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science stories

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European Science Stories

Dear Reader

Detlef Günther, Michael Schaepman, Agatha Keller and Sofia Karakostas.

Since 25 years, scientists of both ETH Zurich and the University of Zurich have been participating very successfully in various European Framework Programmes for Research. These programmes have changed substantially in terms of structure and focus over the past years; yet, what has remained unaltered are the international research collaborations and the establishment of numerous networks in fascinating research domains that contribute to addressing societal challenges:

Cyber crime is a topic of international interest. Consequently, it makes perfect sense that research on cyber security requires international cooperation. Myriam Dunn Cavelty and Matteo E. Bonfanti of the Center for Security Studies (CSS, ETH Zurich) are part of the EU project TAKEDOWN with 18 partners from 13 countries, in which the various phenomena of cyber threats are analysed. The goal of the project is to prevent cyber crime through understanding the causes, structures and dynamics of perpetrators. Beneficial side effects of working in such an international team are the acquisition of knowledge, establishing new networks and gaining management skills.

Perseverance and a high-risk explorative approach are key for visionary research. These qualities define the research career of Andreas Plückthun, Professor of Biochemistry (University of Zurich) and creator of functional proteins. His numerous European and other international research projects prove the success of this attitude. The passion for the unpredictable and the creation of new proteins by «directed evolution» already led to the development of new therapies against cancer and retinal disease. This visionary research is highly complex and strongly depends on collaboration with other partners with complementary knowledge.

In his ERC project about fluid mechanics in collective behaviour (FMCoBe), Petros Koumoutsakos, Professor and Head of the Computational Science and Engineering Laboratory (ETH Zurich), simulates fish schooling and blood flow. By fusing models, algorithms, data and using high performance computing, these phenomena can be understood and learned from. However, computational science is limited by the physical restrictions of digital technology. Koumoutsakos and his research team are involved in developing new methods, systems and the next generation of emerging and sustainable computing.

All of these topics are currently highly relevant and likely for decades to come: These success stories vividly demonstrate that research depends on and benefits from international networking and collaboration. Therefore, the Horizon 2020 programme is an extremely important mechanism for Swiss scientists! Our EU GrantsAccess team offers their experience and competent support during every stage of your project; get to know the members of our Legal Team on the last page of this issue of the Science Stories.

Enjoy reading.

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Extensions of the human brain

Computational science – expanding the range of thinking.

What connects Aristotle to modern computing, why the digital age soon comes to an end and what will follow next. A visit to Petros Koumoutsakos.

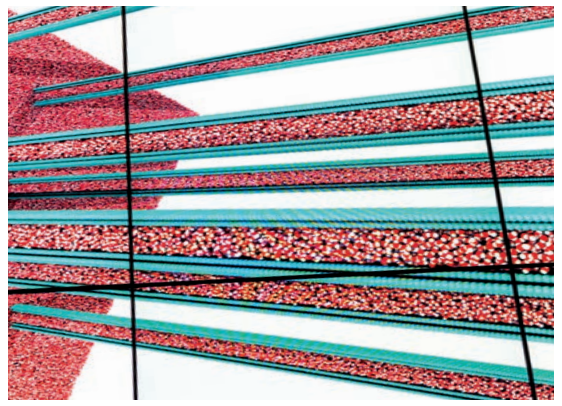
We meet Petros Koumoutsakos in his office on the top floor under the roof of an old former residential building. The small flats of this five-story house were turned into offices and seminar rooms to accommodate the Chair of Computational Science of ETH Zurich. Climbing up the steep stairways, we pass colourful pictures painted on the walls. Portraits of Aristotle, Newton and Bayes kindly smile at us on the third floor and a pod of dolphins welcomes us on the fourth. When we finally reach the fifth floor, slightly breathless, we first want to know more about these paintings. After a warm welcome, Petros Koumoutsakos tells us that these pictures have been painted by a former «artist in residence» in his lab, a young graffiti artist originally educated in Byzantine painting at the School of Fine Arts at the National Technical University of Athens. While we sit down at the table, he explains what these pictures have to do with computational science: «I would call computing an augmentation of the human brain that extends the range of our thinking. But the human brain is always at the centre. Modern computational science is rooted in a long tradition of human thinking, based on the findings and conclusions of Aristotle, Newton and Bayes. That is why I have their portraits painted on the wall.» And with a smile he continues: «The four causes (material, formal, efficient and final cause) of Aristotle are at the core of the definition of multiscale modelling.

