finished product is what counts. Politicians need to see this.

MAGAZINE How far can science influence political decisions – in this case the regulation of CRISPR/Cas for the development of new crop plants?

Anja Steinbeck That is lobbying work and universities need to perform such work in the same way as the automotive or pharmaceutical industries. It is also a motive for science communication: We are going into the German Parliament and explaining the background. But it's just as important to reach out to citizens, too. CEPLAS was one of the first facilities to systematically develop dialogue with both stakeholders and citizens.

MAGAZINE How successful has CEPLAS been in bringing the topic of crop plant research to a broader public?

"CEPLAS was one of the first facilities to systematically develop dialogue with both stakeholders and citizens."

Professor Dr A. Steinbeck - President

Andreas Weber We feel that event formats which involve citizens directly work best – from guided tours of the Botanical Garden to science slams and the "Pint of Science" format. During the pandemic, direct dialogue was unfortunately not possible but we are now looking forward to finally being able to talk directly to citizens about research again. We have always received very good feedback about our events and noted great interest in plant research as well as real openness to innovative breeding methods. We are increasingly involving citizens directly in research through citizen science projects. For example, we are currently developing a carbon dioxide fixation project with schools in which students are identifying how much CO2 can be fixed in

plant biomass in a specific area through photosynthesis. **Anja Steinbeck** I find it important and inspiring that students and young scientists in particular are getting involved here with innovative formats. They are networking away from established professional organisations, for example to counter dogmatic hostility towards genetic engineering with progressive approaches.

MAGAZINE Has the political attitude towards CEPLAS and the research conducted in it changed in recent years; have you noted influences from governments with different focuses?

Andreas Weber The political environment in the area of fundamental research has improved somewhat over the last decade. At state level in particular we are observing significant movement. However, plants and plant breeding are barely mentioned at all in the current coalition agreement concluded by the Federal Government. Only two terms are mentioned: "population types" and "crowd breeding". This won't help meet the EU objectives of the Green Deal and solve the challenges of man-made climate change.

MAGAZINE How has CEPLAS tried to influence politics? Is there a greater openness towards green genetic engineering?



Professor Dr Anja Steinbeck President of HHU Düsseldorf

Employees at CEPLAS

53 working groups involved

63
employees financed through
CEPLAS (PhD students, postdocs, science
management)

134 Cluster members

45% internationalisation (29 different countries)

Prizes and awards

3 Alexander von Humboldt professorships (1 HHU)

3 ERC Advanced Grants (1 HHU)

3 ERC Consolidator Grants (1 HHU)

2 successful applications for research buildings pursuant to Art. 91b (ZSL, PEAC) (both HHU)

9 members in the Leopoldina German National Academy of Sciences (4 HHU)

Andreas Weber CEPLAS has played and continues to play an advisory role in a variety of ways, in the form of hearings in committees at state and federal level, through talks with MPs and through events in the political arena such as parliamentary breakfasts. We frequently see a great deal of openness towards innovations in the area of breeding in one-to-one discussions, but it rarely translates into decision making and legal framework conditions. We need to enter a new era here to meet the requirements of the future.

New PEAC research building

MAGAZINE So a different perception and a better understanding of developments also changes the possibilities for applying CEPLAS research results, i.e. the translation of research into practice?

Anja Steinbeck Translation is a big topic here. At the university we are making great efforts to promote translation in the sense of establishing spin-offs on a broad basis. And we are starting with the students: It's important to get that "founding gene" into their minds. However, translation at CEPLAS is on a different level entirely. Andreas Weber In Germany and Europe, the instrument of public-private partnerships (PPPs) is highly successful in the plant sector. Cooperation between companies and research is supported, enabling significant transfer from the laboratories into practice. There

are a large number of medium-sized companies in the seed sector in Germany and such companies in particular benefit greatly from PPPs.

MAGAZINE How is the university supporting the ongoing work of CEPLAS?

Anja Steinbeck We have just laid the foundation stone for a new research building: PEAC, the "Plant Environmental Adaptation Center". This building is unique in Europe and has been very well-received across the board thanks to the planning of Professor Rüdiger Simon. Here, from 2024, it will be possible to test the influence of different environmental conditions on plants on a targeted basis, which is technologically very demanding. PEAC is being funded by the Federal Government and the state of NRW, while the university is also investing significant internal funds in the project. And we already have the Centre for Synthetic Life Sciences (ZSL) and the new buildings for biology which offer optimum, state-of-the-art working conditions for the entire subject. These are all HHU investments for CEPLAS 3, with which we want to enter the next round of the Excellence Strategy; the process is expected to start at the end of this year. To be successful in this, we are also actively seeking new cooperation partners.

