Geneva chemistry & biochemistry days 2014

TH 16 January 2014, 9.00–17.40
FR 17 January 2014, 9.00–12.30

Sciences II – auditoire P.F. Tingry A150
30, quai Ernest-Ansermet – 1205 Genève
No registration required

Prof. Gisou van der Goot
École Polytechnique Fédérale de Lausanne

Prof. Eric V. Anslyn
the University of Texas at Austin

Prof. Jean-Claude Bünzli
École Polytechnique Fédérale de Lausanne – Korea University

Prof. Gregory D. Scholes
University of Toronto

Junior speakers: **David Alonso • Pierre Charbonnaz • Pierre Cottet • Julien Graff • Annika Hohendahl • Dawid Kedracki • Marius Koch • Alice Lefranc • Romain Letrun • Bastien Néel • Ilyes Safir • Christelle Serba • Damien Simond • Cecilia Tortoreto • Romain Touilloux • Cansel Ustunel • Xiaojiang Xie • Xiuwen Zhou •**

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FACULTÉ DES SCIENCES
SECTION DE CHIMIE ET BIOCHIMIE

UNIVERSITÉ DE GENÈVE

Foreword:

The steering committee of the "Geneva Chemistry and Biochemistry Days" organised by the *Section de chimie et biochimie*, University of Geneva, is proud to announce the 4th edition of this now traditional event.

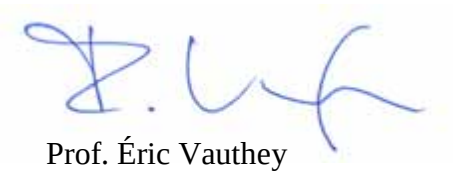
The "Geneva Days" are aimed at giving our students who are close to finishing their PhD studies the opportunity to present their research to a large audience from academia and industry. Our BSc and MSc students are also welcome to smell the very flavour of the research held in our School and learn a bit more about how to present results to a scientific audience.

Four distinguished lecturers will enrich the programme. They have been invited by the Departments of our School (*Département de chimie minérale et analytique*, *Département de chimie organique*, *Département de chimie physique*, *Département de biochimie*) and will seek to illustrate the breadth and quality of chemical and biochemical research in the world today.

This 1.5-day symposium has become the annual *Geneva rendez-vous* between chemists and biochemists from academia and the industry. The event will help stimulate fruitful discussions between young and advanced researchers, and give our students the opportunity to further prepare their professional careers.

We believe that it will give our guests an opportunity to appreciate the high quality of the different aspects of fundamental research performed in our School.

We hope that you will enjoy the lectures and interactions!



Prof. Éric Vauthey
Président de la Section de chimie et biochimie

Steering and organising committee:

Prof. Jean Gruenberg	jean.gruenberg@unige.ch *Département de biochimie*
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Dr Didier Perret	didier.perret@unige.ch *Chargé de communication de la Section de chimie et biochimie*

PROGRAMME – THURSDAY 16 JANUARY 2014

Session 1 – Morning	Chairmen: **Prof. Thierry Soldati + Dr Gaston Crespo**	
09:00--09:15	**Prof. Eric Vauthey**	Welcome message Introduction
09:15--10:05	**Prof. Gisou van der Goot** École Polytechnique Fédérale de Lausanne	Mechanisms of Biological Membrane Perforation by Bacterial Toxins
10:05--10:20	Coffee break	Main hall of Sciences III
10:20--10:40	**David Alonso**	Gradually Twisted Push-Pull Oligothiophenes and their Planarization in Confined Space
10:40--11:00	**Dawid Kedracki**	Polymer-Aptamer Hybrid Emulsion Templating Yields Bio-Responsive Nanocapsules
11:00--11:20	**Marius Koch**	Charge Separation Investigated by Ultrafast Time-Resolved Infrared Spectroscopy
11:20--11:40	**Pierre Cottet**	Copper-Catalyzed Asymmetric Conjugate Addition of Alkenyl- and Alkylalanes to α,β-Unsaturated Lactams
11:40--12:00	**Damien Simond**	A Metalloligand Containing a Three-Fold Axis as Molecular Brick for Supramolecular Self-Assemblies

12:00--14:00	Lunch (all invited lecturers + all PhD students)	Restaurant-pizzeria Sole Mio, boulevard Carl-Vogt

Session 2 – Afternoon	Chairmen: **Prof. Stefan Matile + Prof. Aurélien Roux + Dr Arnulf Rosspeintner**	
14:00--14:20	**Romain Touilloux**	Direct Arsenic(III) Sensing by a Renewable Gold Nanoparticle Plated Ir-Based Microelectrode
14:20--14:40	**Christelle Serba**	Divergent Synthesis of Sesquiterpene Lactones
14:40--15:00	**Bastien Néel**	Towards a Reliable Potentiometric Detection of Nutrients in Sea Water
15:00--15:20	**Annika Hohendahl**	Role of Crescent-Shaped Proteins in Membrane Fission during Endocytosis
15:20--15:40	**Cecilia Tortoreto**	Unprecedented Reactivity of CpRu Stabilized Acceptor/Acceptor Carbenes with Cyclic Ethers
15:40--16:10	Coffee break	Main hall of Sciences III
16:10--16:30	**Ilyes Safir**	Chitosan-Grafted-ssDNA: Self-Assembly and Crystallization
16:30--16:50	**Julien Graff**	Asymmetric Bromine-Lithium Exchange: Application toward the Synthesis of Natural Product
16:50--17:10	**Xiuwen Zhou**	Spectral Tuning of Rhodopsin and Visual Cone Pigments
17:10--18:00	**Prof. Eric V. Anslyn** the University of Texas at Austin	Supramolecular Analytical Chemistry

18:00--19:00	Verre de l'amitié	Main hall of Sciences III
19:00-	Banquet (speakers + chairmen + organisers)	

PROGRAMME – FRIDAY 17 JANUARY 2014

Session 3 – Morning Chairmen: **Prof. Eric Vauthey + Prof. Claude Piguet + Prof. Alexander Adibekian**		
09:00--09:50	**Prof. Gregory D. Scholes** University of Toronto	Photosynthetic Machines and Ultrafast Energy Transfer
09:50--10:10	Coffee break	Main hall of Sciences III
10:10--10:30	**Pierre Charbonnaz**	Multicomponent Surface Architectures with Central Perylenediimide Stacks
10:30--10:50	**Cansel Ustunel**	Phospholipids and Intralumenal Vesicles
10:50--11:10	**Romain Letrun**	Ultrafast Electron Transfer reactions in Liquid Solution: Beyond Kasha-Vavilov's Rule
11:10--11:30	**Xiaojiang Xie**	Photo-Switchable Ion-Exchanging Nanospheres Containing Neutral Ionophores
11:30--11:50	**Alice Lefranc**	Organocatalytic Domino Michael/Aldol Reaction of 3-Halogeno-1,2-Diones to α,β-Unsaturated Aldehydes
11:50--12:40	**Prof. Jean-Claude Bünzli** École Polytechnique Fédérale de Lausanne	Rare Earths: Indispensable Vitamins in Science and Technology
12:40--12:45	**Prof. Eric Vauthey**	Concluding remarks

Mechanisms of Biological Membrane Perforation by Bacterial Toxins

Prof. Gisou VAN DER GOOT

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The mode action of different families of pore-forming bacterial toxins will be discussed, both from a structural point of view and in terms of cell response. The presentation will be focused however on Aerolysin, the founding member of a super-family of ß-pore forming toxins for which the pore structure is unknown. How X-ray crystallography, cryo-electron microscopy (EM), molecular dynamics and computational modeling were combined to determine the structures of aerolysin mutants in their monomeric and heptameric forms, trapped at various stages of the pore formation process, will be presented. A dynamic modeling approach based on swarm intelligence was applied whereby the intrinsic flexibility of aerolysin extracted from new X-ray structures was utilized to fully exploit the cryo-EM spatial restraints. Using this integrated strategy, a radically new arrangement of the prepore conformation and a near-atomistic structure of the aerolysin pore, which is fully consistent with all biochemical data available so far, was determined. Upon transition from the prepore to pore, the aerolysin heptamer shows a unique concerted swirling movement, accompanied by a vertical collapse of the complex, ultimately leading to the insertion of a transmembrane ß-barrel.