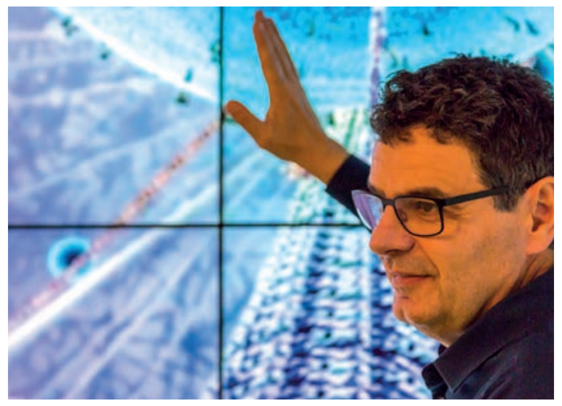
> Computational science is a domain of knowledge, aiming at understanding nature and solving complex problems with the help of computers and mathematics.

But Aristotle just provided a framework for thinking. Isaac Newton was the first who put down principles in mathematics quantifying natural phenomena by physical principles and mathematical formula. However, today we find that Newton's deterministic approach does not take into account uncertainties and the inherent stochasticity of physical systems. So here, the English mathematician and Presbyterian minister Thomas Bayes comes in. He stated that every model has its parameters depending on data. Today, with the massive availability of data and supercomputers, we revisit physical laws. Data-driven, Bayesian uncertainty quantification is a key research field in our lab. Bayes' theory requires the computation of integrals in high dimensional spaces which we can accomplish thanks to the available efficient machines.»

A powerful tool

Computational science, the fusion of models, algorithms, data and high-performance computer, has opened completely new horizons in tackling scientific and even societal problems. It allows us to solve complex problems in relatively little time and to perform «what if?» studies and optimisation. What Petros Koumoutsakos fascinates most about computational science is the





translation of highly difficult problems into algorithms enabling the computers to output facts-based reliable answers. The analysis of the models, simulations, data and visualisations help scientists to understand physical phenomena or suggest feasible solutions to engineers. A key topic he and his group are focusing on are the problems of fluid mechanics of collective behaviour.

> Modern computational science is rooted in a long tradition of human thinking based on the findings of Aristotle, Newton and Bayes.

Fluid mechanics are fundamental to collective behaviour in nature and technology, as fluids pervade complex systems at every scale, ranging from schools of fish and flocking birds to bacterial colonies and nanoparticles for drug delivery. Little is known about the role of fluid mechanics in such applications. Is schooling the result of vortex dynamics synthesised by individual fish wakes or the result of behavioural traits? Is fish schooling energetically favourable? How does blood affect the collective transport of nanoparticles in cancer therapy? To all these crucial questions Petros Koumoutsakos and his team want to find the answers through computational methods that resolve the interaction of fluids and multiple, deforming bodies across several scales from macro to nano.

Understanding fluid mechanics

Therefore, in 2013, Petros Koumoutsakos applied for an ERC Grant on «Fluid Mechanics in Collective Behaviour: Multiscale Modelling and Applications» which he received in 2014. Since the project has started, he and his group have achieved quite a number of results. Based on data and existing equations, they have developed the first ever physically accurate simulation of fishes swimming together. «These simulations allow us to understand the fluid forces that fish must overcome in order to swim the way they do and how they are sensing and reacting to their environment,» he tells us while showing the impressive flow visualisation on a large screen. This simulation is much more than a highly sophisticated software based on computational science methods. It has a direct impact on applications. «What we learn and abstract from the fish swimming could be used to put together wind turbines in a windfarm or fly drones in an optimal swarm formation, which could drastically reduce the consumption of energy and improve efficiency,» Petros Koumoutsakos explains. To develop a computer model to understand how nanoparticles flow through blood vessels is another topic he is focusing on within his ERC project. Cancer might be treated by nanoparticles transported through the body of a patient and delivered precisely into the tumour. But there are quite a couple of questions still unanswered. Blood cells have a soft structure, while nanoparticles are quite rigid. How will they interact with each other? Similar questions arise for the detection of other cells, such as circulating tumour cells in the blood stream. There is one circulating tumour cell per billion of red blood. How can we detect it?

> What we learn from the fish swimming could be used to put together wind turbines in a windfarm or fly drones in an optimal swarm formation.

Hence, similar to the school of fish, nanoparticles and tumour cells in a blood stream are collective fluid mechanics phenomena, which Petros Koumoutsakos and his group want to understand and create reliable computer simulations thereof that will help their prediction.

On the eve of a new age of computing

But computational science is more than solving problems by computing and computers. It also deals with key problems of computers themselves. During the last 50 years, according to Moore's law, the number of transistors in a dense integrated circuit has doubled every two years. But this expansion has come to an end due to physical limits. You simply cannot pack additional numbers of processors onto the same area. Moreover, the speed of the machines cannot be exceeded any further as

ERC Advanced Grant

«FMCoBe: Fluid Mechanics in Collective Behaviour: Multiscale Modelling and Applications»

Duration: 2014-2019.

