# eu grants access science stories

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# European Science Stories Dear Reader



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

The European Framework Programmes for Research and Innovation are vital for Zurich. Collaborative projects – along with projects funded by the European Research Council – have always played a central role within the EU Framework Programmes and this has definitely not changed within Horizon 2020. Such projects enable cross-border cooperation between universities, SMEs and industrial enterprises. Therefore, we want to dedicate this issue of Science Stories to three collaborative projects coordinated by the ETH or the University of Zurich:

Clouds, their formation and development, are at the heart of Ulrike Lohmann's scientific interest. As a coordinator of the collaborative EU project BACCHUS, she has teamed up 21 partners from 13 different countries to deepen the understanding of the interaction between aerosol particles, clouds and climate. However, numerous scientific findings, publications and the development of an extensive «Ice Nucleation DataBase» are not the only outcome of the project. Some of the pleasant side effects included the opportunity to gain influence on the sustainable climate policy of the European Union, intensified relationships with the partners, project-management experience and many follow-up projects.

The University of Zurich has been a pioneer in the research on overcoming the regeneration block of the injured spinal cord with the antibody NOGO. The EU project NISCI is on the verge to start testing this promising drug on acute patients to see whether the functions of injured spinal cords can be improved. Armin Curt, coordinator of this translational project, explains how this challenge can only be tackled with a multinational team-effort. At least twelve spinal cord injury centres in Europe are involved in the clinical trials. The greatest challenges so far were obtaining all the necessary approvals, standardising the trials at the different locations and having the drug produced at such a large scale. And now begins the wait for first results.

The MAMI project shows that one does not necessarily need to be an established professor to submit and successfully lead an EU collaboration project. Mirja Kühlewind and Brian Trammell, both postdocs at ETH Zurich, have been coordinating the MAMI project since 2014. Together with six partners from five European countries, they aim to rearchitect the internet in order to make it work better for everyone. Naturally, they are experts when it comes to transport protocols and internet architecture. To allow them to focus on their research, an experienced research manager of EU GrantsAccess reinforces their management team.

You will see that collaborative projects have much more to offer than scientific findings and results: increased visibility, career promotion for young scientists as well as synergy benefits to name but a few. And don't be afraid of the many project administration tasks. Our EU GrantsAccess team will be happy to support you. Learn more on the last page.

We wish you an exciting read.

Michael Schaepman

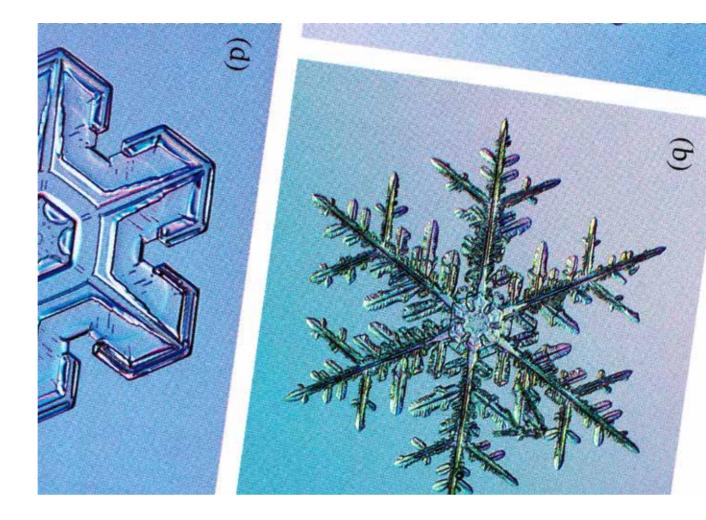
Detlef Günther

Vice President for Veterinary Medicine and Science, University of Zurich

Vice President Research and Corporate Relations, ETH Zurich Sofia Karakostas and Agatha Keller

Co-Heads EU GrantsAccess

the database on ice nucleating particles is at the heart of our joint research / 3



# «The database on ice nucleating particles is at the heart of our joint research»

Ulrike Lohmann analyses the formation and development of clouds as well as the interaction between them and climate. Together with her project manager, Monika Burkert, she just finished an EU project involving 21 partners.

The media call her the «cloud lady». The real name for what she does is by far less poetic: Ulrike Lohmann is a Professor for Experimental Atmospheric Physics at ETH Zurich. Her research focuses on the formation and development of clouds as well as on the interaction between them and climate. Unsurprisingly, the researcher's office is located somewhat nearer to the clouds than others: from the ninth floor of an ETH Zurich building, she has a spectacular view over Zurich West. Three floors above her is the rooftop terrace, from which she can observe the weather and cloud formations. However, Ulrike Lohmann likes it best even higher up. She loves to watch the clouds beneath her: «A sea of clouds with blue sky above is the most beautiful scenery ever,» she says.

She searches for particles – since cloud droplets and ice crystals need aerosol particles as seeds. The dark thundercloud, the fleecy clouds floating in the sky like tiny cotton balls or the impressively twisted cumulus clouds: They all consist of cloud droplets, ice crystals or both. ter and particles only when the media announce «blood rain», as they did for 13 April 2018; when the clouds rain down on us in various colours: red (Saharan dust), yellow (pollen) or black (soot).

A layperson looks for faces, animals or fantasy sculptures when watching the clouds; Ulrike Lohmann, the scientist, looks deeply into the clouds. «I have never been asked to participate in so many EU projects as right now.»

Ulrike Lohmann is interested in the ice crystals and what is inside them. Ice crystals can only form with the help of a grain of sand from the Sahara, a soot particle, a pollen grain or an organic particle from the ocean to which they can attach themselves. As we usually live way below the clouds, we become aware of the fact that they consist of wa-

#### Aerosol particles influence the climate system

These so-called aerosol particles acting as centres for ice crystals hover in our atmosphere and, despite their small size, have a major influence on the formation of clouds, their thickness and phase as well as on the quality of the air that we breathe (particulate matter, smog). Aerosol particles also have an effect on the climate. Some particles contribute to the global warming as they absorb radiation similar to greenhouse gases. Others contribute to the global cooling as they reflect parts of the sunlight back to space similar to a parasol; by this, less solar energy reaches the surface of the earth. Some aerosol particles also destroy stratospheric 4 / the database on ice nucleating particles is at the heart of our joint research





ozone. «Once we get a deeper understanding of how aerosol particles are related to the formation of ice clouds, we will also be able to unravel some reasons behind climate change and precipitation formation,» Ulrike Lohmann explains.

#### EU funding for basic research

For almost 20 years, Ulrike Lohmann has pondered on how and why ice crystals are formed. «I realised early on that we know very little about ice clouds and have therefore started my own experimental group.» Ulrike Lohmann is considered a pioneer in the field of ice crystal modelling within the climate model.