References:

1. Degiacomi M.T.[#], Iacovache I.[#], Pernot L., Chami M., Kudryashev M., Stahlberg H., van der Goot F.G.[*] and Dal Peraro M.[*] The molecular assembly of the aerolysin pore reveals a unique swirling membrane-insertion mechanism. *Nature Chemical Biology* **2013**, *9*, 623-629. DOI: 10.1038/nchembio.1312
[#] Co-first author, [*] Co-senior corresponding author

Supramolecular Analytical Chemistry

Prof. Eric V. ANSLYN

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The senses of taste and smell operate via a series of cross-reactive protein-based receptors that are non-selective, but create patterns that discriminate solution and vapor composition, respectively. This talk will focus on the use of synthetic and designed receptors for the analysis of complex analytes by mimicking how the mammalian senses operate. Analytes in beverages, chiral mixtures, and blood/saliva have been targeted. The receptors derive from a combination of rational chemical design and modeling, with combinatorial synthesis techniques. Optical signaling derives either from indicator-displacement, or indicator-uptake, assays. It will be shown that a union of designed receptors targeted to a class of analytes, with combinatorial methods, gives fingerprints that differentiate between the individual members of the class. The strategy is to use a core-binding element that imparts a bias to each and every member of the library, ensuring affinity of the library members for the class of analytes being targeted. The design of this core derives from standard molecular recognition principles: preorganization, complementary, pair-wise interactions between receptor and analyte, and desolvation. Combinatorial techniques impart the differential behavior and cross-reactivity desired in an array sensing application. The fingerprints of the solutions are created using artificial neural networks, principle component analysis, and/or linear discriminate analysis. The technique represents a marriage of supramolecular chemistry and pattern recognition protocols, resulting in a versatile artificial method that acts analogously to the mechanisms of taste and smell.

Rare Earths: Indispensable Vitamins in Science and Technology

Prof. Jean-Claude G. BÜNZLI

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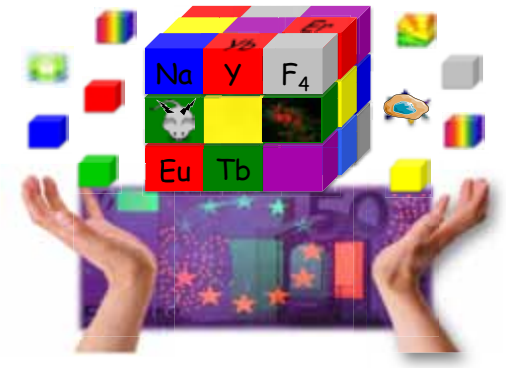
In the 1890's, Carl Auer von Welsbach started what proved to be a unique and perennial industrial endeavour by inventing the gas mantle and the Mischmetall, and by founding the first rare-earth chemical company. Today, about every high-technology object we use contains rare earths: lighting devices, displays, magnets, rechargeable batteries, catalysts, hard-drive disks, optical fibres and amplifiers, smart phones, bioanalyses kits, contrast agents for bioimaging… The point is that only minute quantities of these elements are often needed: a smart phone contains 9 of them, totalling 150-200 mg; an optical quartz fibre doped with less than 1‰ of erbium is an efficient amplifier for optical telecommunications; highly sensitive immunoassays use only about 1 µg of luminescent lanthanide. Rare earths therefore deserve well their denomination of vitamins of technology. In a first, general part, this presentation gives an overview of rare earths resources, properties, and uses[1]; it then focusses more particularly on applications taking advantage of luminescent properties[2].



The second part describes aspects investigated in the author's laboratory and in collaboration with other laboratories. A first example deals with the design of highly luminescent complexes[3] and color-tunable coordination polymers. The second example addresses the need for adequate up-converting materials for telecommunications and solar-energy conversion. Indeed, Er^{III} up-conversion has recently been demonstrated in molecular compounds thanks to a clever engineering of a supramolecular Cr-Er-Cr edifice[4]. A final example is linked to supramolecular assembly of highly stable and luminescent dinuclear helicates in water at physiological pH from ditopic hexadentate ligands with benzimidazole core. The helicates can be bioconjugated to avidin and various monoclonal antibodies[5]. When combined with microfluidic devices, the dinuclear bioprobes allow simultaneous imaging of two receptors expressed by human cancerous cells and tissues[6,7].

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7. Chauvin A.-S., Thomas F., Song B., Vandevyver C.D.B., Bünzli J.-C.G. *Phil. Trans. Roy. Soc. A* **2013**, *371* (1995), Art. Nr. 20120295. DOI:10.1098/rsta.2012.0295.

Photosynthetic Machines and Ultrafast Energy Transfer

Prof. Gregory D. SCHOLES

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Photosynthetic solar energy conversion occurs on an immense scale across the earth, influencing our biosphere from climate to oceanic food webs. Photosynthetic light harvesting complexes are sophisticated multichromophoric assemblies used to regulate and concentrate photo-excitations for delivery to reaction centers under wide-ranging incident irradiances[1]. They provide wonderful model systems to study energy transfer mechanisms in well-defined structures. I will describe a few recent examples of ultrafast energy transfer in photosynthetic light harvesting.

References:

1. Scholes G.D., Mirkovic T., Turner D.B., Fassioli F., Buchleitner A. Solar light harvesting by energy transfer: From ecology to quantum mechanics. *Energy Environ. Sci.* **2012**, *5*, 9374–9393.

Gradually Twisted Push-Pull Oligothiophenes and their Planarization in Confined Space

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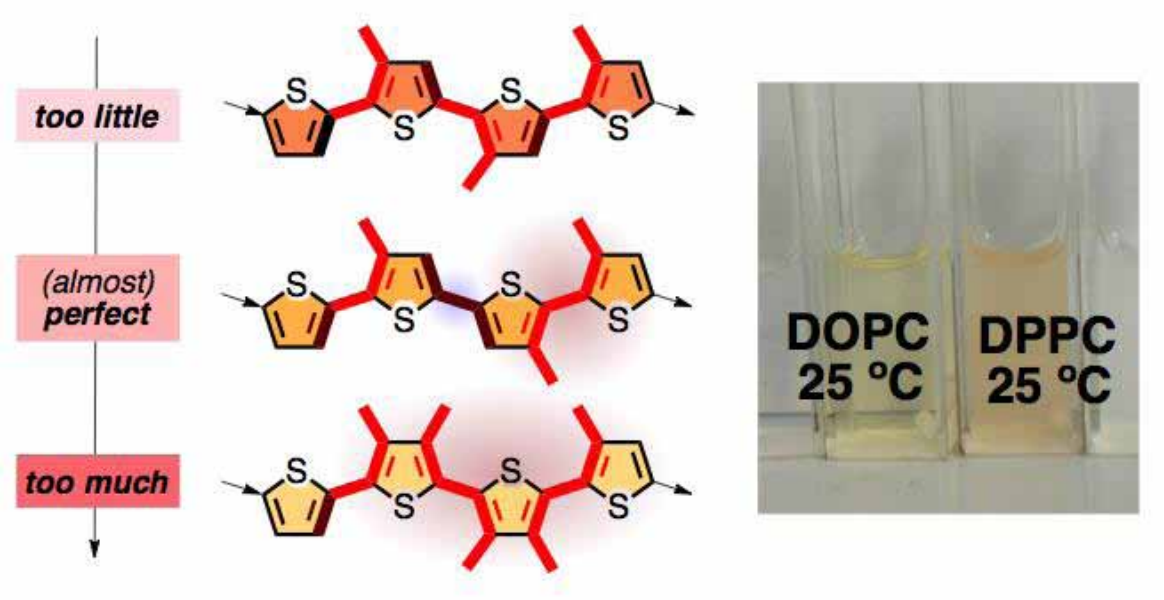
In nature, the combination of chromophore planarization and polarization occurs in processes reaching from the chemistry of vision to the pigmentation of lobsters[1]. Increased conjugation, and thus improved communication between the polarizing groups, is responsible for a dramatic red shift upon flattening of these chromophores. These lessons from nature suggest that planarization and polarization could be combined to obtain conceptually innovative membrane probes.