MAGAZINE Let's take a further look into the future in conclusion: If the application for CEPLAS 3 is successful, we will ultimately be looking at a crop plant research programme at HHU that has been running for almost 20 years; is the topic then exhausted?

Andreas Weber No, definitely not. Climate change, the growing global population and competition for limited arable land mean we face major challenges in the long term. The ongoing rise in temperatures is increasing stress for crop plants – we are also experiencing this in NRW with drought years and ever more frequent storms. So we need new, adapted crop plants.

Anja Steinbeck After such a long period, we must also think about making a research programme like CEPLAS permanent. That's an issue for the government, which really needs to create permanent structures for such well-established and successful topic areas. In my opinion, this must be taken into account in the Excellence Strategy in future.

The interview was conducted by Arne Claussen and Victoria Meinschäfer.





Synthetic biology

Where biology

meets
engineering

BY ARNE CLAUSSEN

Applications in plant research for industrial processes and in biomedicine – Professor Dr Matias Zurbriggen and his research group leader Jun-Prof Dr Hannes Beyer from the Institute of Synthetic Biology see potential applications for their young field of research everywhere. But what exactly is synthetic biology and how can it contribute to the objectives of the Düsseldorf Cluster of Excellence CEPLAS?



he synthetic biology researchers view themselves as being a little like engineers who work with living organisms. "We approach living material with the perspective and working style of engineers," says Professor Zurbriggen. "With a precise understanding of all underlying principles and processes, we want to modify and optimise biological systems and adapt them to new conditions or to have novel functionalities. Or even create new ones from scratch."

What is "synthetic" biology?

But how exactly does it differ from conventional biology? Jun-Prof Hannes Beyer, who received a Freigeist Fellowship from the Volkswagen Foundation for his work at Zurbriggen's Institute last year: "Engineers have an exact product in mind, which should have defined properties. They develop this product on the basis of similar objects using known processes. They design it on the computer and simulate its behaviour on the basis of known physical and chemical properties. This results in a prototype, which is tested and optimised further." A targeted process.

→ Optogenetics: Light-induced, spatiotemporally resolved control of signalling and metabolic processes in microbial, animal and plant systems. CEPLAS researchers are utilising such novel, experimental approaches in their efforts to understand fundamental biological processes and mechanisms, and introduce new properties into crop plants.

"With a precise understanding of all underlying principles and processes, we want to modify and optimise biological systems and adapt them to new conditions."

Professor Dr Matias Zurbriggen — biologist

Professor Zurbriggen: "In the past, biologists usually worked in a different way and were much more dependent on chance. For example, to find plants with new or at least improved properties, mutagenesis – a process in which mutations are randomly generated in genetic material by means of radiation or chemicals – was often used. The many seeds altered in this way are then cultivated and only when the plants have grown does it become evident whether individual specimens have gained interesting properties that should be bred further." This is time-consuming, expensive and not necessarily successful.

Synthetic biology, a discipline established around 20 years ago, aims to practice biology systematically and adapt or optimise organisms on a targeted basis for a variety of applications. This has only been possible since genome sequencing became cost-effective, making the genetic

properties of many thousands of living organisms accessible. Now, sequencing is being carried out to see what the blue-prints of e.g. specific subsystems of a cell – such as those of enzymes – look like and when exactly which genes can be switched on and off to enable a cell to react to changing environmental conditions.

"Once we know all this, we can also think about how the properties of a crop plant can be changed in such a way that the plant is better adapted to climate changes, less water or a shortage of nutrients, more capable of fighting pathogens or more productive," says Zurbriggen, explaining potential applications with a view to the objectives of the CEPLAS Cluster of Excellence on Plant Sciences.

One important tool used in synthetic biology approaches is the CRISPR/Cas method, which can be used to edit the genome precisely – letter by letter, so to speak. "This method also allows e.g. harmful mutations, which lead to diseases and where only a few genetic letters are affected, to be repaired," Beyer says.

But synthetic biology can do much more. Microorganisms such as coli bacteria or yeast cells are already being used to produce chemical substances on an industrial scale. New information containing the blueprints for the desired substances is inserted into the genetic material of these well-understood single-celled organisms. These sequences may have been taken from other organisms. The molecular factories in the cells then use the blueprint for their work.