For the past four and a half years, she has been the coordinator of an EU project on the formation of ice clouds, involving 21 partners. «Roughly 15 percent of the resources awarded went to our institute; this enabled us to accelerate our own research,» the ETH researcher says. The EU prothose produced by humankind (such as soot, fine particulates, etc.) on cloud formation and climate. The BACCHUS project had Ulrike Lohmann and her team also dealing with how the cloud formation in the Arctic will be influenced should maritime traffic increase due to the melting of ice. Ships emit soot particles as well as CO<sub>2</sub>.

It was Ulrike Lohmann's first EU project that she headed herself. The FP7 project has just been completed. The final meeting was held at ETH Zurich at the end of April 2018. For the last time, the project participants from 13 different countries presented their results by means of lectures and a poster session. The around 50 attendants discussed climate models, measurement data and methods. The discussions were engaged in a somewhat familiar atmosphere. «Indeed, we have achieved good relationships with the partners over the course of these four and a half years» Ulrike Lohmann recounts. She too, enjoyed the open dialogue. «This is something you can never take for granted, with so many different personalities involved.»

the Center for Climate Systems Modelling at ETH Zurich. «Project management obviously enhances your career-promoting skills,» Ulrike Lohmann states delightedly. The predecessor's management experience with BACCHUS was one of the reasons why she was appointed to her new executive function. Monika Burkert filled in as her successor and brought along the necessary skills: She holds a PhD in Atmospheric Physics and works in Lohmann's group. She is one of those scientists who enjoys «dealing with details of ice nucleating particles in the laboratory,» she says.

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«Roughly 15 percent of the resources awarded went to our institute: this enabled us to accelerate our own research.»

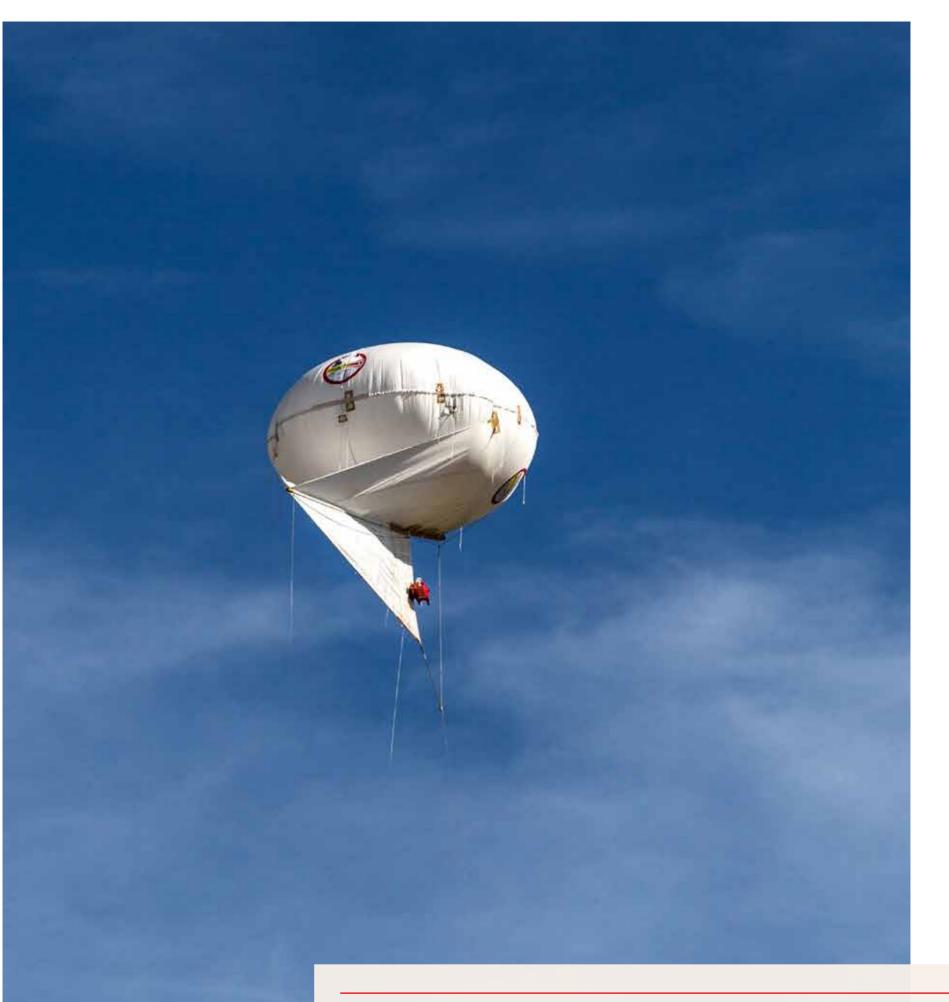
Her passion for detail, her accuracy and the fact that she enjoys interacting with people proved highly advantageous for the project management tasks. When she listed all of the management activities during the final meeting of the BACCHUS group, the crowd was getting rather dizzy. She organised all the meetings, workshops and participations of the group at international conferences. For a while, she maintained the ice nucleating particle database herself. She ensured that the group's members published their results: at the time of the final meeting, the BACCHUS group already published 120 peer-reviewed papers. The project manager organised advanced training for young scientists, was responsible for media presence and the BACCHUS website. She provided the European Commission with reports and made sure that the gender balance improved noticeably

ject is worth 8.7 million € and is called BACCHUS. One of its goals is to set up an Open Access Database with international ice nucleating particle measurements so that users eventually will be able to search for detailed aspects of these measurements and will be able to find possible linked complementary measurements. «We finally want to amalgamate the knowledge gathered,» Ulrike Lohmann states. Another goal was to get a deeper understanding of the interaction between aerosol particles, clouds and climate in order to achieve better projections for future climate and establish improved principles for a sustainable climate policy within Europe. One of the issues raised thereby was to study the effect from natural aerosol particles (such as pollen, algae, salt, etc.) versus

#### Career-promoting project management

Monika Burkert, sitting next to her in the office with a view, nods in approval. She was involved the most with said personalities. Monika Burkert organised and held together the BACCHUS project as a project manager. «I quickly learned to treat the different characters with different approaches,» she laughs.

A project involving this many international partners requires a tight project management. Monika Burkert joined the project half way through, after her predecessor was promoted Executive Director of



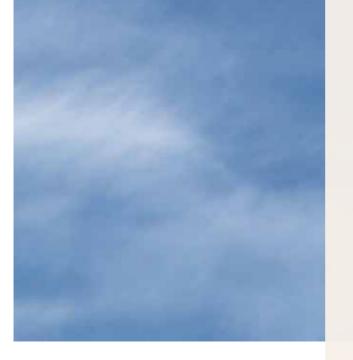
# EU funded projects currently running

#### Projects funded by FP7

• «BACCHUS - Impact of Biogenic versus Anthropogenic emissions on Clouds and Climate: towards a Holistic UnderStanding», collaborative project

Duration: 2013-2018

Coordinator: ETH Zurich, CH



Partners: 21 research institutions from 13 different EU countries.

