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10th Young Faculty Meeting, 6th June 2017

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Every year at the beginning of June, the «Platform Chemistry» of the Swiss Academy of Sciences (SCNAT) organizes the «Young Faculty Meeting», which has become a very attractive appointment in the agenda of young group leaders working in Swiss universities. Traditionally, the meeting consists of a day of lectures focusing on both fundamental and applied research, covering a multitude of topics from different fields of chemistry, together with talks and discussions focused on career advice. The participation of researchers at different stages of their career, including senior guests and representatives of chemical companies, make this meeting a rather unique opportunity for young group leaders to get inspiration from their peers and to learn from the experience of the most successful researchers working in the country. This year the meeting took place in the wonderful location of the Haus der Universität (Bern) and was organized by ***Fabien Cougnon*** (University of Geneva), ***Albert Ruggi*** (University of Fribourg) and ***Leo Merz*** (SCNAT), with the generous support of the Kontaktgruppe für Forschungsfragen (KGF): BASF, Hoffmann-La Roche, Novartis and Syngenta. To properly celebrate the 10th edition of the meeting, a gorgeous program was offered, including five scientific lectures given by young group leaders, one presentation given by a representative of Roche and three career-related talks given by professors at different stages of their careers. The meeting was concluded with a dynamic and informal panel discussion, which involved the senior guests and the participants in a very stimulating exchange of ideas and experiences.

Participants during the morning session.

Prof. ***Konrad Tiefenbacher*** (University of Basel) opened the day reporting a fascinating example of enzyme-like supramolecular catalysis, applied to the synthesis of cyclic terpenes. In nature cyclic terpenes are synthesized from linear substrates, following a cascade reaction known as tail-to-head terpene cyclization. Such processes are assisted by the internalization of the substrate in the hydrophobic enzymatic pocket (cyclase). Structural preorganization and stabilization of the cationic intermediates within the enzymatic pocket enable the controlled formation of different products (*e.g.* eucalyptol, limonene, α-terpinene) from a single substrate (*e.g.* geranyl pyrophosphate) under mild (pH = 6–7) conditions and with high selectivity. In contrast, this type of reaction is difficult to control using the conventional methods of chemistry. Tiefenbacher's group uses a self-assembled resorcinarene-based molecular capsule as an artificial enzyme mimic. The reaction is initiated by an external acid and takes place inside the cavity of the capsule where the aromatic moieties enable stabilization of the intermediate carbocations *via* cation-π and cation–dipole interactions. This strategy gave striking results with monoterpenes. For instance, the capsule catalysed the transformation of geranyl acetate into α-terpinene, and that of nerol into eucalyptol with yields in the order of 35%. The same capsule was used for other chemical transformations, and enhances enantioselectivity in iminium-catalysed 1,4-reduction of α,β-unsaturated aldehydes. In this case, the capsule binds the iminium species *via* cation-π interactions, providing a steric shielding which favours the reaction on the less hindered side, and improves enantiomeric excess by up to 65% as compared to the experiment without capsule.

Prof. Raffaella Buonsanti

Following up on a different note, Prof. ***Raffaella Buonsanti*** (EPFL Sion) presented the use of colloidal nanocrystals as light harvesting units and electrocatalysts, and showed some intriguing results regarding the influence of their composition and morphology on their properties. Her group develops synthetic methodologies to generate nanocrystals of different shapes, sizes and crystalline structures. After an overview on the synthesis of nanocrystals, Buonsanti covered two main topics in her lecture: the use of copper nanocrystals as electrocatalysts for CO_2 reduction and the use of perovskite nanocrystals for light harvesting. While CO_2 reduction is an attractive strategy to obtain sustainable fuels or useful chemicals, the selectivity towards multicarbon products still constitutes a formidable challenge. Most notably, the ratio between the atoms located on the faces and on the edges of the nanocrystals plays a crucial role in determining the products obtained. The electroreduction of CO_2 by Cu nanocrystals of different shapes (cubic and spherical) and sizes (from 7.5 nm to 63 nm) was investigated. The 44 nm Cu nanocubes were found to exhibit the highest selectivity for the conversion of CO_2 into ethylene, explained by a unique balance in the ratio of face/edge atoms. The second part of the talk covered the applications of nanocrystals as light harvesting materials. Caesium lead halide perovskites are promising light harvesting materials because of their outstanding optoelectronic performances, but the low stability of perovskites in the presence of water, air and light constitutes a major obstacle to develop their application in integrated photoelectrochemical devices. Buonsanti's group has recently developed a method to stabilize perovskite nanocrystals by protecting them with

amorphous alumina deposited by atomic layer deposition. By using this methodology, it is now possible to obtain perovskite nanocrystals that remain stable after 8 hours of solar irradiation, when immersed in water and can be stored under ambient light for more than 45 days.