Professor Zurbriggen: "However, productivity may be so low that this production process would not be cost-effective. But we know other cells that can generate the substances more quickly and in greater quantities. We can also develop new enzymes with new properties that do not yet exist or combine genes differently. As these alternative production processes are genetically encoded, they can now potentially

"We want to create optogenetic organoids, i.e. three-dimensional structures in test tubes that can fulfil the

organs such as the liver."

functions of human

Jun-Prof Dr Hannes Beyer — biologist

also be transferred to a bacteria, yeast or plant cell to induce it to produce (new) molecules efficiently."

The pharmaceutical industry was the first to apply such methods. They found out that biological syntheses can also produce highly complex active ingredient molecules where conventional chemistry failed. Beyer: "The mRNA vaccines against the coronavirus are also created in a very similar way."

This technology was originally developed to find drugs to fight cancer, the intention being to use mRNA molecules that encode tumour-specific proteins to teach the immune system to recognise and attack diseased cells, while leaving healthy ones untouched. The first phase II clinical trials are already underway. "These approaches can be developed further towards personalised medicine and therapeutic agents tailored precisely to individual patients, their specific medical conditions and immune system," says Zurbriggen.

Designing new biological process chains

With regard to the fundamental and applied plant research at CEPLAS, Zurbriggen's team is pursuing so-called reconstruction strategies. The first step is to understand all the individual sub-processes in a biological process so well that it can be reconstructed from scratch. Once all these modules and their functionality are known, a new biological process chain can be designed from them and optimised. The objective is "smart plants".

"In CEPLAS, we are for example looking at how a plant absorbs and stores carbon dioxide, and how it uses water or other nutrients," explains Professor Zurbriggen. He continues: "If we know one other plant that has learnt how to grow well and build up biomass in arid conditions, we can perhaps add precisely this optimisation to crop plants to improve their ability to cope with climate change."

A synthetic leaf could be an objective. It does not need to look like a natural leaf but it would fulfil all the functions a plant requires of a leaf, such as carbon dioxide fixation via photosynthesis. Such synthetic leaves could be used not only to study and understand fundamental processes better, but also to develop new properties. The two biologists take tomatoes as an example to demonstrate that these approaches are really not that complex: "Tomatoes were originally virtually inedible tiny fruits, but they were more resistant e.g. to disease. Colleagues found out that only five mutations are necessary to obtain tomatoes much similar to the ones we know today from the original form." Synthetic biology can thus also be used to reconstruct and improve evolution.



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Jun-Prof Dr Hannes Beyer and Professor Dr Matias Zurbriggen in the laboratory at the Institute of Synthetic Biology.

One of the focuses in Düsseldorf being addressed in Beyer's "Synthetic Model Biosystems" research group is optogenetics. "Light is an excellent tool for controlling processes: It can be precisely localised – in part in areas within a cell – and permits extremely quick switching," says Beyer. With his team, he is inserting optical switches – so-called photoreceptors – into biological control units.

Controlling metabolism using light

Plants and bacteria that have to adapt to changing light conditions have such photoreceptors. Plants for example need to ramp up their photosynthesis in good time at the start of the day and they need to know when it is time to shed their leaves in autumn when the days get shorter. Biologists can insert such photoreceptors into signalling chains to switch e.g. metabolic processes on and off using light. Or they can use them to ensure that certain DNA sequences are only read out when they are enabled via a pulse of light, allowing cellular processes

in bacterial, plant and animal systems to be controlled. Dr Beyer: "We want to create optogenetic organoids, i.e. three-dimensional structures in test tubes that can fulfil the functions of human organs such as the liver. These structures are so small that it is very easy to influence them optically." Using the light switch, specific metabolic processes can be disrupted in the same way as during illness to see how this affects the system as a whole.

Organoids can serve as disease model systems to test the effect of medication. Beyer: "Creating the organoid from patient tissue would even make personalised medication tests possible, which would in turn make it possible to find a therapy optimally tailored to each individual, although this is of course still a long way in the future."

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n this context, it is important to know that the health sector worldwide accounts for around 4.4% of the global CO₂ footprint through energy, anaesthetic gases, other pharmaceuticals, materials, consumables and waste. And, as a Canadian study shows, anaesthetic gases account for approx. 50% of the harmful emissions from the operating theatres of a hospital.

Scientific pilot project

This prompted Professor Dr Peter Kienbaum and his team to initiate a scientific pilot project: The widely used "volatile anaesthetics" are persistent halogenated hydrocarbons. Kienbaum explains: "Most of us are familiar with the abbreviation CFCs, which stands for chlorofluorocarbons. Their use has been restricted worldwide as they exacerbate the greenhouse effect and thus contribute to global warming. We wanted to make a contribution towards significantly reducing this harmful effect."