A series of systematically deplanarized push-pull oligothiophenes has been designed and synthesized to determine the perfect twist for maximal spectroscopic response to their planarization within various different lipid bilayer membranes[2,3].

These new dynamic fluorescent amphiphiles with this poorly explored coupled process are sensitive to their environment and allow the solid-ordered (So) and liquid-disordered (Ld) bilayer membranes to be discriminate with the naked eye.



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2. Dal Molin M., Matile S. *Org. Biomol. Chem.* **2013**, *11*, 1952-1957.
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Multicomponent Surface Architectures with Central Perylenediimide Stacks

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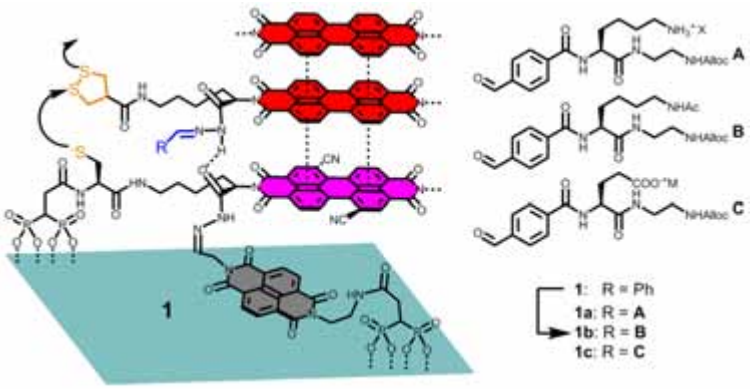
Self-organizing surface initiated-polymerization (SOSIP) has been recently introduced to precisely organize functional molecules on indium tin oxide (ITO), a widely used transparent conductive material. In brief, after functionalization of the oxide surface with a monolayer of initiators with diphosphonate "feet," disulfide-exchange polymerization is used to covalently capture propagator molecules that feature two strained, five-membered cyclic disulfides. Non-covalent interactions, most prominently π-π stacking and hydrogen bonds, are installed to ensure a correct preorganization of the reaction partners toward formation of ladderphane-like structure.[1] Benzyl hydrazones along the central stacks are used as templates that can be removed after SOSIP and replaced by new components of interest. This process is referred to as templated stack-exchange (TSE).[2]

The perylenediimide (PDI) chromophore is a recognized n-type organic semiconductor that can also transport holes, has a high extinction coefficient and forms well-defined aggregates through face-to-face π-π stacking. When applied to SOSIP, this material showed a unique capability to generate significant photocurrents also in the presence of only one charge-transporting channel systems, thus emerging as a model for the investigation of factors influencing the generation and transfer of charges in single-channel architectures. For example, the effects of permanent charges and dipole moments on the rate and directionality of electron transfer is documented by several reports in the literature.[3] It is envisioned that the post-SOSIP TSE along central PDI stacks with either negative or positive entities would remotely modulate the photocurrent. Synthetic details as well as experimental results will be presented.



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2. a) Sakai N., *et al. J. Am. Chem. Soc.* **2011**, *133*, 18542-18545. b) Sforazzini G., *et al. Chem. Sci.* **2013**, *4*, 1847-1851. c) Bolag A., *et al. ChemistryOpen* **2013**, *2*, 55-57. d) Sforazzini G., *et al. J. Am. Chem. Soc.* **2013**, *135*, 12082-12090.
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Copper-Catalyzed Asymmetric Conjugate Addition of Alkenyl- and Alkylalanes to α,β-Unsaturated Lactams

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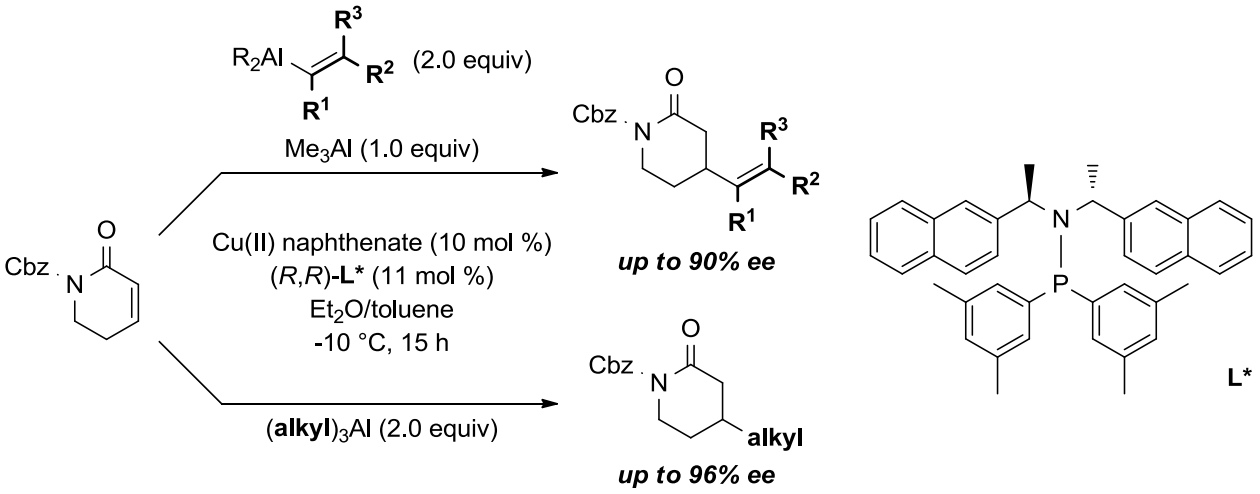
Since nitrogen-containing heterocycles are ubiquitous in compounds of pharmaceutical interest, much effort has been dedicated to the development of new methodologies allowing for the formation of optically active derivatives of such compounds. Among the main reactions in organic synthesis, the asymmetric conjugate addition of organometallic species is one of the most powerful tools for enantioselective C-C bond formation.

In this context, alkenyl and alkyl groups have been successfully introduced to six-membered α,β-unsaturated lactams via a copper-catalyzed asymmetric 1,4-addition of the corresponding alanes.[1] Moderate to good yields and good to excellent enantioselectivities can be achieved by using a combination of the very cheap copper(II) naphthenate and a readily available phosphine amine ligand. The creation of an all-carbon quaternary stereogenic center, via Michael addition to a trisubstituted conjugated lactam, was also disclosed for the first time.



References:

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Asymmetric Bromine-Lithium Exchange: Application toward the Synthesis of Natural Product