Financial contribution from FP7: 8,746,587 € (1,391,044 € for ETH Zurich)

«DACCIWA – Dynamics-Aerosol-Chemistry-Cloud Interactions in West Africa», collaborative project
Duration: 2013-2018

Coordinator: Karlsruhe Institute of Technology, DE

Partners: U16 institutions from 6 different countries.

Financial contribution from FP7: 8,746,982€ (340,200 € for ETH Zurich)

#### Projects funded by Horizon 2020

• «ATM-METFIN - Quantifying atmospheric ice nucleating particle (INP) concentrations via advances in measurement techniques and field studies of ice nucleation»

Marie Skłodowska-Curie Actions: European Fellowship

Duration: 2017-2019

Financial contribution from H2020: 175,418 €

#### 6 / the database on ice nucleating particles is at the heart of our joint research



## Ulrike Lohmann

Since October 2004, Ulrike Lohmann is a Professor for Experimental Atmospheric Physics at the Institute for Atmospheric and Climate Science of ETH Zurich. Born in Berlin, she studied Meteorology at the Universities of Mainz and Hamburg. In 1996, she obtained her PhD in Climate Modelling from the Max Planck Institute for Meteorology. She was a postdoctoral fellow at the Canadian Centre for Climate Modelling and Analysis in Victoria and an Assistant and Associate Professor at Dalhousie University in Halifax. She was awarded a Canada Research Chair in 2002, received the AMS Henry G. Houghton Award in 2007 and was elected as a fellow of the American Geophysical Union in 2008 and of the German National Academy of Sciences, Leopoldina, in 2014. Ulrike Lohmann has published more than 200 peer-reviewed articles. She was a lead author for the Fourth and Fifth Assessment Reports of the Intergovernmental Panel for Climate Change (IPCC), who received the Nobel Peace Prize. The award, which she received as an IPCC member, is hanging in her office.

(30 percent of the project participants were female). And this just lists a few of her many responsibilities. She was the contact point for all 21 partners.

How did she manage to do it all? Monika Burkert knows the secret - the coaching of EU GrantsAccess. «They supported me proficiently. Whenever I needed counselling, the information and advice office of the University of Zurich and ETH Zurich was there to help swiftly with their profound experience in international research projects. For example, they could tell me in detail what to do in terms of scientific, administrative and financial reporting.»

However, professional knowledge is not the only asset that facilitates the management of such a large project: you also need personal skills. «The main thing is to quickly get to know the project participants. Knowing each other makes everything easier,» Monika Burkert says. Reminding people was her most difficult task. Certain project participants had to be reminded repeatedly of deadlines. Others did not read emails properly and had to be reminded regularly of the publication policy. «I then had to pick up the phone,» the project manager recounts. «At any rate, I certainly massively enhanced my multitasking skills during this project.» in an international project and establish contacts themselves. The BACCHUS group also attracted the attention of the scientific community, as, for example, they had their special session at the annual conference of the European Geosciences Union in 2016 and because the project participants published continuously. «I have never been asked to participate in as many EU projects as right now,» Lohmann says. The project also produced new or enhanced collaborations spontaneously, for example a joint measurement campaign on Cyprus and in Ireland: The clouds over Cyprus often form on Saharan dust, whereas in Ireland marine and continental clouds forming on various aerosol particles can be observed. «This collaboration opens doors to new possibilities.»

«The main thing is to quickly get to know the project participants. Knowing each other makes everything much easier.» se is set up and will continue to be enlarged even when the BACHHUS project is completed,» Ulrike Lohmann states. She is very happy that the longawaited database is finally a reality. «It is at the heart of the international collaboration.»

# Reducing «aggressive» CO2 and air polluting emissions

Of course, the EU project could not conclusively answer the question raised concerning the interaction between aerosol particles, the formation of clouds and climate. The research conducted in the Arctic showed, roughly summarised, that the emissions of increased ship traffic within the area are less important for the changes in Arctic clouds than the augmented evaporation of an ocean free of ice: the latter creates thicker clouds.

According to Ulrike Lohmann, the impact of aerosol particles from human activities on ice clouds is smaller than assumed. Earlier studies had shown that clouds forming on anthropogenic particles reduced the greenhouse effect by 30 percent; the warming of the earth's atmosphere would have been even higher without them. However, this does not mean that humanity can continue as previously done, because the pollution of the air has a strong impact on people's health around the world. «These findings show that we have to reduce CO2 emissions and air pollution simultaneously and even more aggressively than before. There is simply no alternative.»

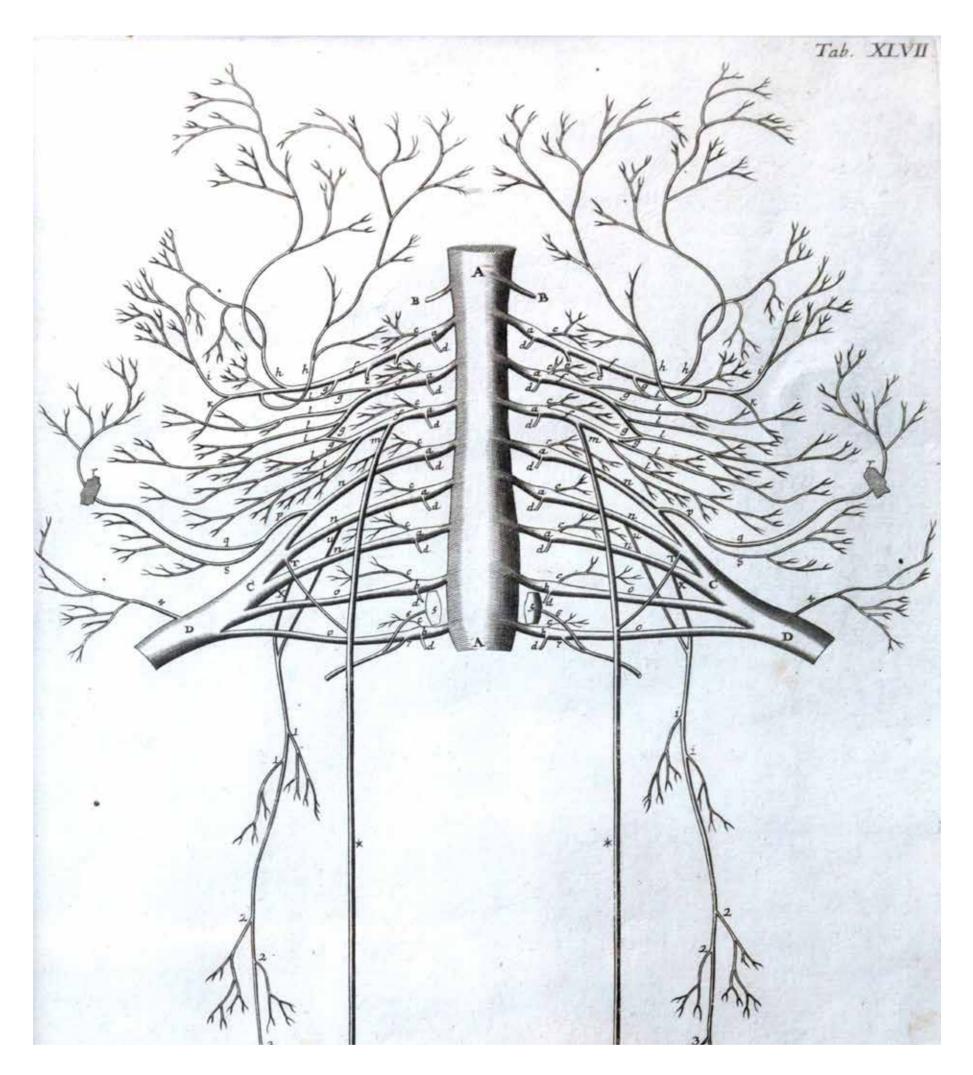
# Attracting the attention of the scientific community