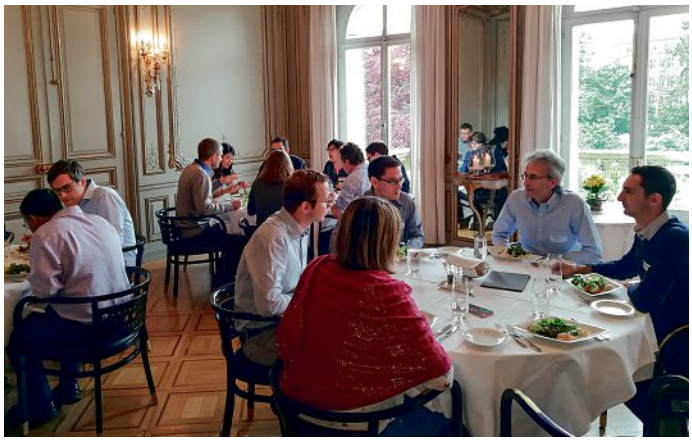
After the coffee break, Dr. ***Matthias Nettekoven*** (F. Hoffmann-La Roche, Basel) introduced the structure of Roche with a focus on its research activities. He explained that Roche is constantly looking for knowledge and innovation, which opens doors for creative scientists to join or collaborate. Meanwhile, Roche is striving for immersion of chemistry students into industrial research by offering one-year internships at the bachelor level. Additionally, internships or postdoctoral collaborations for other scientific disciplines at their research facilities were presented.

For a treatment of Spinal Muscular Atrophy (SMA), a rare genetic disease, Nettekoven gave an insight into Roche's pharmaceutical research. Testing millions of small molecular substances for biological activity can easily be achieved through high throughput screening. But optimizing other properties of an active molecule, such as solubility, lipophilicity or even toxicity, while retaining, or even better, increasing its biological activity is a challenge that only knowledgeable scientists can achieve. A drug development project of this magnitude requires a huge workforce. By investing in such projects, Roche gathers insights and knowledge that might be transferable to other challenging projects in the future.

Prof. Kaori Sugihara

In the following talk, Prof. ***Kaori Sugihara*** (University of Geneva) discussed her research in the field of cell membrane physics and chemistry. The electrical and mechanical properties of cell membranes are mostly elusive due to lack of technique to characterize them quantitatively. Atomic-force microscopy, for example, is limited to the detection and the manipulation of vertical forces. Her group is currently working on the development of a friction force microscope, which can detect both vertical and lateral forces. The current bottleneck in using this technique in biology is its limited detectable force ranges. Recently, her group has identified that the problem originates from the macroscopic friction law used in the method, where the weight of the object governs the strength of the friction force. At nanoscale, where the weight of the object is negligible, adhesion between the substrate and the object plays the more dominant role. By solving this problem, they have demonstrated the calibration of friction force microscopy at pico-Newton forces. This operation force range that matches with typical biological forces is important for their long-term goal to map mechanical forces in biological membranes. Using this method, they are now on the way to correlate the fluorescence signals of mechanochromic polymer, polydiacetylene, with local forces for its application as a cell membrane force sensor. Sugihara also presented a second research topic focused on the electrophysiological characterization of membrane pores formed in the presence of two antimicrobial peptides, defensin and cathelicidin. The presented results show that these peptides exhibit a negative cooperativity towards human cells but a positive cooperativity towards bacteria, explaining why co-localization of these peptides is capable of decreasing their respective toxicity while maintaining a high therapeutic efficiency.

In comparison to the well-studied effects of oxidative stress, little is known of the antagonist deregulation of redox homeostatis: reductive stress. The production of exclusively reductive cellular environments has been, however, correlated to a variety of pathologies such as cardiomyopathy, diabetes and inflammations. Prof. ***Pablo Rivera-Fuentes*** (ETH Zürich) described his interest on the topic and reported the design of photoactivable luminescent phosphine probes to investigate the effects of reductive stress in biological processes. A series of probes was synthesised upon derivatization of suitable fluorescent dyes with a trialkylphosphine, which causes a strong quenching of their fluorescence. The photoactivable derivatives are uptaken by HeLa cells where, upon irradiation with UV light, they release the trialkylphosphine that consequently induces reductive stress. Concomitant release of the dye triggers fluorescence, allowing for a visual mapping of the process. In their work, the group demonstrated that the released phosphine is capable of reducing the oxidized form of glutathione, thus perturbing the redox homeostasis of the cellular environment. The induced reductive stress promotes protein aggregation. The group is currently working on improving the spatial resolution of their technique and expanding its scope, notably by targeting cell organelles.