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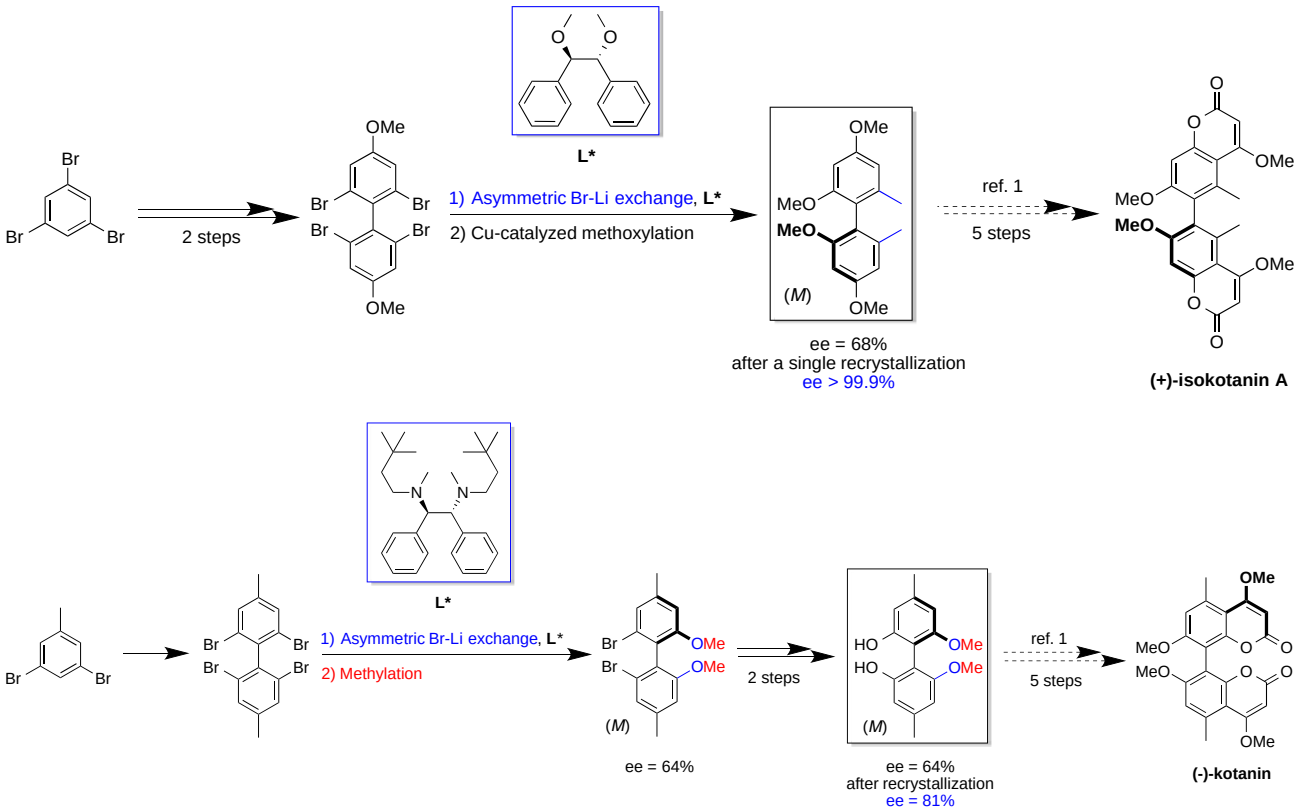
Axial chirality is present in a wide range of biologically active compounds.[1] One of the most famous example of this is glycopeptide vancomycin, possessing important antibiotic activities and isolated for the first time in 1953 from a soil bacterium *Amycolatopsis orientalis*. Axial chirality is also present in several other natural product families like bicoumarins (desertoïn C, isokotanin A and kotanin). Furthermore, we decided to select the bicoumarin scaffold to apply our direct asymmetric bromine-lithium exchange strategy. The aim of this work was to synthesize isokotanin A and kotanin chiral building blocks in high yields and ee.[2]



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Role of Crescent-Shaped Proteins in Membrane Fission during Endocytosis

Annika HOHENDAHL

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Biological membranes play an important role for delimiting the cytoplasm from the extracellular space and for establishing intracellular compartments. Processes like endo- and exocytosis allow the transport between the different cellular compartments and the extracellular space. During endocytosis, the plasma membrane is deformed to form a bud. This bud is then separated from the plasma membrane by membrane fission, becoming a vesicle.

We are using an in-vitro system to study the interactions of proteins with the membrane during this process. We are specifically interested in the GTPase dynamin which polymerises around and constricts membrane tubes[1], as well as its physical interactors amphiphysin and endophilin. The latter two proteins contain a crescent-shaped N-BAR domain preferentially binding to curved membranes[2] and tubulating them if highly concentrated. Dynamin and N-BAR proteins form a hybrid coat around in-vitro membrane tubes which resemble in-vivo vesicle necks in cells in which endocytosis is blocked.

While it was previously shown in-vitro how dynamin induces membrane fission upon GTP hydrolysis[3], it remains unclear which role the N-BAR proteins play in membrane fission. Measuring the dependence of the fission time on protein concentration and ratio gave hints about a potential inhibitory role of N-BAR proteins as regulators of the dynamin-induced membrane fission. The protein distribution along the tube and kinetics of the protein binding will give further insights into the more precise way of how N-BAR proteins regulate the fission time.

References:

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Polymer-Aptamer Hybrid Emulsion Templating Yields Bio-Responsive Nanocapsules

Dawid KEDRACKI

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Herein we describe the synthesis of a DNA-polymer, being the nucleotide sequence an aptamer selected in vitro to target specifically the immunoglobulin E (IgE) protein, an allergy biomarker[1]. Subsequent to coupling to poly(2-alkyl-2-oxazoline) with N-protected amino acid side chains, the resulting amphiphilic DNA-polymer hybrid composed of the water soluble DNA fragment grafted to the hydrophobic polymer segment can be regarded as a high molecular weight analogue of a surfactant.

The IgE-aptamer polymer hybrid has been successfully synthesized by solid phase synthesis according to well established chemistry routes. This macromolecule can be regarded as a high molecular weight analogue of a surfactant with the major advantage of being constituted of a bioinspired biocompatible synthetic polymer segment coupled to a biological stimulus-responsive nucleotide sequence. Results obtained from CLSM, AFM and reflectometry evidence that the aptamer remains functional subsequent to coupling to the polymer and engagement in the stabilization of the emulsion and shows high specificity. Further stabilization could be achieved by UV-irradiation of the cross-linkable pendent groups which were not modified with cysteine for subsequent grafting to the aptamer sequences. Since this cross-linking step occurs at the oil water interface, the function of the aptamer is not affected.

Engagement of the aptamer in the emulsion stabilization does not hinder its specificity of binding to its target, which paves the wave for further developments of capsules for sustained and targeted delivery through the synergistic combination of site specific aptamer recognition of the encapsulated load[2].

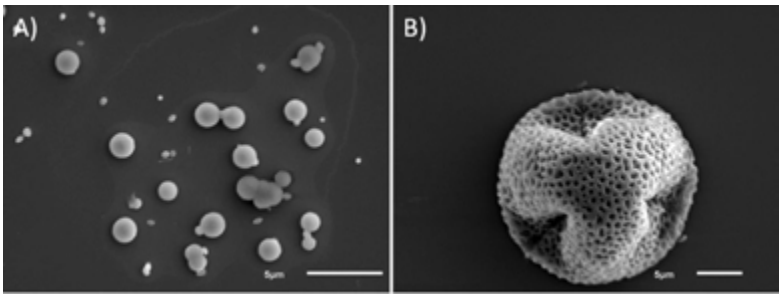

Fig. 1 Scanning electron micrographs of PBOX-aptamer capsules after cross-linking by irradiation with UV light.
A) Cross-linkage is performed subsequent to filtration.
B) Large porous structures are observed when no extrusion is performed to reduce the size: fusion of the droplets might occur.

References:

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Charge Separation Investigated by Ultrafast Time-Resolved Infrared Spectroscopy

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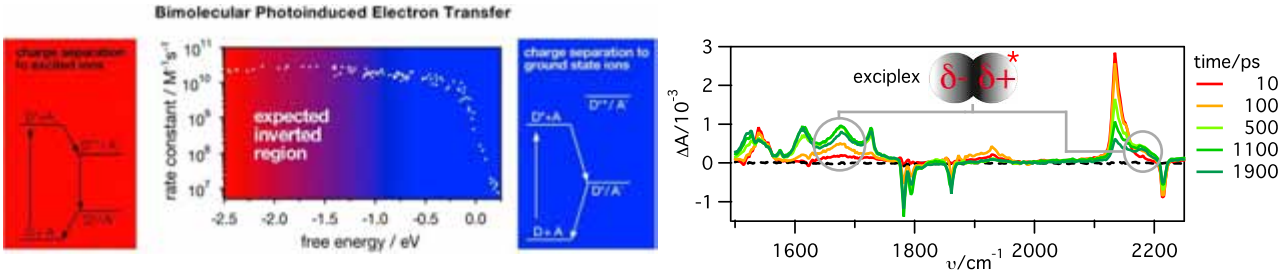
Photoinduced electron transfer (PET) is one of the simplest chemical reactions and experimental results have been explained since more than five decades in the context of Marcus' Theory. The bimolecular case of PET has nevertheless exhibit strong discrepancy with this theory, e.g. the independence of electron transfer rate constants on the driving force above -0.5 eV (inverted regime). Although the observation of this inverted regime has been reported more than 30 times in micelles or ionic liquids, our results revealed these spurious observations as artefacts, rising from the complexity of diffusion-influenced reactions.[1,2]

To furthermore explain the still remaining absence of the inverted regime, we constructed an ultrafast time-resolved infrared spectroscopy setup (TRIR). By measuring the internal temperature of the participating intermediates, this setup made it possible to distinguish radical ions in the ground- and electronic excited state, which allows to explain the absence of the inversion in the experimental results.[3] A detailed explanation will be given in a first part of the presentation.