Coordinating a European project with 21 partners is very demanding – yet, the project certainly had enormous benefits, Ulrike Lohmann says. Not only that her research group received funds for their research, they also strengthened and enlarged their network, the PhD candidates and postdocs were able to acquire experiences The BACCHUS project had focused on mixedphase clouds containing water and ice. It examined clouds up to an altitude of 3.5 kilometres. Ice nucleating particle measurements were taken on the Jungfraujoch, captive balloons and cable cars with holographic cameras and so-called skywalkers were sent into the clouds in various countries and one group brought measurement data back from an ocean research cruise, which took them from Bremerhaven to Cape Town with side trips to the Antarctic and back home. The database has been filled with ice nucleating particle measurements from our partners, yet it is not complete. «The main thing is that the databa-

#### • Denise Battaglia

#### Interview clip:

www.grantsaccess.ethz.ch/en/sciencestories



# Repair of the damaged spinal cord

An interview with Armin Curt, Professor of Paraplegiology

# at the University of Zurich.

How a clinical trial with a novel antibody brings new hope to people with a spinal cord injury and why

Armin Curt has been dedicated to this extraordinary project for years.

There are about 250,000 people in Europe suffering from spinal cord injuries. What do these patients hope for?

For people with spinal cord injuries, the desire to find a cure and to recover never stops. Most of the patients find a way to adjust and live with the handicap, but heartfelt hopes do remain that there might be a cure one day. When you ask persons with a spinal cord injury what function they would like to get back if they could choose just one, walking is astonishingly not always mentioned. They ask for hand functions and bladder/ sexual functions. Walking is of course a big desire but there are many other less recognised challenges as well. What can these people hope for from the NISCI project?

The goal of the NISCI (Nogo Inhibition in Spinal Cord Injury) project is not to cure a complete paralysis. It is about finding first steps for a treatment to improve functions in the patients. Within this clinical trial, we focus on tetraplegic (quadriplegic) pati-



## Armin Curt

Injured nerves in the human body are able to regenerate and regrow. But there is one terrible exception: The fibres of the central nervous system of the spinal cord. Therefore, people suffering from a spinal cord injury are partly or fully paralysed for the rest of their lives. Up to now, there is no therapy that repairs the damaged spinal cord nerves. In 1985, Martin Schwab, Professor of Neuroscience at the University of Zurich (since 1985) and ETH Zurich (since 1997) postulated the concept of «inhibitors of neurite growth» as a cause of the absent regeneration of injured fibre tracts in the central nervous system. Subsequently, he isolated one of the most potent nerve fibre growth inhibitors, a protein called Nogo-A. When this protein was blocked, regeneration and functional repair could be shown for the first time in adult rats and monkeys after spinal cord injuries. In a next step, Martin Schwab and his team developed an antibody against Nogo-A which was tested in trials with animals in the early 2000s. The first trial in human beings (2006 – 2008) proved that the antibody is safe and tolerable. In autumn 2018, a second clinical proof of concept trial will start with 140 acute patients suffering from a spinal cord injury to test the efficacy of this antibody therapy. After 33 years of research and trials, there is hope to develop a therapy that helps to repair the damaged spinal cord nerves and make them recover.

ents who suffer from an acute cervical injury (at the level of the neck), which results in an impairment of the legs but also of the arms and hands - a terrible condition indeed. About 50 percent of patients suffering from a spinal cord injury are tetraplegics (quadriplegics). In our clinical trial, patients will be administered a novel drug – the antibody against Nogo-A – to see how this modulates nerve function and hopefully improves the condition of the patients, specially the hand and arm functions. The trial is not a fishing expedition, we will not apply the drug and just see what may happen.

#### «This trial is not sponsored by big pharma. We even have to produce the drug.»

There are clear considerations as to what we look for, what we are going to test and what we expect. developing and standardising recovery profiles for many years. Today, we have gathered the data of more than 4,000 patients within the network. Thanks to this data, we know the degree of recovery quite well that a patient with a specific spinal cord injury can achieve with the existing therapies and we also understand the timelines. Based on these data, we have developed prediction rules which work fairly well. So, when a patient comes to the hospital with an acute spinal cord injury, we can apply clinical test batteries and predict the likelihood for and degree of regaining arm/leg functions with the help of the existing therapies.

#### NISCI started in January 2016. What is the status of the project, two and a half years later?

We have set up the network, we have put together the protocol design and we have just handed in the applications for the trial to the regulatory bodies and ethics committees in Switzerland and the other EU countries involved in the project. Now we are close to the get-go and hope to start the clinical trial in September or October this year. The administrative efforts we have to manage are very demanding, they are on the highest level you can imagine, and it takes a great amount of time to pass all the regulatory hurdles. But we think it is worth to go through this lengthy and challenging process because it is about the safety of patients and, ultimately, we also must assure ourselves to be on solid ground. EMSCI network is that it includes experienced and dedicated SCI (spinal cord injury) centres that are dealing with this kind of patients. They are already trained to look at the patients in doing these assessments and we know what kind of patients they typically see and how many patients they treat per year.

#### «It is not about writing nice papers, it is about getting our patients out of the wheelchair.»

So, we cooperate with these centres to perform the clinical trial with their acute patients. Each of these centres will follow the same procedure. When new patients come in suffering from an acute spinal cord injury, they go through a checklist of inclusion and exclusion criteria and the data will be fed into a prediction calculator, which we share within the EMSCI network. When a patient enters the clinic either in Heidelberg or in Italy or wherever, he or she undergoes a standardised assessment and a prediction. And if the prediction indicates that after the conventional therapy he or she will end up with a very severe, disabling or a moderate impairment, we will invite this patient to enrol for the clinical trial.