However, dispensing with volatile anaesthetics is not an option: The gases are highly effective, easily controllable and gentle on patients. Even high-risk patients recover quickly and very well from an anaesthetic thanks to their use, which has been tested and proven in billions of cases worldwide. They are indispensable in operations on severely ill patients or children. To date, however, it has usually been the case that these volatile anaesthetics exhaled by patients are directly extracted from the anaesthetic machine and emitted into the outside air.

The solution was to collect and even reuse the gases. "And it works," Kienbaum is delighted to report. The anaesthetic gases exhaled by a patient while under anaesthetic are collected via an activated carbon absorber connected directly to the anaesthetic machine and then stored. The technical effort involved is comparatively low. The absorber system already exists in intensive care medicine, but extensive preparations were required before its concrete application in the operating theatre. "I sat down with a pharmaceutical company for this. After all, the manufacturers really ought to consider how to dispose of their products in a sustainable way. It was also necessary to conduct a risk assessment with the medical technicians at the hospital beforehand," says Kienbaum.

In the next step, the absorbers are collected and dealt with by the manufacturer. The anaesthetic gases retain their full effectiveness and quality, so they can be safely used for further patients. This makes volatile anaesthetics the first drugs that can be reused in the future. A further positive effect of the recycling system: The resources used in drug production and provision are significantly reduced, which in turn reduces energy use and waste.

"Depending on the patient and duration of the operation, just under 50% of the volatile anaesthetic used can be recycled under favourable conditions."

Professor Dr Peter Kienbaum — anaesthetist

Within the framework of the pilot study, the Department of Anaesthesiology is now using the absorbers in five operating theatres at Düsseldorf University Hospital to enable scientific evaluation of their use. The results of the study headed by Professor Kienbaum also show however that some of the anaesthetic gases inhaled by patients and absorbed into their bodies are still stored in their bodies after they have recovered from the anaesthetic. The exact amount of these gases is still being investigated and probably depends on various factors such as the duration of the operation or the weight of a patient. This amount is only exhaled in the hours after the anaesthetic and cannot therefore be collected via the anaesthetic machine.

Climate- and patient-friendly

Peter Kienbaum draws a positive conclusion: "We are very satisfied with the results to date. Depending on the patient and duration of the operation, just under 50% of the volatile anaesthetic used can be recycled under favourable conditions. Thanks to this more climate-friendly anaesthetic, anaesthesiologists can continue to use the full range of available medication for safe and patient-friendly anaesthetics in the future, while also protecting the climate."

MacNeill, A. J., Lillywhite, R. & Brown, C. J. (2017). The impact of surgery on global climate: a carbon footprinting study of operating theatres in three health systems.

→ https://doi.org/10.1016/S2542-5196(17)30162-6

Economic sanctions against Russia

Fundamental principles and limits of international law



BY CAROLIN GRAPE

Since the end of the Cold War, the United Nations and in particular western governments have increasingly relied on international sanctions to resolve conflicts, for example as an instrument for punishing breaches of international law, human rights violations, the development of weapons of mass destruction or terrorism. Dr Matthias Valta, Professor of Public and Tax Law at the Faculty of Law, considers the fundamental international law principles of sanctions.

wide range of financial and trade sanctions, e.g. a trade embargo, import, export and investment restrictions or financial controls, all fall under the heading of economic sanctions. Since the beginning of the 21st century, so-called "smart sanctions" have been employed with the aim of reducing the negative impact on the wider population of the targeted countries. Personal sanctions such as travel bans, account freezes and similar target the government elite, its supporters and key areas of the economy. The usual purpose of all restrictions is to achieve the economic and diplomatic isolation of a state or a group of people (essentially the elite of a country). Yet they must also comply with international, European and national legal provisions.

With its military invasion of Ukraine on 24 February, Russia violated the prohibition of the use of force (Art. 2.4 of the UN Charter), the principle of non-intervention (Art. 2.7 of the UN Charter) and the principle of the sovereign equality of member states, thus clearly breaching international law and calling its validity into question. The UN General Assembly condemned the invasion with a broad majority but the UN Security Council was paralysed by Russia's veto right. Following an early decision against military intervention, the USA, the European Union and other states quickly resolved to supply weapons and significantly intensify the targeted smart sanctions in place since the annexation of the Crimea in breach of international law in 2014. The intention is to cut off the Kremlin's financial and technological means to finance the war, impose tangible economic and political costs on the political elite in Russia responsible for the invasion and weaken the Russian economy by sanctioning key industries in the medium to long term in order to generate (domestic) political pressure to bring about political change and eliminate the economic basis for the current policy.