Financial contribution from FP7: 2,498,800 €

there will not be sufficient energy in the near future to run the expanding numbers of computers. They also may effect enormous environmental problems, as cooling the big machines pollutes the environment even more than air traffic. It seems that we soon reach the end of the digital age of computing as we know it. So, what will be the next technology, we ask Petros Koumoutsakos. He names three options to replace digital computing by 2040: Quantum computing, neuromorphic computing (processing information similar to the human brain) and reducing the accuracy of the existing digital computing. For example, instead of up to 25 digits, computing could be restricted to two digits to save energy. Today, scientists and engineers all over the world are thinking of ways to reinvent computing, searching for new methods and systems - and Petros Koumoutsakos is one of them. Together with 50 colleagues from ETH Zurich, the EPFL (École polytechnique fédérale de Lausanne), the University of Zurich and the USI (Università della Svizzera italiana), he is currently preparing a project proposal for the NCCR* on emerging and sustainable computing.

> Cooling the big computers pollutes the environment even more than air traffic.

«Future computing algorithms will merge the classical way of deterministic physical principles and new ways of integrating data in our predictions and thinking processes, bringing Bayes and Newton together. This will have another gigantic impact on our society. Fusing these ideas with new computing architectures and hopefully making a contribution to some societally relevant applications - this is how I see my work for the next ten years,» Petros Koumoutsakos tells us at the end of our visit.

> You start by thinking, you end by thinking and the computer is just an augmentation of our human capabilities.

On the stairways down from the fifth floor, passing the portraits of Aristotle, Newton and Bayes that continue to smile at us from the walls, we remember what Petros Koumoutsakos told us before we left his office: «Even in the new computer age you start by thinking, you end by thinking and the computer is just an augmentation of our human capabilities.»

● Rolf Probala

Petros Koumoutsakos

Petros Koumoutsakos has received his diploma in Naval Architecture at the National Technical University of Athens in 1986 and the Master's degree at the University of Michigan, Ann Arbor, in 1987. In 1992, he acquired his PhD in Aeronautics and Applied Mathematics from the California Institute of Technology (Caltech). After his PhD, he worked as an NSF fellow in parallel computing from 1992 to 1994 at the Center for Research on Parallel Computation at Caltech and as a research associate at the Center for Turbulence Research at NASA Ames/Stanford University from 1994 to 1997. In 1997, he was elected Assistant Professor of Computational Fluid Dynamics at ETH Zurich and in 2000 Founding Director of the ETH Zurich Computational Science & Engineering Laboratory as well as Full Professor of Computational Science. He is an elected Fellow of the Society of Industrial and Applied Mathematics, the American Physical Society and the American Society of Mechanical Engineers; in addition, he led the team that won the 2013 ACM Gordon Bell Prize in Supercomputing of the Association of Computing Machinery. Since February 2018, Petros Koumoutsakos is an elected foreign member of the US' National Academy of Engineering (NAE). This prestigious distinction is seen as one of the highest professional honours accorded to an engineer.

* NCCRs, the Swiss National Centres of Competence in Research, promote long-term research networks in areas of strategic importance for Swiss science, economy and society.

Interview clip:
www.grantsaccess.ethz.ch/en/sciencestories

«This project forces us to think transnationally»

The cyber security specialists Myriam Dunn Cavelty and Matteo E. Bonfanti participate in a European project with 18 partners. Precisely the many partners are very important for their research.

Are we to expect an increase in cyber terrorism in the future?

Myriam Dunn Cavelty: Cyber crime is a real danger and most people are aware of it due to various incidents. However, cyber terrorism is pure fiction.

Is there hardly any cyber terrorism?

Dunn Cavelty: It was once assumed that terrorists would use the virtual network as a cheap means to apply violent pressure. However, fact is that terrorists achieve greater effects and obtain more attention by using bombs and other acts of violence than by attempting cyber attacks. However, there is an increase in connecting organised crime and terrorism: Terrorists use cyber resources for recruiting, for propaganda and their funding by means of fraud, money laundering, blackmailing or the dark net trade.

How imminent is this danger?

Dunn Cavelty: Assessing this danger is rather difficult due to a lack of data information. Nevertheless, a number of incidents have demonstrated that information security is being neglected at many institutions. Last May, the malicious software programme «WannaCry» encrypted data on over 230,000 computers in roughly 150 countries. Many hospitals were attacked as well

and subsequently forced to pay a great amount of money to the perpetrators for the encrypted patient data. Technically, this attack was simple. Many companies and institutions are now aware that they could be attacked; yet, they still invest too little in precautionary measures. Attacks on financial institutions or credit card fraud are unpleasant indeed; however, attacks on so-called critical institutions that would damage our basis of life would be much more serious. This is what people dread most.