The trial is designed to answer a distinct question: How can we improve arm and hand functions? If you ask tetraplegic (quadriplegic) patients whether they prefer to be able to stand and walk or to use their hands, the patients will answer: Give me back my hands! I can live with a wheelchair but not being able to use my hands poses the greatest obstacles in terms of independence.

To what extent can you predict the degree of recovery of a spinal cord-injured person?

What will then happen to the patient who agrees to enrol for the trial?

Within the European Multicenter Study about Spinal Cord Injuries Network (EMSCI)\*, we have been When the trial starts in autumn, how will it be performed? How will you find the participating patients? First, this patient undergoes various standardised and basic clinical tests as well as some additional advanced assessments based on the protocol of the study. This test battery has been trained by the centres. They do them already now, on their

The great advantage of having this large European

<sup>\*</sup> https://www.emsci.org/

#### repair of the damaged spinal cord /9



regular patients. These are clinical tests on what the patient can feel, how he can move, there are imaging tests of the spine from which you see how the spinal cord looks like, where exactly the lesion is located and how grave it is. There will also be some measurements of nerves fibres of arm and legs. All these data will be the base for the enrolment of the patient.

#### And how will the drug then be administered?

The antibody will be injected into the cerebrospinal fluid (CFS) compartment at the lumbar backbone of the patient. It is a typical CSF punch, which you also do when you are looking for meningitis or any inflammation in the CSF. The injection, the dosing, the time interval is exactly the same as we did already in the phase 1 study from 2006 - 2008.

ly the same in each centre. The physicians and nurses performing the trial on site are trained to apply the drug and deal with the patient. But here comes the difficult point. This is a randomised controlled double-blind study, the highest level you can have. Hence, when I treat a patient here in Zurich, I do not know if I am going to inject the drug or just a placebo. Only after a while we can unblind the study and see which one did better, the drug or the placebo.

Half of the patients participating in the trial receive the drugs and may benefit. But the other half receive a placebo and miss a possible improvement. How do you deal with this ethical challenge?

This has been a fundamental problem ever since there have been clinical trials. And to be honest, it is also a challenge for us. But for the rigour of a trial, this is exactly what is needed. All these approval studies are typically designed in this double-blind pattern with placebo and real treatment. There is no way yet on this level of drug development to overcome this challenge. It is an unsolved problem. But it is important to understand that if you have novel drug treatments that are applied for the first time to humans, you must acquire truly valuable clinical data. It cannot be imprecise, as afterwards you may treat thousands of people. When you start with a flaw design and flawed outcomes, this will affect the other thousands of patients to follow. It is a difficult topic.

The University of Zurich is the main sponsor. We have co-funding from the EU (Horizon 2020) and the Wyss Zurich\* is also involved. We even have to produce the drug. This process to produce and get the antibody ready for application is an enormous effort, steered and managed by Martin

\* http://www.wysszurich.uzh.ch/projects/wysszurich-projects/cenereg/

## The long way from basic research to a novel therapy

Injured nerves in the human body are able to regenerate and regrow. But there is one terrible exception: The fibres of the central nervous system of the spinal cord. Therefore, people suffering from a spinal cord injury are partly or fully paralysed for the rest of their lives. Up to now, there is no therapy that repairs the damaged spinal cord nerves. In 1985, Martin Schwab, Professor of Neuroscience at the University of Zurich (since 1985) and ETH Zurich (since 1997) postulated the concept of «inhibitors of neurite growth» as a cause of the absent regeneration of injured fibre tracts in the central nervous system. Subsequently, he isolated one of the most potent nerve fibre growth inhibitors, a protein called Nogo-A. When this protein was blocked, regeneration and functional repair could be shown for the first time in adult rats and monkeys after spinal cord injuries. In a next step, Martin Schwab and his team developed an antibody against Nogo-A which was tested in trials with animals in the early 2000s. The first trial in human beings (2006 - 2008) proved that the antibody is safe and tolerable. In autumn 2018, a second clinical proof of concept trial will start with 140 acute patients suffering from a spinal cord injury to test the efficacy of this antibody therapy. After 33 years of research and trials, there is hope to develop a therapy that helps to repair the damaged spinal cord nerves and make them recover.

«My dream is to see the first approach that truly helps to repair the damaged spinal cord and make it recover.»

This was a study on safety and feasibility from which we learned that the drug has no negative impact on the patient and the way of application has been proven to be safe. Based on the results of this phase 1 study, we will do the clinical trial now in phase 2. There will be six injections within four weeks after the injury, when the nervous system is still plastic enough, allowing to obtain some improvements or increase plasticity. The patient will then be guarded for six months to evaluate the result. The procedure will be exact-

What is the other main challenge you are facing within this project?

First of all, this is an investigator-initiated trial (IIT), meaning this trial is not sponsored by big pharma.

10/ repair of the damaged spinal cord





Schwab and his group at the Wyss Zurich and the University of Zurich. It's a great challenge. That is one part. The other part is that this is a multinational trial including at least twelve centres and I as the clinical PI have to shepherd all these centres and people into the same direction. Moreover, I also have to look for additional funding. We have the EU funding, which covers about 75 percent of the costs. We also gained funding from the Swiss Paraplegics Association and from Wings for Life in Austria. But I have to make sure that we are not running out of fuel. The NISCI project is a very ambitious undertaking that only works because we have a very good setup here at Balgrist with people in clinical care, SCI research, as well as experienced study nurses and many others to help. It is not a one-man show, it is truly a big, big team effort.

## Project funded by Horizon 2020

#### You are very experienced in coordinating complex translational projects. What does this NISCI project mean to you?

The concept of neuroplasticity and the concept to overcome the inhibition that blocks the regeneration of injured fibre tracts in the central nervous system has been pioneered here in Zurich and has a long exciting tradition to work on. After such a long journey, we definitely want to see now if this is really able to change the outcome for our patients. I am a clinician, I see patients on a daily basis and I feel with my patients. I want to see a change. Having all these experiences with this antibody approach and all these preclinical studies, we would like to witness it in humans. Hence, we have a very strong interest to observe this based on the scientific background but also on a day-to-day basis when we treat our patients. It is not about writing nice papers, it is about getting our patients out of the wheelchair. Therefore, we have a strong desire to do something. This clinical trial offers very special conditions. We had other trials with stem cells, with robotics; they all had their special ideas and approaches. However, having the first drug to allow the nervous system (i.e. spinal cord) to be more plastic and achieve an improvement of functions

who suffer from the result of a spinal cord injury. There are more chronic than acute patients. First, however, we need to establish this treatment, showing its worth and open the field to further exploration and investment. Another big challenge is the fact that big pharma has shied away from this extremely difficult field so far. They can earn money more easily with other projects and larger recipient numbers. But we would like to prove that there is reason enough to invest in this treatment.