The personal sanctions imposed restrict the freedom of the oligarchs, seize their assets and also affect President Putin and Foreign Secretary Lavrov. Financial sanctions have cut Russian banks, including its Central Bank, off from western financial markets and the partial exclusion from the SWIFT payment system has isolated the Russian financial system worldwide, forcing it to seek costly alternative solutions.

The limits of economic sanctions under international law

In response to the question of whether the implemented sanctions remain compliant with international and European law, Matthias Valta explains: "Sanctions represent a serious intervention in the international economic order and are not legally permitted "just like that". Firstly, they affect global trade law as they discriminate against and exclude goods and services from the targeted countries from the market. Under European law, the decision on whether and how economic or financial relationships to one or more third countries can be suspended, restricted or terminated entirely must be taken in a multi-step process. Russia's exclusion from SWIFT also hinders the payment transactions of third countries who may choose not to impose sanctions."

"The legitimate purpose of the sanctions is to prevent or bring an end to the international armed conflict."

Professor Dr Matthias Valta — lawyer

The sanctions are at odds with the regulations of the General Agreement on Tariffs and Trade (GATT) of the World Trade Organisation (WTO) in the sense that trade advantages granted to one contractual partner must be granted to all partners in the interests of equality (most-favoured-nation principle). However, the safeguarding clause in the GATT permits exceptions to enable key national security interests to be maintained, in particular in cases of war and crises in international relations. So the sanctions imposed on Russia do not violate world trade law.

In addition, it must be ensured that the sanctions do not run counter to the international law principle of non-intervention. As a norm under customary international law, this principle prohibits or restricts the influence of a state in the domestic affairs of another state and is intended as a protective mechanism for sovereign states. However, the sanctions can be justified under the right to take countermeasures, which is also recognised as "customary international law". The idea: "In the event of a violation of obligations under international law such as in the case of an invasion, every state should in principle be permitted to work towards restoring peace," says Matthias Valta. The legal expert explains: "However, in the international law practice of the member states, the conviction has developed that not every interest rep-

The principle of non-intervention versus customary international law

resents sufficient justification. It must outweigh the interests of the sanctioned state. However, unaffected third-party states are permitted to impose sanctions against serious human rights violations, relevant threats to international security and violations of universal international law. The occupation and annexation of the Crimea and occupation of eastern Ukraine already counted as serious

The Swedish furniture company IKEA has temporarily stopped all exports and imports from and to Russia and Belarus. The same applies for production in Russia.



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Protest against the war in Ukraine: Demonstrators call for embargoes on Russian oil and gas.

violations of the prohibition of the use of force and the territorial sovereignty of Ukraine. And this applies all the more to the current large-scale military invasion by Russia aimed at forcing a change in government and the further violation of territorial integrity." This is also confirmed by the right to collective self-defence (Art. 51 of the UN Charter), according to which even military assistance against the aggressor would be permitted, meaning that sanctions are quite definitely allowed.

As set out in the case law of the European Court of Justice on the sanctions already imposed in 2014, there is also no violation of the principle of proportionality as it applies in international and human rights law. Matthias Valta comments: "The legitimate purpose

Matthias Valta addressed the topic of sanctions in the lecture series recently organised by the Faculty of Law entitled "Law in conflict situations – perspectives on the war in Ukraine".

of the sanctions is to prevent or bring an end to the international armed conflict. The proportionality of the sanctions should be measured against this. In any case, they are suitable for achieving this purpose: Even though it is difficult to influence political calculations in the case of Russia, sanctions encourage political change and limit the consequences by maintaining the normative claim of international law. With regard to proportionality, securing peace fundamentally outweighs even significant economic disadvantages."

The principle of proportionality

The right to life represents a further limit: Sanctions must include humanitarian exceptions that ensure the supply of water, food and medical products. "However, no life-threatening supply gaps are foreseeable as a consequence of the targeted sanctions against the Russian financial and energy industries," says the legal expert.

Valta concludes: "Consequently, there is a solid legal basis for the economic sanctions already imposed and even for further escalation. To a certain extent, they are actually the prerequisite for ensuring that international law is not undermined. What escalation would encourage a change in Russian behaviour and what costs each sanctioning state is prepared to bear itself over what periods are therefore primarily political questions."





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