Which type of data is interesting for hackers in Switzerland?

Dunn Cavelty: Popular targets are research and development data. Political information are interesting as well: On location of diplomatic talks in Geneva, for example, spy software was found. Banks are also popular targets; however, they are usually relatively well protected as they invest greatly in cyber security.

What are the effects that cyber crime might have on citizens?

Dunn Cavelty: For instance, it is annoying to have your digital identity stolen, as there are several possibilities how this can be misused online. Credit card fraud is common, yet the money stolen is usually compensated. Attacks leading to the fact that we could no longer perform digital transactions over a longer period would be strongly disabling as well. It would become very difficult or even dangerous if a cyber attack were to cause a longer electricity cut.

In order to develop strategies against cyber attacks, your initial approach within the EU project «TAKEDOWN» is to achieve a deeper understanding of cyber crime and cyber terrorism.

Matteo Bonfanti: Indeed. The motivations for cyber attacks are very diverse and depend on the objectives of the corresponding individuals or groups. These objectives may be of financial or propagandistic nature, some perpetrators merely wish to scare people or interrupt their communal life. We collect data on cyber crime and cyber terrorism in order to understand the various phenomena as much as possible. We also analyse the means used in case of attacks, so that institutions can protect themselves better in the future. The basis of prevention is to understand the causes, structures and dynamics of these groups.

You launched the project with a large survey. What were the questions?

Bonfanti: We conducted a Europe-wide survey addressing policy-makers, law enforcement officials, and other first-line practitioners to understand their needs and challenges in fighting and preventing cyber crime and cyber terrorism. For example, we investigated the existing policies and approaches and how they can be improved. As strong transnational cooperation is needed for the fight against cyber attacks, we also asked about how this cooperation can be enhanced. We also inquired on the desired tools and technologies to be employed for countering cyber threats. One of the objectives of this project is to identify the right technologies or other tools to institutions or companies to increase their data security.

How can you support potentially affected parties?

Bonfanti: Our aim is to develop two platforms: TAKEDOWN offers a public platform for the wide European civil society with tools that inform them in detail about cyber crime, terrorism and radicalisation, of how they can identify them and protect themselves against them. This ranges from security guidelines for the everyday user, via guidance for teachers suspecting that a student could become radicalised, up to tips concerning the data protection of companies. This platform also provides access to experts on the subjects for all people interested. What is more, we collect data on cases with which the public or companies were confronted.

What about the second platform?

Bonfanti: This second platform is password-protected and only accessible to national institutions

Matteo E. Bonfanti

Matteo E. Bonfanti is a Senior Researcher at the Center for Security Studies (CSS) of ETH Zurich. He holds a PhD from the Scuola Superiore Sant'Anna di Pisa, Italy. Before joining the CSS, he was a researcher at the Institute of Law, Politics and Sustainability of the Scuola Superiore Sant'Anna, the Centre for Science, Society and Citizenship in Rome and the Central European University in Budapest, Hungary. In 2008, he served as research assistant at the office of the European Data Protection Supervisor (EDPS) in Brussels. Since 2010, Matteo E. Bonfanti has been involved as a researcher in several projects in the field of counter-terrorism, crime prevention, crisis management and cyber security. He also acts as a privacy and personal data protection advisor for private entities.

and law enforcement agencies across Europe. They receive information about mature or emerging technological security solutions (or services) that protect against cyber crime and cyber terrorism. We would like to offer a list of technologies and a list of technology providers. We do not develop the digital solutions ourselves, but we provide an overview of the solutions available and best suited for the parties affected.

18 international partners participate in this project. What makes it special for you?

Dunn Cavelty: Many of the project partners have been working in the areas of terrorism and cyber crime for many years. This profound knowledge has captured our interest. It is also important that the project involves many different countries. Cyber crime and cyber terrorism do not stop at the national borders.

What do you expect from this cooperation in terms of your research?

Dunn Cavelty: We hope for rewarding contacts, a strong network. As the project extends from Bulgaria to Romania to Israel, we will learn about what other countries worry about and what they do about it. Knowing of other perspectives enriches our own research.

Can you give us an example of other perspectives on the phenomenon?

Bonfanti: For instance, our partner in the UK is most worried about cyber crime. The project participants from Romania and Bulgaria are mainly interested in the detection and prevention of corruption; others intend to focus above all on corporate crime.

Dunn Cavelty: What we need are transnational solutions. This is why it is important to conduct collective research on how these groups think, work and how they come into being in the first place.