#### What would be your dream?

My dream is to find the first treatment to improve the neurological recovery after a spinal cord injury. By today there is simply no treatment available to repair the damaged cord. We can offer rehabilitation around the damaged cord. So far, this is the only proven treatment to help the patients and the existing rehabilitation interventions have a good impact on their lives. But obviously they are still limited. I have always wondered why this silly spinal cord refuses to recover (laughing). So, I would like to see the first approach that truly helps to repair the damaged spinal cord and make it recover.

«NISCI - Antibodies against Nogo-A to enhance plasticity, regeneration and functional recovery after acute spinal cord injury, a multicenter European clinical proof of concept trial», Collaborative Research and Innovation Action

Duration: 2016-2020

Coordinator: Universität Zürich, CH

Partners: Universitätsklinikum Heidelberg, DE; Max Planck Gesellschaft zur Förderung der Wissenschaften, DE; Fundacio Institut Guttmann, ES; Fakultni Nemocnice v Motole, CZ; Berufsgenossenschaftlicher Verein für Heilbehandlung Murnau, DE; Fondazione Santa Lucia, IT; Klinikum Bayreuth, DE; Ruhr-Universität Bochum, DE; Ecrin European Clinical Research Infrastructure Network, FR; TP21 GmbH, DE

Financial contribution from H2020: 4,774,444 € (1,928,534 € for Universität Zürich)

https://nisci-2020.eu/index.php?id=1449

- that is what we would like to have.

Is there realistic hope that a patient steps out of the wheelchair after the use of this drug?

Based on my experience, this is very unlikely. There are no miracles. Currently, we do this trial with acute patients to see whether this approach has the potential to improve plasticity and might potentially help our patients. Nevertheless, we also Interview clip: intend to test it eventually on chronic patients

Interview: Rolf Probala

www.grantsaccess.ethz.ch/en/sciencestories

masters of protocols / 11



# **Masters of protocols**

How young researchers of ETH Zurich make the Internet work better for everyone. A journey with Mirja Kühlewind and Brian Trammell.

It's an icy Monday morning in March 2018 in London. While the busy traffic rolls over Edgware Road and commuters pass by, an international meeting on the Internet inside the Hilton Metropole hotel has just been opened. Within the coming five days, more than 1,200 experts - network designers, operators, vendors, researchers and software developers of the Internet Engineering Task Force (IETF) - will meet at the Hilton London Metropole to exchange knowledge, discuss new solutions and work commonly on new standards. The IETF is a large international community of Internet experts who share one common commitment: to make the Internet work better to the benefit of all. Anyone can participate in the IETF provided that the person is willing to contribute his or her technical expertise in an open process to improve the Internet. There is no formal membership or a membership fee. Participants of IETF make their contributions as volunteers, developing jointly relevant high-quality technical documents for the design, use, and management of the Internet. While the Internet is a huge complex global network of networks of millions of computers, the IETF is a network of brains from all over

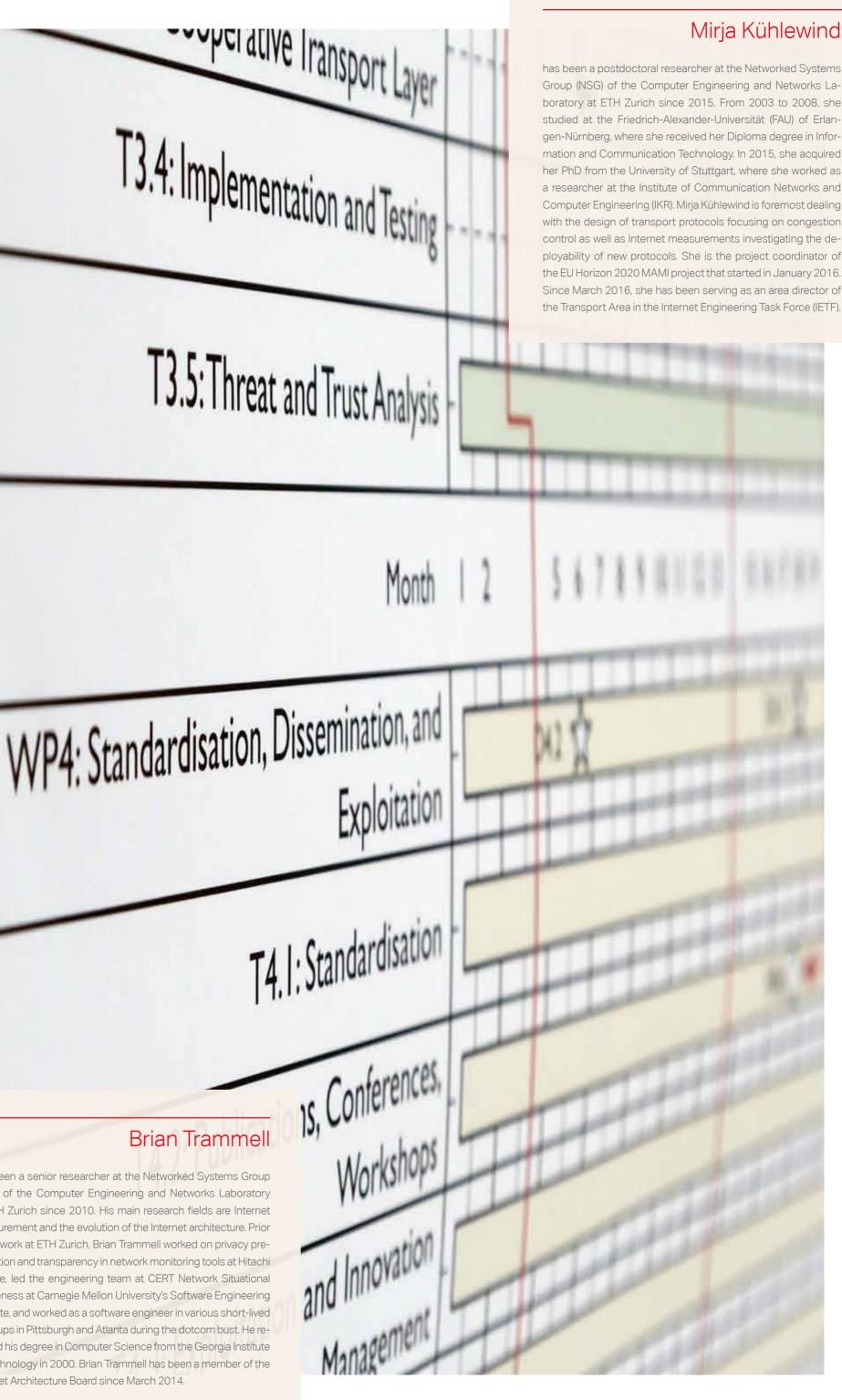
the world, dedicated to keep the Internet operating smoothly. Most of the IETF work is done in specialised working groups whose members are cooperating all year round via mailing lists. However, three times a year, the IETF community assembles for a meeting where the results of the working groups are presented and discussed. At the end of a long process based on «rough consensus», the IETF can set a technical solution as a new standard and recommend its deployment, which is subsequently usually well-accepted by the Internet world." ged in several working groups and committees. Just before the start of the London meeting, Brian was confirmed for another two-year term as a member of the Internet Architecture Board (IAB), which is part of the IETF. And Mirja has just started her second term as an area director of the Transport Area of the IETF, which comprises several working groups dealing with transport and forwarding problems. Mirja happened to join the IETF when she was a PhD student because of a project she was running with a colleague at that time. As she participated very actively in the discussions of the working groups, her colleagues in the IETF motivated her to become first working group chair and then finally one of the directors of the Transport Area in 2016. «My role as an area director is mainly to coordinate and keep the process running properly,» she explains when we meet for a coffee in the hotel lobby between two morning sessions. «I read all documents from every working group in all areas and add my comments before they finally get published. Our aim in the Transport Area is to adapt existing transport protocols or to develop new ones that will be eventually published as so-called Requests for