In a second part, we show that TRIR is not only able to differentiate molecules with different internal temperature but also intermediates with slightly different electronic environment. In an investigation of systems with very low driving force, we observed then for the first time a vibrational band of an excited complex (exciplex). The clear spectroscopic signature allows the detailed analysis of this omnipresent intermediate and details about the kinetics as well as structural information are given in this second section.



References:

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Organocatalytic Domino Michael/Aldol Reaction of 3 Halogeno-1,2-Diones to α,β-Unsaturated Aldehydes

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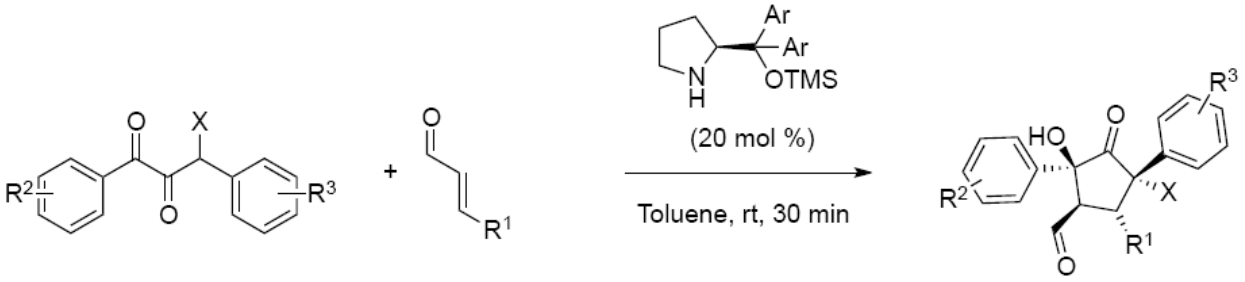
1,2-dicarbonyl compounds such as 1,2-ketoesters or amides represent very attractive scaffolds due to their versatile reactivity and have recently found a widespread use in asymmetric organocatalytic transformations.[1] Many research groups have focused on the development of different activation modes increasing their nucleophilicity instead of the generally observed self-condensation. In contrast, 1,2-diones have rarely been described as pronucleophiles in organocatalytic reactions.[2] In this context, we report the first organocatalytic domino Michael/aldol reaction of acyclic 3-halogeno-1,2-diones to α,β-unsaturated aldehydes to form challenging cyclopentanone derivatives with four contiguous stereogenic centers in excellent diastereoselectivities (>20:1 *dr*), good yields (69-97%) and enantiomeric purity (up to 94% *ee*).[3]



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Ultrafast Electron Transfer Reactions in Liquid Solution: Beyond Kasha-Vavilov's rule

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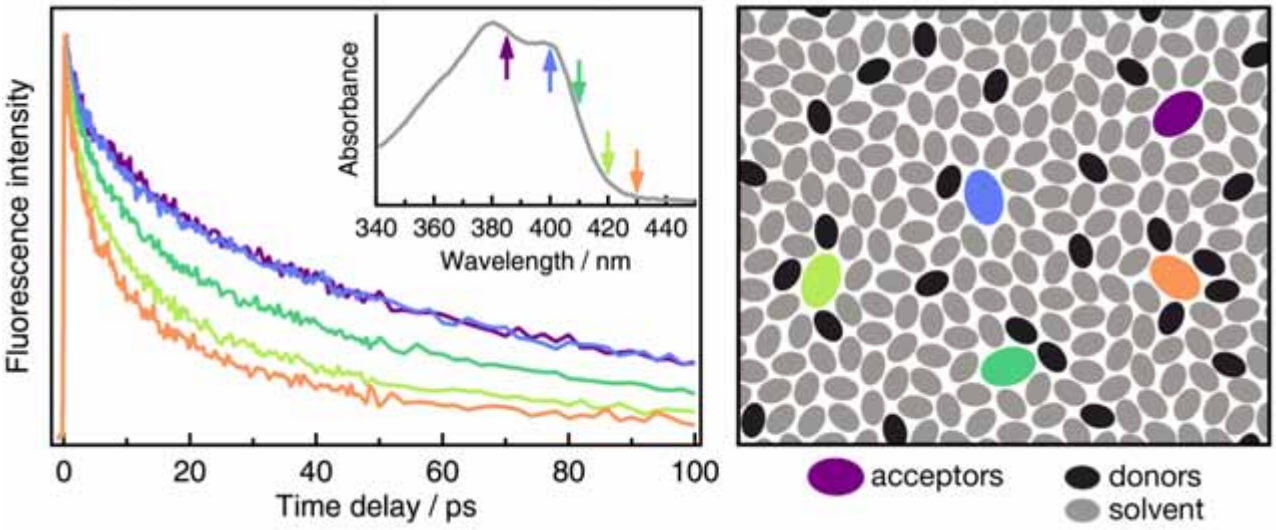
Understanding the dynamics of fundamental chemical reactions like proton and electron transfer is of paramount importance due to their ubiquitous nature and can be achieved by using ultrafast spectroscopy, thanks to the development of short pulse lasers over the past decades. The currently achievable time resolution allows studying reactions that take place on a sub-picosecond time scale, that is, in parallel or even faster than solvent rotational and/or translational motion in liquid solution. Such ultrafast reactions therefore happen in non-equilibrium and do not obey Kasha-Vavilov's rule any more, one of the most important rule in photochemistry, which states that the fluorescence quantum yield and photochemical processes of organic molecules are independent of the excitation energy.

To investigate this phenomenon, we are using ultrafast electron transfer reactions whose dynamics can be followed by time-resolved fluorescence. Our study reveals that, for inhomogeneous systems reacting on a time scale similar or shorter than solvent relaxation, the dynamics are strongly wavelength dependent and affected by the environment of the fluorophore (acceptor) at the time of its optical excitation. Non-specific interactions between reactants can lead to such inhomogeneities, yielding a wide variety of electron donor-acceptors arrangements that co-exist in solution, each having a different dynamics, as pictured in the figure below.



Towards a Reliable Potentiometric Detection of Nutrients in Sea Water

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A better understanding of our environment begins by a better monitoring of relevant chemical and biological parameters. Potentiometry, by measuring the activity of specific ions, is a widely used technique because of its cost-effectiveness and its easy implementation. While limits of detection for lipophilic anions can reach nanomolar levels – as for iodide or perchlorate – potentiometric devices selective for more hydrophilic ions do not share the same performances either for the detection limit or for selectivity, for example for nitrite, nitrate, or phosphate. Moreover, measuring anions in seawater meets the challenge of chloride interference, where it is several orders of magnitude more abundant than these other ions.

There are ways to improve the selectivity of potentiometric sensors, and we have explored two of them. On one hand, the efficiency of the ionophore – the molecule that brings selectivity to the potentiometric detectors – can be tuned and we will present results obtained with a new nitrite-selective ionophore. The cobalt(II) tert-butyl-salophen ionophore[1] was synthesized in-house and its performances (limit of detection, selectivity and robustness) were evaluated, altogether with its ability to quantify nitrite in urine. On the other hand, the interfering ions can be suppressed in order to improve the limit of detection of the main analyte. This is achieved with a desalination setup developed by our group on the basis of Nafion[2], a cation-exchanging membrane that allows for the in-line desalination of a sample and subsequent analysis.

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Chitosan-Grafted-ssDNA: Self-Assembly and Crystallization

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Natural deoxyribonucleic acid (DNA) is a fundamental biological macromolecule involved in a plethora of biochemical mechanisms such as protection and propagation of the universal genetic information or gene silencing. Owing to their inherent biochemical properties, compounds based on synthetic nucleic acid strands have thus been synthesized and do show promising results as potential therapeutics[1-3]. However, to infer bioavailability to the nucleotide sequence, conjugation through covalent binding to water soluble polymer chains consisting of a carbohydrate, a poly (amine) or a poly (ethylene glycol) segment needs to be performed.