Bonfanti: This project forces us to think transnationally.

Dunn Cavelty: The perspective of the EU is key for us also in that they are way ahead in terms of the balancing act between cyber security on the one hand and the protection of privacy and individual liberties on the other hand. The EU harmonises laws and introduces an obligation to register for those who have been attacked. It is unpleasant for companies when they have to admit that somebody viewed their data or even stole them. Therefore, the hope is for the companies to increase their security level instead. Switzerland currently discusses a similar obligation to register.

Which EU Member States are most aware of these issues?

Dunn Cavelty: Germany is very active and deals carefully with privacy matters. The UK is also quite ahead of other countries and the Netherlands is one of the best. However, Switzerland is not doing that bad either.

What are the biggest challenges with so many project partners?

Bonfanti: Coordination is difficult with 18 partners from 13 states, with diverse institutions, stakeholders, different cultures, perspectives, interests and languages. I have learned that it is best if you pro-actively approach the partners, set deadlines and remind each other of arrangements. This triggers a domino effect and gradually everyone acts in concert. Such large entities are challenging, that is true, but behind every partner is a human being with a personality, an agenda and personal interests. Throughout this project, I have acquired many management skills that will be very helpful for future projects. In addition, the potential with this many European partners is significant.

Dunn Cavelty: In principle, it is important for Swiss institutions to participate in European projects. We are in the middle of Europe and should therefore cultivate this collaboration and take care of it.

Myriam Dunn Cavelty

Myriam Dunn Cavelty is a Senior Scientist and Deputy for Research and Teaching at the Center for Security Studies (CSS) of ETH Zurich. She studied International Relations, History and International Law at the University of Zurich. She was a visiting fellow at the Watson Institute for International Studies (Brown University, USA) in 2007 and a fellow at the *Stiftung Neue Verantwortung* in Berlin, Germany, from 2010 to 2011. Her research focuses on the politics of risk and uncertainty in security politics and changing conceptions of (inter)national security due to cyber issues (cyber security, cyber war, critical infrastructure protection) in specific. She also advises governments, international institutions and companies in the areas of cyber security, cyber warfare, critical infrastructure protection, risk analysis and strategic foresight.

Will our data ever truly be safe?

Dunn Cavelty: Indeed, we will never see absolute data security; it is an illusion. We have to change our way of thinking: We should not ask how we can achieve absolute security, but instead focus on the consequences of cyber attacks and what to do when they happen. We should deal more with coping strategies.

Yet, ever since the terrorist attacks of 9/11, security is at the top of every political agenda.

Dunn Cavelty: Yes, the attacks have demonstrated how vulnerable our societies are. Now we think that if we focus on security, we will be safe. Some countries have introduced extreme laws at the expense of freedom and privacy to maintain this feeling of security, yet the success thereof is debatable. What we need is a broader debate on what security stands for today in the first place, as well as profound public information about the risks, protections and prevention.

You are dealing with worst-case scenarios on a daily basis, some warn against cyber war. What are the biggest threats at the moment?

Dunn Cavelty: I am more worried about politicians threatening the world with a fusion bomb than about the myth of cyber war. Cyber tools cannot achieve an even remotely physical destruction; therefore, they are secondary.

What is currently the most effective protection against cyber crime and cyber terrorism for institutions and companies?

Bonfanti: It is vital that they invest in the right technical security solutions, hire specialists and regularly instruct their employees regarding data security.

And how can private computer users prevent attacks?

Dunn Cavelty: By consistently updating their computer, by changing passwords, by controlling credit card statements, by not opening everything received via e-mail and by assessing where they post and with whom they communicate online. At home, you would never let everybody inside, just because they knocked at your door. The same precaution should prevail when using the Internet.

Bonfanti: One repeatedly forgets: Once something is on the Internet, you cannot remove it. Nobody knows exactly what the social media companies are storing and for how long. Security starts with the computer users themselves.

● Interview: Denise Battaglia

Interview clip:
www.grantsaccess.ethz.ch/en/sciencestories

Project funded by Horizon 2020

«TAKEDOWN - Understanding the Dimensions of Organised Crime and Terrorist Networks for Developing Effective and Efficient Security Solutions for First-line-practitioners and Professionals», European collaborative Research and Innovation Action.

Duration: 2016-2019
Coordinator: Synyo, GmbH Austria
Partners: 18 institutions from 13 different European Countries
Financial contribution from H2020: 3,421,062 € (274,687 € for ETH Zurich)

www.takedownproject.eu

«The greater the obstacles, the more I am fascinated by them»

Everything is interrelated on multiple levels

Andreas Plückthun designs synthetic proteins as therapeutics, for example against cancer. The current European project now supports his important high-risk basic research.