#### Committed to the Internet community

Among the experts gathering for the IETF session on this Monday morning in London are Mirja Kühlewind and her colleague Brian Trammell, two young researchers and Internet protocol specialists from the Computer Engineering and Networks Laboratory at ETH Zurich. Both have been involved with the IETF for several years and enga-

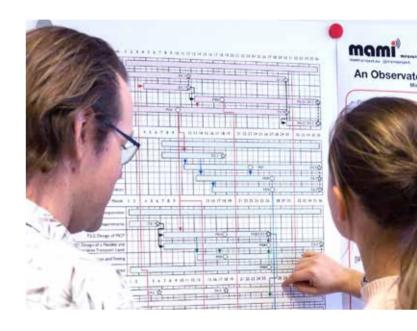
\* https://www.ietf.org

# Mirja Kühlewind



has been a senior researcher at the Networked Systems Group (NSG) of the Computer Engineering and Networks Laboratory at ETH Zurich since 2010. His main research fields are Internet measurement and the evolution of the Internet architecture. Prior to his work at ETH Zurich, Brian Trammell worked on privacy preservation and transparency in network monitoring tools at Hitachi Europe, led the engineering team at CERT Network Situational Awareness at Carnegie Mellon University's Software Engineering Institute, and worked as a software engineer in various short-lived start-ups in Pittsburgh and Atlanta during the dotcom bust. He received his degree in Computer Science from the Georgia Institute of Technology in 2000. Brian Trammell has been a member of the Internet Architecture Board since March 2014.

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Comments (RFCs). These are the standard documents produced by the IETF that are needed for large-scale deployment in the Internet. But this is a long way to go, as not only technology but also politics play a role. You have to convince the community and win the support of the key players of the Internet.» Mirja spends a great deal of her time on work she is doing in the IETF and during the six days of the IETF meeting in London she is facing a tough time, chairing sessions, participating in discussions, and meeting people. But as her research topic at ETH Zurich matches perfectly with the problems she is dealing with as an area director, her engagement is beneficial for both her research at ETH Zurich and the IETF.

#### Privacy versus functionality - conflicting demands

Since her time as PhD student, Mirja Kühlewind has been dealing with the design of transport protocols, congestion control, and the measurement of the Internet. We just take it for granted that emails reach their destination precisely, websites will open in no time and documents, pictures and videos can be downloaded or streamed whenever and wherever. But to make these tremendous communication services of the Internet work, a sophisticated technology of «protocols» is needed. They ensure that the data packets are transported safely through the network in the most optimal way and reach their destinations reliably. TCP (Transmission Control Protocol, which manages transmissions between computers connected to the Internet) and IP (Internet Protocol, which makes sure that packets get across the network) are two of the most common standardised protocols applied by

almost all systems. But the Internet is constantly changing due to new technologies, services, needs, and demands. Consequently, the Internet protocols also have to be adapted to keep the Internet operating smoothly. Apart from new needs and technologies, there is also another development that challenges the hitch-free functioning of the Internet: The growing desire of the users to protect their privacy by encrypting their data as it crosses the network.

#### «The IETF is a network of brains from all over the world, dedicated to keep the Internet operating smoothly.»

While increasing security and privacy for the users is an important goal for many people working in the IETF, it also means that in some cases less information is available to the network that has previously been used to optimise the packet flow through it. As a result, data packets might get unintentionally stuck, changed, or sorted out somewhere on their way through the Internet; they might even slow down the system as a whole. It is like ship containers being packed into special boxes, changing their shapes, preventing anyone from detecting the content of the containers and then provide the boxes with encrypted addresses. Of course, this would cause great confusion along the entire global transport chain.

needs some information about the data packets it transports in order to handle them safely and efficiently. If we start to encrypt everything, this information is lacking. Therefore, about four years ago, inspired by the discussion within the IETF, Brian and I started thinking about the information the network absolutely needs in order to work properly and how we can provide this information only, not more and not less.» To address this problem in depth, Mirja and Brian took the chance when there was a call from the European Commission in 2015 for collaborative projects within the Horizon 2020 program. They wrote a proposal, arranged a consortium of seven partner institutions (four universities, two companies, one research laboratory), convinced the Commission and received the funds for their MAMI project (Measurement and Architecture for a Middleboxed Internet), which started in January 2016.

#### The MAMI project

As a researcher and area director of IETF, Mirja is aware of the conflicting interests between the demands for privacy and the smooth internet traffic management. «I fully agree that privacy is a key priority in the Internet,» she says, «but the network

By the MAMI Project, Mirja, Brian and their partners of the consortium try to overcome three conflicting trends in the Internet: The expanding deployment of encryption to protect end users' privacy, the increasing use of in-network functionality provided by middleboxes and the expansion of new applications like interactive videos demanding for new protocols which will then be impaired with the middleboxes. The aim of the project is to restore the balance between encryption, innovation in protocols and functionalities provided by middleboxes in a cooperative way. Hence, the key target addressed by the MAMI project are the so called «middleboxes» devices that transform, inspect, filter or otherwise manipulate traffic for other purposes than just

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forwarding packets. Middleboxes can be firewalls, network address translators, etc.\*

While we order another coffee from the waiter in the hotel lobby, Mirja explains their approach: «Originally, the only purpose of a network router was to look at the packet in order to see where it should go and then forward it, or, if necessary, drop it. But there are so many additional services in the network today, especially in mobile networks, where middleboxes optimise a great deal. The problem is that they have so many functions, nobody knows what they are doing. So, your transmission might suffer because now it encrypts something that wasn't encrypted before and has been used as input for one of the middlebox functions on the path. In order to overcome this problem, we developed a middlebox cooperation protocol which can be used together with the Transport Control Protocol (TCP) as well as new transport protocols that are currently standardised such as Quick UDP Internet Connections (QUIC), which will then provide the middleboxes with the necessary information but, at the same time, secure privacy of all other data.» For the development of this solution, Mirja and her

team have carried out extensive measurements of the Internet within the months past. Tests showed that their middlebox cooperation protocol works and could be implemented. «The goal of the project has been to get this new protocol defined as standard by the IETF and recommend its deployment,» Mirja explains.