To induce structure formation, we coupled single stranded nucleic acid strands to chitosan, a bioavailable and biocompatible amphiphilic polymer. Chitosan-grafted-ssDNA hybrids (C-g-ssDNA) were synthesized through solid phase synthesis to induce self-assembly in solution and on surfaces. The chemical characterization of the resulting C-g-ssDNA was performed by mass spectrometry (MALDI-TOF) whereas structure formation is observed by optical and atomic force microscopy.

Due to the chemical incompatibility between the hydrophilic ssDNA fragment and the amphiphilic chitosan polymer, self-assembled spherical nanostructures organize in solution (Figure 1) whereas crystalline structures are observed on surfaces.

Ongoing investigations are devoted to the understanding of the intra-and intermolecular interactions between the polymer segments that drive structure formation.

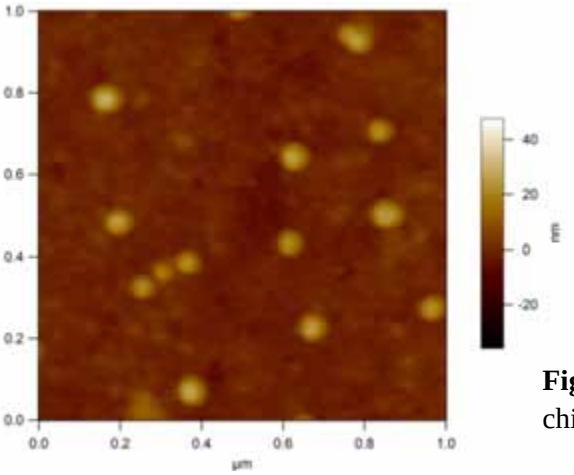

Fig. 1 Representative Atomic force micrograph of chitosan-g-ssDNA structures self-assembled in solution.

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Divergent Synthesis of Sesquiterpene Lactones

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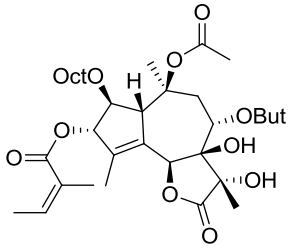
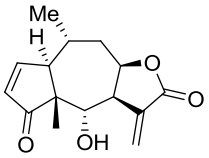
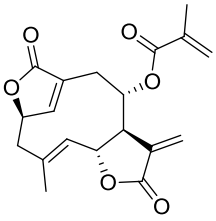
The sesquiterpene lactones are a large family of natural compounds found in plants with a wealth of biological activity that has been harnessed for centuries for indications ranging from inflammation regulation to oncology.[1] In a number of cases, the presence of Michael acceptors is intimately linked to their bioactivity by engaging their target covalently.



thapsigargin
inhibits the sarcoplasmic or endoplasmic reticulum Ca^{2+}-ATPase

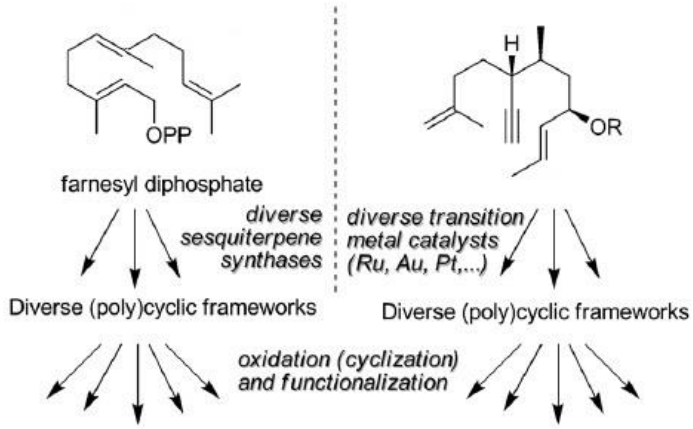


helenalin
inhibits the NF-kB pathway



deoxyelephantopin
inhibits primary tumor growth and metastasis in mice

Following a resurging interest in covalent inhibitors, we reasoned that a synthetic strategy leading to different members of this family and extending the diversity to modifications inaccessible by the biosynthetic machinery should afford an interesting collection of molecules to modulate protein activity. Herein, we will report new strategies which successfully lead to natural compounds and analogues.[2,3]



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A Metalloligand Containing a Three-Fold Axis as Molecular Brick for Supramolecular Self-Assemblies

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Because it is impossible to obtain an extended two-dimensional network with five-fold symmetry subunits, a closed pseudo-spherical species is formed.[1] In the same manner, by mixing four-fold and a three-fold axes, held together with an angle of approximately 55° to each other, a cluster with cubic symmetry should be obtained.[2] An octahedral hard metal centre coordinated to three chelating ligands generates a three-fold axis. Square planar transition metals such as copper(II) or palladium(II)[3] provide the required four-fold axis.

The investigations reported herein detail the differences in the coordination chemistry of the metalloligand Al**L**$_3$ (**L**=3-(pyridin-4-ylmethyl)acetylacetonate) (Figure 1) in both solution and the solid state. Solution studies as NMR, spectrophotometric and conductometric measurements show good evidence for the formation of a discrete species with a composition in agreement with that of an octahedral cage $[(Al\mathbf{L}_3)_8M_6]^{12+}$ ($M=Cu^{2+}$, Pd^{2+}). In the solid state, however, extended two-dimensional coordination polymers are obtained instead of discrete objects.

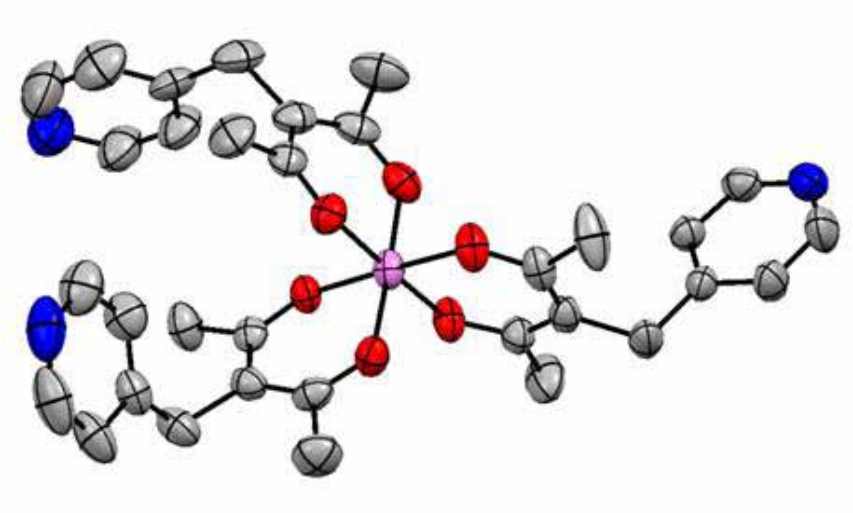

Fig. 1 Crystal structure of the metalloligand Al**L**$_3$.