Andreas Plückthun is a designer and a creator. He creates synthetic proteins. To create something new, to build new substances, has fascinated him ever since his adolescent days. Therefore, he went on to study chemistry in Heidelberg. «I wanted to understand how life works and comprehend the chemical and physical processes behind it all,» he says. However, Andreas Plückthun did not merely wish to understand the processes. Instead, he wanted to use the findings for the creation of something new. During his studies, he specialised in proteins and spent seven years in the US, at Harvard University among other institutions, in order to acquire the skills and knowledge of genetic engineering. This field became popular in the early 1980s in the United States, and Plückthun remembers those days clearly: «I worked in an intellectually highly inspiring environment among many visionary researchers.»

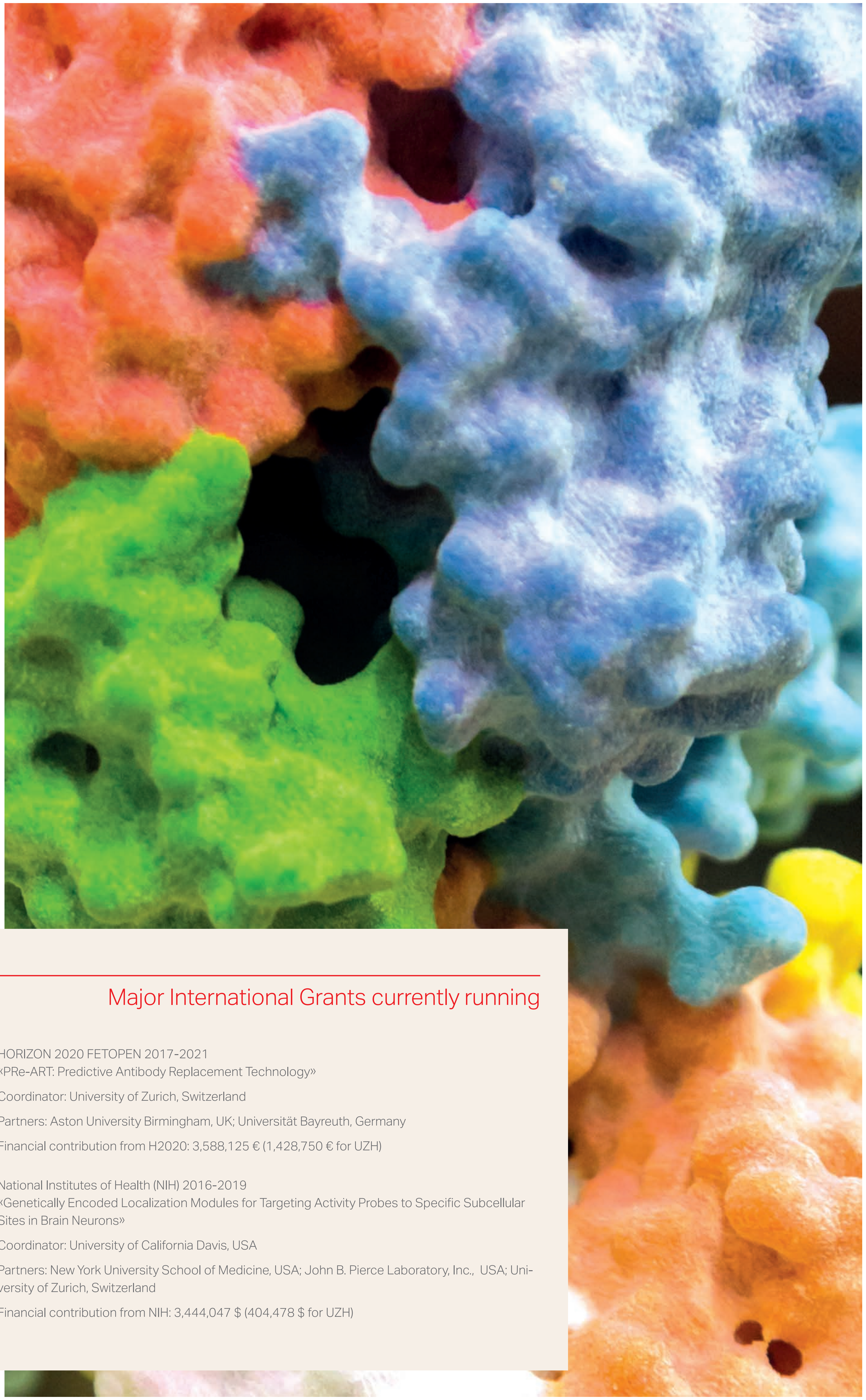
For many years now, Plückthun has been a visionary researcher himself. He is a Professor at the Department of Biochemistry at the University of Zurich, creating synthetic proteins to great success. He has received numerous awards and prizes and has helped to found three spin-off companies over the course of three decades, all three of them developing therapies against diseases on the basis of synthetic proteins. The German biotechnology company MorphoSys, the oldest of the three companies, currently employs 430 members of staff.