Discussions continued through the lunch break.

Prof. ***Marc-David Ruepp*** (University of Bern) opened the afternoon session describing his investigation on the pathomechanisms of neuronal death in relation to Amyotrophic Lateral Sclerosis (ALS), a neurodegenerative disorder caused by the selective degeneration of upper and lower motor neurons resulting in muscle wasting and paralysis. The large majority of ALS cases are sporadic. However, some patients suffer from an inherited form of ALS and in most of these cases the responsible mutations have been identified. Some of these cases are caused by mutations in the gene expressing fused in sarcoma (FUS) protein, a ubiquitously expressed RNA-binding protein. The mechanisms by which its mutations induce ALS are unclear. The main goal of Ruepp's group is to investigate the physiological functions of FUS and the pathomechanisms of ALS-linked FUS. One of the major challenges in this investigation is the choice of a good disease model. Since early disease events are initiated by intrinsic factors of motor neurons, Ruepp and co-workers model the disease with motor neurons derived from several isogenic ALS-linked human induced pluripotent stem cell lines created by TALENs and CRISPR/Cas9. The identical genetic background, apart from the mutation, allows the direct comparison between healthy and ALS-linked FUS expressing motor neurons. The alterations caused by ALS-linked FUS are identified by bulk and single cell RNA sequencing. The Ruepp group will then investigate the candidates identified in the transcriptomic profiling to identify potential therapeutic approaches and biomarkers for diagnostics.

Prof. Christian Hinderling

The second part of the meeting was dedicated to lectures focusing on career advice and tips for the young faculty members. Prof. ***Christian Hinderling*** (University of Applied Science, Wädenswil/Zürich) initiated this second session with a presentation of the Universities of Applied Science. Hinderling first presented a general comparison with 'classical' Swiss universities, in terms of aims and organisation, and commented on career opportunities as a lecturer or a professor. He then focussed on his own institution, the Institute of Chemistry and Biotechnology (ICBT). The unique teaching philosophy at ICBT was illustrated through the example of a first semester lab course. Students are encouraged to work with freedom of action and self-control in order to promote their full responsibility and commitment, rather than passivity. The program offered there is an excellent alternative to that of traditional universities, and the students are generally highly sought-after on the job market. At each major stage, the program also offers to their students the possibility to join a traditional university or to enter directly the professional world. Although teaching is the main objective at the UAS, research is an integral part of the landscape: ICBT is composed of 10 sections, divided by fields, with a total of 26 research groups spanning a variety of research interests from environmental biotechnology to physical chemistry. Research often tackles interdisciplinary problems, mostly financed by third-party funding.

Prof. ***Kevin Sivula*** (EPFL Lausanne) provided useful tips on acquiring grants using his own experience as a young independent group leader. He listed the main Swiss and European funding sources that contributed to the expansion of his group within the first few years of his career: the SNF grants (individual investigator grant), ERC grants (starting grant) and Marie Curie Actions (postdoctoral fellowships). He spoke on the topic with contagious enthusiasm and energy, and mentioned little-known but non-negligible opportunities to collaborate with industry on certain research subjects.

Prof. Christian Bochet

This topic was further expanded in the last talk by Prof. ***Christian Bochet*** (University of Fribourg), wittily entitled "Do academics really need to cross the desert alone?". Bochet described with good humour the perks and difficulties of being a young academic in Switzerland. He provided a wealth of strategic career suggestions including a presentation of the different SNF granting schemes and a summary of the evaluation criteria used for hiring at the University of Fribourg. Committees often evaluate the quality of the research performed, along with teaching experience and fund-raising history. He spoke lengthily about the expectations that must be met by young scientists if they want to become successful, and gave a brief guideline of the *do's and don'ts* of an academic career. Advice to be taken with a pinch of salt, as Bochet prompted in the conclusion of his talk, because being successful is a complex equation and there is no general recipe. Nevertheless, it is always good to be reminded that one should never get too comfortable at any stage of their career if they want to remain competitive.

The day was concluded with a panel discussion during which the audience freely interacted with the senior scientists ***Christian Bochet***, ***Christian Hinderling*** and ***Mattias Nettekoven***, joined by ***Volker Herdtweck*** from Roche Human resources. The discussion, which lasted for over an hour, allowed each of the senior scientists to further develop the advice touched upon during their respective lectures and to answer more personally all the questions coming from the participants.

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