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Unprecedented Reactivity of CpRu Stabilized Acceptor/Acceptor Carbenes with Cyclic Ethers

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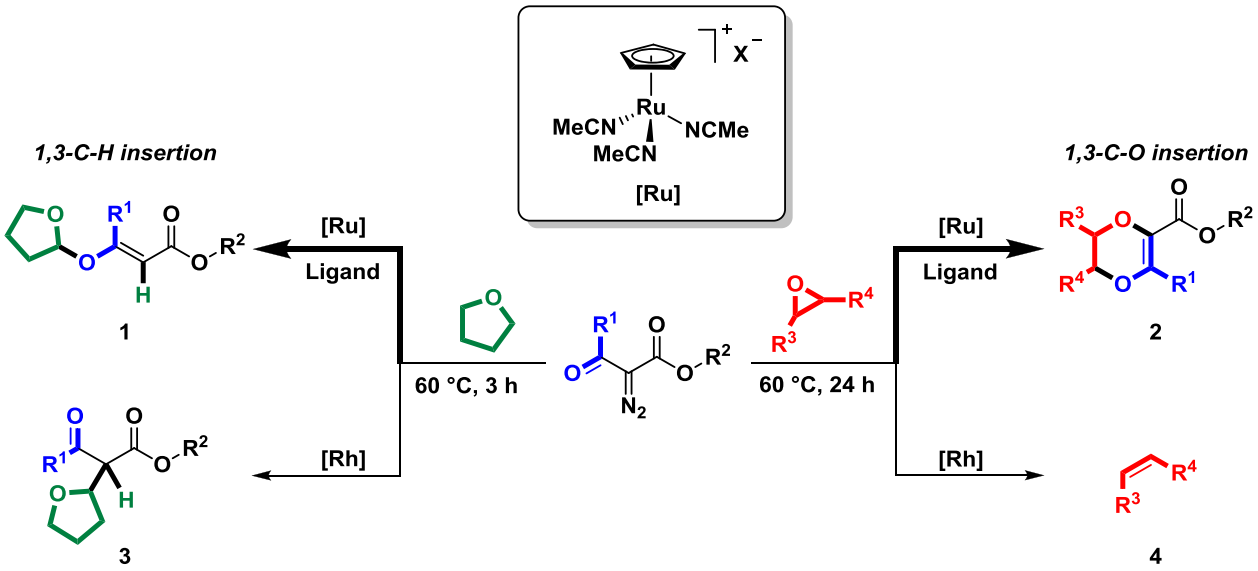
Cationic CpRu complexes are interesting alternatives to copper and dirhodium species for the catalyzed decomposition of diazo compounds.[1] In this context, our group has recently shown that combinations of $[CpRu(CH_3CN)_3][PF_6]$ and diimine ligands catalyze the decomposition of α-diazo-β-ketoesters and allow further condensation and O-H insertion reactions.[2]

Herein, we report that such decomposition reactions lead to novel enol-acetal motifs (**1**) through unprecedented C-H insertion reactions into tetrahydrofuran moieties.[3] In a new development, that uses epoxides as substrates, we describe the direct formation of unique dioxene species (**2**).[4] Both processes are only possible through ruthenium cyclopentadienyl catalysis as, under Rh(II)-mediated reactions, products **3** and **4** are predominantly obtained.[5]

Mechanistic insights will be given into these unusual three atoms insertion reactions and stereoselectivity issues will be particularly discussed.



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Direct Arsenic(III) Sensing by a Renewable Gold Nanoparticle Plated Ir-Based Microelectrode

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We aim to determine arsenic (III) in natural aquatic systems at the nanomolar range and at natural pH. For this purpose we introduce here a microelectrode capable of quantifying As(III) that consists of a gold nanoparticle plated Ir-based microelectrode (AuNP-IrM)[1]. The innovation of the analytical approach proposed is the electrochemical control of all key steps, *i.e.*: Ir substrate cleaning, AuNPs deposition, As(III) detection, AuNPs oxidation for their renewal (Fig.1). This strategy is an attractive basis in view of future on-field applications of the reported AuNP-IrM for direct arsenite analysis in aquatic systems.

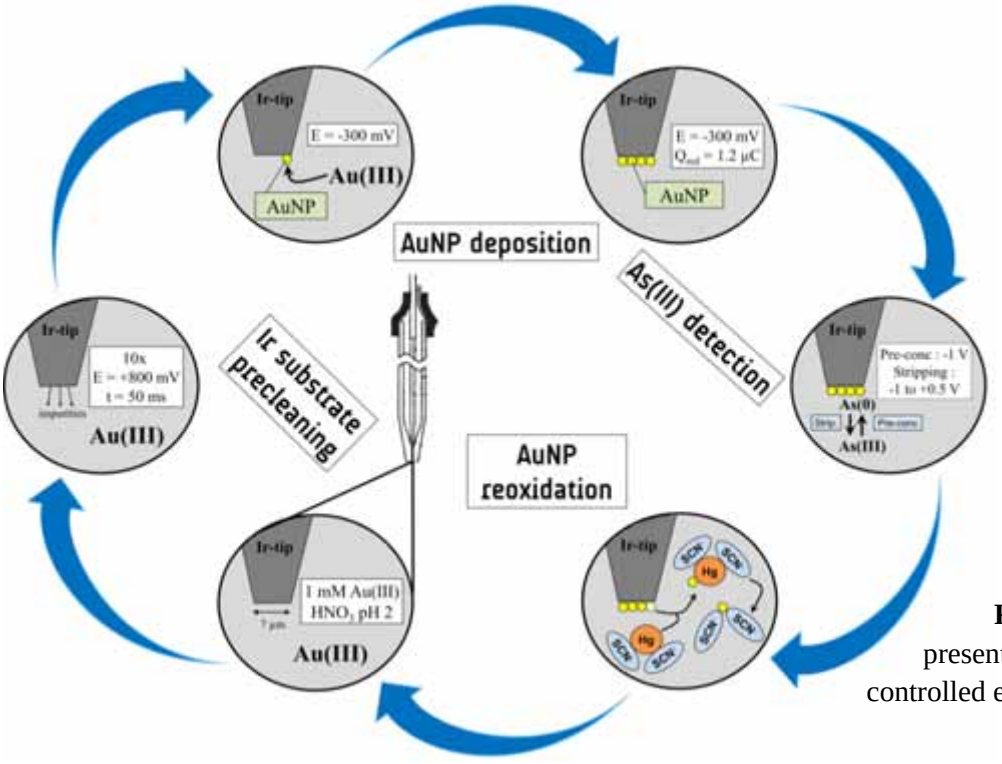

Fig. 1 Schematic presentation of all steps controlled electrochemically

The microsensor was electrochemically characterized by Square Wave Anodic Stripping Voltammetry. The obtained results demonstrate that the stripping peaks exhibit reproducible linear calibration curves (RSD of 2.2%) at pH 8 for As(III) concentrations between 10 and 50 nM using a 3 min pre-concentration time. Sub-nanomolar As(III) quantification is achieved using a pre-concentration time of 20 min. Copper interference is negligible for Cu:As concentration ratios of ≤10:1. The AuNP layer has a lifetime of at least 1 day. The measurements are reproducible over time for a given AuNP layer and between refreshed gold layers (RSD of 8.7%).

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Phospholipids and Intralumenal Vesicles

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Growth factor receptors, upon binding their ligands on the plasma membrane, trigger a signaling response that will eventually change the cell transcriptional program. Cells control the signaling program by receptor degradation in lysosomes, a process termed down-regulation. In this process, activated receptors are internalized into early endosomes and ubiquitinated, which are sorting platforms for endocytosed cargo proteins. Ubiquitinated signaling receptors including EGF receptor are sorted for downregulation into the intralumenal vesicles (ILVs) of multivesicular endosomes by Hrs and ESCRT complexes, which are also involved in membrane deformation and the ILV formation process. These multivesicular endosomes are transported to late endosomes and eventually fuse with lysosomes where their cargo is degraded. Evidence shows that other proteins — or perhaps mechanisms — may also be involved in ILV formation, and these may be involved in exosome formation or cholesterol transport [1].

Previously we reported that Sorting Nexin 3 (SNX3), a PtdIns3P- binding protein belonging to the Sorting Nexin Family, is involved in the biogenesis of multivesicular endosomes and controls the formation of intralumenal vesicles that contain EGF receptor[2]. I study the mechanisms that control ILV formation, and in particular the precise role of SNX3. We found that SNX3 shares high sequence homology with SNX12, and I found that this protein also acts as a functional homolog. When overexpressed, SNX12 restores ILV formation in SNX3- or Hrs-deficient cells [3]. Our data provides evidence that Snx3 and Snx12 are involved in intralumenal vesicle formation through a PI3P-dependent mechanism. This is consistent with the role of ESCRTs in the down-regulation of signaling receptors, which requires PI3P.

While PI3P is necessary for ESCRT function and ILV formation in early endosomes, lysobisphosphatidic acid (LBPA) is found only in late endosomes and it plays a key-role in ILV formation within late endosome, but the relationship between these mechanisms is not known. These lipids may thus serve as molecular markers for these two pathways. However, essentially nothing is known about the possible relationships between these lipids, not even their levels after interfering with the ILV formation or lipid biosynthesis. Quantification of PI3P and LBPA will help clarifying the relationship between the lipids and the mechanisms of ILV formation. The precise role of each lipid and its partner proteins in endosome biogenesis will be studied precisely.