«The Internet is so important to freedom of society. As I have the technical skill to improve the Internet it makes sense to me to do it.»

But so far, she, Brian and the MAMI team have not yet succeeded to convince the IETF community. So, they currently work on integrating the developed mechanisms directly into new protocols, such as QUIC, instead of having a separate protocol that could be used in combination with all future transport protocols the same way. Finally, the MAMI project will end quite successfully in a few months. Besides a new protocol that offers a technical solution to a burning problem of the Internet, the team also gained much knowledge and experience through their measurements, which will be available to the research community and contribute to a better understanding of the Internet. nobody else volunteered, I said I'd figure it out and do it. It is the first time I coordinate an EU project.» One good reason Mirja finally agreed to take over the coordination was the support offered by Katharina Eggenberger of the EU GrantsAccess office. Katharina is an experienced research manager of this service institution, provided jointly by ETH Zurich and the University of Zurich, knowing the rules and regulations for EU grants and the formal management procedures for EU projects very well. So right from submission up to now she has been accompanying the MAMI team as an administrative manager and coach. «Katharina has dealt with all the contract issues with the legal people of the partners. She is also preparing the management and financial reports we have to submit and she helps us in every way to manage the project. I only have to add the technical part to the reports and can focus entirely on the scientific and technical aspects of the project. It's great,» Mirja rejoices. Before we have to end the coffee break as the next session starts, I ask Mirja about the reasons behind her dedication to improve the Internet: «On the wall in my office at ETH Zurich, there is a world map showing the freedom of press. I think the Internet is so important to society, for the freedom of speech, the freedom of press and for an open world. And as I have the skill to work in the technical area to improve the Internet it makes sense to me to do it. And beyond all that - it's fun,» she answers and rushes to the next IETF session on this cold Monday morning at Hilton London Metropole.

\* https://en.wikipedia.org/wiki/Middlebox

#### Coordinating a collaborative EU project

Project funded by Horizon 2020

Project funded by Horizon 2020

«MAMI - Measurement and Architecture for a Middleboxed Internet»; European collaborative Research and Innovation Action.

Duration: 2016-2018

Coordinator: ETH Zurich

When Mirja and Brian launched the MAMI project in 2014, the question arose: Who will coordinate it? «Neither Brian nor I intended to coordinate the project, because at that time it was not clear whether Switzerland would still participate in the Horizon 2020 programme,» Mirja declares. «But as

#### Rolf Probala

#### Interview clip:

www.grantsaccess.ethz.ch/en/sciencestories

# Project Management @ EU GrantsAccess

Large collaborative projects are fun! They allow researchers to learn and benefit from each other; synergies can be exploited, interdisciplinary fields explored. Within a consortium, young scientists can start building their networks, train their presentation skills and get direct feedback on their research methodology and results. Furthermore, the participation in international projects increases the intercultural skills of researchers. In many cases, partners initiate follow-up projects already at consortium meetings, make plans for student exchanges and joint publications – and long-lasting collaborations evolve.

EU-funded collaborative projects must be set up according to a predefined project management structure. This certainly helps a lot during the project implementation. Consequently, the project coordinator and the management team are busy with monitoring deliverables and milestones, organising meetings, writing minutes, communicating with the European Commission, chasing financial reports from partners, observing possible risks and ethical requirements, translating complicated EU regulations for partners, overseeing the publication output of the consortium and mitigating conflicts. These are tasks that are not usually taught in the course of a scientific career but require specialised skills and experience.

Unfortunately, this mountain of management tasks discourages many researchers from coordinating a project. With some extra help, however, the experience of coordinating a project can be very positive and rewarding. To ease the burden, EU GrantsAccess offers various levels of support to coordinators. During proposal preparation, we can assist you with the consortium budget, participate in partner meetings, give input on the management structure and governance, take care of the completion of the electronic forms in the participant portal and connect you with knowledgeable experts for prescreening of your proposal. We also assist and support in answering various questions from project partners.

During the project implementation phase, you can choose between two support models:

- Coaching: The coordinator hires a project manager who is ideally from the scientific field of the project. At the same time, a person of our office is appointed to advise and coach the project manager throughout the lifetime of the project in matters of administration, financials, specific legal issues and project management. The intensity of the coaching is determined entirely by the project manager. He or she can ask for support whenever needed. In our experience, one or two meetings per year plus a few phone calls and several emails are enough.
- Project involvement (only for ETH Zurich/UZH coordinators): A research manager of our office is directly involved in the project. He or she implements communication tools, project processes and management guidance, communicates with partners and the EU Project Officer, defines performance indicators, provides templates, coordinates the reporting and translates EU regulations for the consortium. Ideally, the exact level of support is defined during the proposal phase or, at the latest, before the project starts. Costs for EU GrantsAccess management tasks during the project lifetime, such as personnel costs, travel and consumables, can be charged to the project.



Katharina Eggenberger



Regina Notz

Framework Programme	Akronym	Title	Amount funded
FP6	SIBMAR	Obtaining atomically resolved structural information on individual bio molecules using electron holography	1,434,096€

FP7	ASMENA	Functional assays in for membrane protein on nanostructured supports	3,940,098€
FP7	RESUMENET	Resilience and Survivability for future networking: framework, mechanisms, and experimental evaluation	3,046,594€
FP7	V-Charge	V-Charge - Autonomous Valet Parking and Charging for e-Mobility	5,630,000€
FP7	RNPnet	RNP structure, function and mechanism of action	4,246,947€
FP7	DIVA	Data Intensive Visualization and Analysis	3,355,212€
FP7	Vista-TV	Video Stream Analytics for Viewers in the TV Industry	1,995,000€
FP7	Lakeside zurich	Researchers' Night 07 at the Zurich lakeside - A celebration of European Research in Switzerland	70,000€
FP7	lakeside night	Researchers' Night at the Zurich lakeside - a science festival for all senses	110,000€
FP7	Zurich meets Europe	Researchers' Night 2009 in the heart of Zurich	150,000€
FP7	Tandem	Talent and Extended Mobility in the European Innovation Union	278,628€
H2020	Flourish	Aerial Data Collection and Analysis, and Automated Ground Intervention for Precision Farming	4,780,047€
H2020	Mami	Measurement and Architecture for a Middleboxed Internet	2,901,500€

Coordinated projects with direct management involvement of EU GrantsAccess (since 2006).



EU GrantsAccess International Research Programmes

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