Synthetic antibodies and synthetic proteins

Proteins are macromolecules. They are part of the basic building blocks of every cell. In our bodies, there are several hundred thousand different proteins. They are responsible for the cell's structure, but they also serve as molecular machines. They transport substances, such as the blood's iron, they accelerate chemical reactions in the body or slow them down, and, finally, they act as antibodies to fight infections and other diseases.

> Nature is by far a much better creator than myself.

Andreas Plückthun and his team are specialised in the development of synthetic proteins. Creating new protein molecules is done by computer design and by means of the so-called «directed evolution». With this method, the Zurich researchers create simultaneously 100 billion variants of the protein molecules, all of them with small changes (mutations). A few of them then bind tighter to the target molecule - they are enriched, the procedure is repeated and the protein functions increasingly better. «It is our goal to create



antibodies and other proteins that exceed the natural properties and may therefore be used as therapeutics,» the biochemist explains. This revolutionary search strategy was developed by Plückthun some 20 years ago and has been the foundation of his research ever since.

Therapeutics against cancer and retinal disease

Synthetically produced antibodies and other therapeutic proteins, developed according to the procedures from the Plückthun Lab, are currently in clinical trials. One antibody (by the name of Guselkumab), developed by MorphoSys against severe psoriasis, was recently approved by the US Food and Drug Administration as a drug. It is administered by injection every eight weeks. Another class of synthetically created proteins, the so-called DARPins, also show great promise in the clinic. One DARPin for curing macular degeneration, a disease of the eye's retina common in old age, was developed by Plückthun's second company - Molecular Partners - and is currently in the late-stage clinical trial phase. Additional cancer treatment drugs are in clinical trials at both companies.

Plückthun and his team practise their research on the Irchel campus of the University of Zurich in a well equipped laboratory, divided into various special rooms on two floors. In one laboratory, for example, human tumour cells are merged with synthetic proteins to test which of the many variants trigger the desired effect on the cells. The labs are equipped with robots; they analyse thousands of proteins within a few minutes.

So, is Plückthun a creator? He laughs and agrees. «Yes, but a poor one. Nature is by far a much better creator than myself,» he adds. «The closer I get to the core of life, the more humble I have become. The interrelationships and interdependencies are becoming increasingly complex the closer you look.» The perfection of nature's interplay will probably never be reached.

Numerous international research projects

Not that he is frustrated about that. «The greater the obstacles, the more I am fascinated by them. The magnificent aspect of my field is that you can, at least in principle, develop agents for all diseases, for instance, that could fight tumour cells or activate the body's own immune system. All you have to do is find out what the rules are and the effects of each agent.»

> Our research is highly complex and we are therefore dependent on the collaboration with other partners with complementary knowledge.

Plückthun is among those professors at the University of Zurich and ETH Zurich who have raised the most European and other international research project funds. One of the reasons for this success is that he regularly participates in open calls - and that he is persistent: If the first attempt fails, he is not discouraged but focuses on the second try. Together with his team, he participated in the grand total of ten projects of the EU's Seventh Framework Programme for Research FP7, the predecessor of Horizon 2020. He explains his commitment by stating that each project generates research funds, important research findings and new contacts. Being persistent is rewarding: At the end of 2017, he was among only eight out of 190 researchers whose project proposals were accepted by one particular call of the Swiss National Science Foundation.

Coordinator of a FET Open project

His persistence also paid off in view of the current EU funding programme Horizon 2020: In his third attempt, Plückthun received a FET Open project as coordinator. These projects are fiercely contested as well; several hundreds of researchers from all across Europe are participating and only four to five percent of them are awarded. There is a reason for the FET Open's popularity: support is given to research projects with a radical vision, with a pioneering technological goal and with ambitious interdisciplinary research. Already in the early stages, FET Open funds these high-risk projects that might well not ever result in social or economic innovations. Plückthun is delighted that it all worked out. The project is a collaboration between himself, his team and the UK's Aston University as well as the German University of Bayreuth; their goal is to develop a new fundamental platform which replaces the conventional antibody technology. Very simply put, the project team plans to create «Lego® bricks» that improve the diagnosis of diseases in the first place and that, afterwards, may be implemented in therapies, depending on the disease. The project is based on an interdisciplinary approach. The researchers of the three universities combine computer design, the experience from cell experiments, X-ray structural analyses, protein engineering and much more. The Zurich lab is responsible, among other things, for designing proteins, for analysing them and for their synthesis. The partner universities, in turn,