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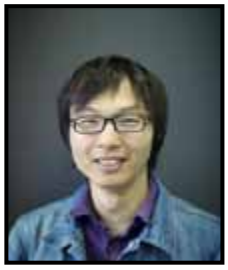
Photo-Switchable Ion-Exchanging Nanospheres Containing Neutral Ionophores



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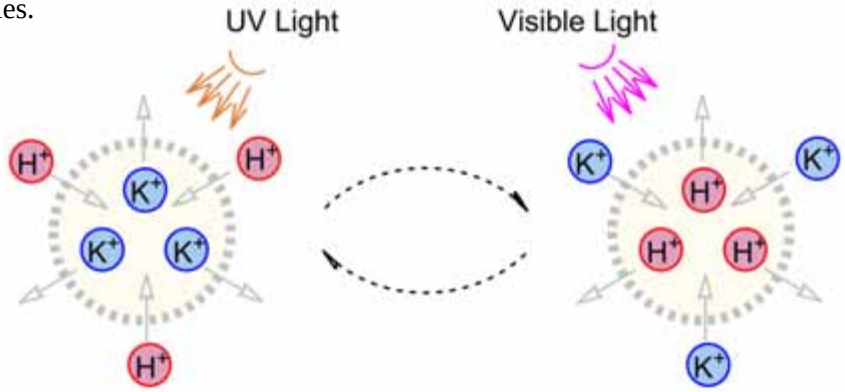
Ion-selective indicators, whose light emission reflects the local concentration of the ion, have been used for chemical imaging purposes. Examples include indo-1, rhod-2 and fluo-3 for Ca^{2+}, lucigenin and SPQ (M-440) for Cl^- , Sodium Green for Na^+. Although these indicators are widely used, they suffer from some drawbacks such as cytotoxicity, transition metal interference (i.e., selectivity), dye leakage and sequestration. Moreover, their synthesis is difficult, making these compounds expensive. The palette of detectable ions can be expanded with ion-selective optodes, which work on the principle of partitioning of ions between the sample and a sensing phase. We present here a convenient precipitation procedure to fabricate ultrasmall fluorescent ion-selective nanosensors that operate on the basis of bulk ion-exchange sensing principles.



The nanosphere matrix is composed of bis(2-ethylhexyl) sebacate and a tri-block copolymer, Pluronic® F-127, which also functions as a surfactant to stabilize the nanoparticle. The particles can be prepared easily in large quantities without resorting to further complicated purification. Dynamic light scattering shows that these particles exhibit a monodisperse size distribution with an average diameter of 40 nm, suggesting that the nanoparticles are among the smallest ionophore-based ion-selective nanosensors reported to date. Na^+ and H^+ selective nanospheres were characterized by absorbance and fluorescence spectroscopy.

Based on this platform, we also created ion-selective nanospheres that can be triggered by light to bring about a localized ion-concentration perturbation. A photoswitchable compound, spiropyran, was incorporated into the nanospheres. Using K^+ as a model ion, we demonstrate that the nanospheres are able to release K^+ into the aqueous surroundings when irradiated by UV (365 nm) light. By illumination of visible light, they are able to uptake the K^+ back in and reduce the K^+ concentration in the surrounding solution. We aim to apply such photoswitchable nanosensors for drug delivery applications in living systems.

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Spectral Tuning of Rhodopsin and Visual Cone Pigments

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Retinal is the light-absorbing biochromophore responsible for the activation of vision pigments and light-driven ion-pumps. Nature has evolved molecular tuning mechanisms that significantly shift the optical properties of the retinal pigments to enable their absorption of visible light. Using large-scale quantum chemical calculations at the density functional theory level combined with the frozen-density embedding theory[1,2] approach, we show here how the protein environment of vision pigments tune the absorption of retinal to the 2.3-2.6 eV (480-530 nm) region by electrostatically dominated interactions between the chromophore and the surrounding protein residues. The calculations accurately reproduce the experimental absorption maxima of rhodopsin (2.49 eV/498 nm), and the red, green, and blue color pigments (2.3-2.9 eV/430-530 nm). We further identify key interactions responsible for the red- and blue-shifting effects by mutating the rhodopsin structure *in silico*. Moreover, we find that deprotonation of the retinyl is likely to be responsible for the blue shifted absorption of retinal in the blue cone vision pigment.

References:

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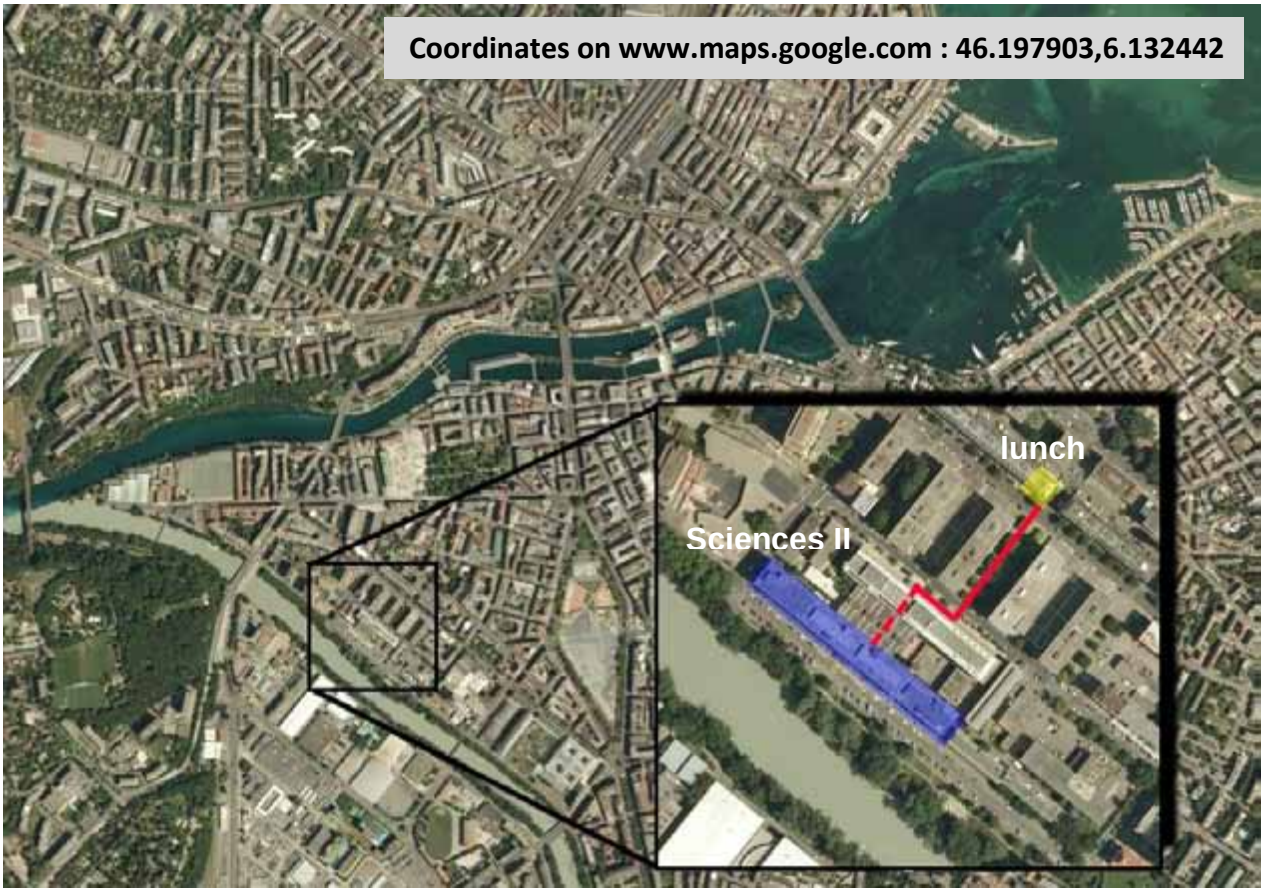

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