Major International Grants currently running

- HORIZON 2020 FETOPEN 2017-2021
  «PRe-ART: Predictive Antibody Replacement Technology»

  Coordinator: University of Zurich, Switzerland

  Partners: Aston University Birmingham, UK; Universität Bayreuth, Germany

  Financial contribution from H2020: 3,588,125 € (1,428,750 € for UZH)

- National Institutes of Health (NIH) 2016-2019
  «Genetically Encoded Localization Modules for Targeting Activity Probes to Specific Subcellular Sites in Brain Neurons»

  Coordinator: University of California Davis, USA

  Partners: New York University School of Medicine, USA; John B. Pierce Laboratory, Inc., USA; University of Zurich, Switzerland

  Financial contribution from NIH: 3,444,047 $ (404,478 $ for UZH)

will be in charge of other, complementary tasks. «Our research is highly complex and we are therefore dependent on the collaboration with other universities and partners with complementary knowledge,» Plückthun says. This kind of research projects, according to him, has great potential, as all parties involved work intensively on the same questions within a relatively short period of time. «They all have a common goal, are greatly motivated and committed.» Plückthun has acted several times as a project coordinator of consortia; however, it is a first as EU project coordinator. It is yet uncertain whether the researchers will reach their goal in this visionary project. «We know what we want, but nothing similar has ever been attempted before; we therefore do not know whether the molecules that we design and create will eventually function as desired. We do know, though, that if they will - it would have a great impact.»

Participation requests from the United States

The protein specialist has also participated in three projects sponsored by the renowned American National Institutes of Health (NIH), one of them is still running. He did not even apply for this NIH brain research project; the University of California had asked for his expertise in protein engineering and his support. The great reputation of the «Plückthun Lab», as his laboratory at the Department of Biochemistry is called, has been noted in the USA.

He also appreciates the explorative characteristics of these projects. Plückthun considers it crucial that researchers dare to «do without the familiar glow of the lamp» and embark on a journey into darkness, trying something new without having to deliver a predefined product. «Unfortunately, most funds are allocated to research projects with predictable results that are quickly achieved, even though the progress itself is only incremental. The high-risk basic research, by contrast, falls behind.» The unthinkable may only be achieved by explorative research, with much patience and the willingness to take risks.

He believes that the hope placed on genetic engineering for the development of new therapies is great and justified. The development of drugs by means of programmed micro-organisms or cell reactors he deems necessary; however, he considers genome modifications on humans completely irresponsible at this point in time. «We simply do not know enough about the possible consequences, about the interactions and relationships.» During the course of his research, he has become increasingly aware of the fact that everything is interrelated on multiple levels. At first glance, it seems surprising that such a complex organism like a human being is directed by a mere 20,000 genes. «But that is because it is not only the 20,000 genes piloting the organism; they are supported by an inconceivably large number of interactions.»

> If the molecules that we design and create will function as desired - it would have a great impact.

A small mutation to a gene can trigger different effects at completely different locations and levels. «Instead of concentrating on the optimisation of the genome, we should step back and admit in all modesty that we simply know far too little at this stage - all we see is the tip of the iceberg, the major parts are still under water.» Editing the tip of the iceberg irrevocably is a complete taboo for him, but not the continuous research of the entire iceberg. And, as we have seen before: Plückthun is fascinated by the unknown, he is motivated by challenges.

● Denise Battaglia

Interview clip:
www.grantsaccess.ethz.ch/en/sciencestories

Andreas Plückthun

Andreas Plückthun studied Chemistry at the University of Heidelberg and received his graduate education at the University of California at San Diego, where he obtained a PhD. He was a postdoctoral fellow at the Chemistry Department of Harvard University (1982 to 85). From 1985 until 1993, he was group leader at the Gene Center Munich and the Max Planck Institute of Biochemistry in Martinsried, Germany. He was appointed as a Full Professor of Biochemistry at the University of Zurich in 1993. His research achievements include fundamental contributions enabling the emergence of antibody engineering, studies on synthetic antibodies which led to the first fully synthetic antibody library, the development of ribosome display and the development of the Designed Ankyrin Repeat Protein (DARPin) technology. His research remains centred on protein engineering, combining protein design, directed evolution, biophysical basic research and biotechnological applications. In 1992, he co-founded the Munich biotech company MorphoSys AG, in 2004 the Biotech Company Molecular Partners AG in Zurich-Schlieren, and in 2014 the Biotech Company G7 Therapeutics in Zurich-Schlieren (now Heptares Zurich).

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