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ALFRED WERNER FUND
MASTER'S STUDENT SCHOLARSHIPS

In this report, the Alfred Werner Scholars' class of 2022–2024 present their Master Thesis research projects. There are twelve scholars of this class who completed their studies earlier this year. One scholar is expected to complete his studies by the end of the year, as he was doing an internship during his Master studies. For the same reason, one report of one student of the class of 2021–2023 is presented with a delay.

The Alfred Werner Fund of the SCS Foundation, established in 2013, supports master's degree studies for excellent students from foreign countries in Chemistry or Biochemistry at a Swiss University or at a Federal Institute of Technology. The Foundation offers scholarships in the amount of CHF 30,000 for international students nominated by the Swiss partner universities.

ETH zürich · EPFL · Universität Basel · UNI FR Université de Fribourg Universität Freiburg · Université de Genève · Université de Neuchâtel unine · u b Universität Bern · University of Zurich[UZH]

The scholarship program is supported by the Swiss chemical and pharmaceutical industry, several private donors, and the Gebert Rüf Foundation.

NOVARTIS · Roche · syngenta · WISSENSCHAFT. BEWEGEN GEBERT RÜF STIFTUNG · dsm-firmenich · MERCK · Givaudan

So far, more than eighty scholarships have been granted to students from over 30 countries, most of them continuing their career in Switzerland. To learn more about the Alfred Werner Scholars, please visit the Gallery of alumni at https://foundation.scg.ch/scholarships/scholar-gallery or download the Alfred Werner Program Impact Report 2013–2021 from the same Web site.

Alfred Werner Master's Scholarships 2024–2026

The Allocation Committee of the Alfred Werner Fund, consisting of representatives from the program supporting companies and the partner universities, granted stipends to nine international students. Two students decided to study at other universities and two students asked to delay the beginning of their studies to next year as they had received a Fulbright stipend and an opportunity for an internship, respectively. Finally, one student received a grant from his home country (Japan) to pursue his studies at EPFL.

Therefore, only four students will constitute the 2024–2026 class of Werner Scholars. This is somewhat disappointing for the program, but it also shows that students selected by the Allocation Committee were of highest quality. Top students can choose the place where they want to study and receive grants from other sources.

The following students received a scholarship (class of 2024–2026):

Mikhail Boym, University of Basel
Higher Schoof of Economics, Russia
Derenk Ong Boon Hong, ETH Zurich National University of Singapore, Singapore
Leonardo Husk Holberg, ETH Zurich
University of Copenhagen, Denmark
Tudor Lile, ETH Zurich
RWTH Aachen, Germany

Alfred Werner Fund Master's Scholarships 2022–2024

Konstantina Kalliopi Armadorou
Nationality: *Greek*
Bachelor: *National and Kapodistrian, University of Athens*
Master at: *EPFL*
Master thesis supervisor: *Prof. Michael Grätzel*
Co-examiner: *Prof. Jovana Milić*

Electroactive Low-dimensional Interlayers for Inverted Perovskite Solar Cells

Perovskite solar cells (PSCs) have attracted increasing attention over the past decade as third-generation photovoltaics. An important factor for fabricating highly efficient and stable PSCs is the use of appropriate stabilizing interlayers with passivating properties on top of the perovskite absorber. These organic molecules often form more stable low-dimensional or layered (2D) structures yet exhibit performance limitations due to their elec-

tronically insulating properties. Herein, we employ functional electroactive molecules as interlayers that can form low-dimensional perovskite structures, providing a minimal trade-off between efficiency and stability in inverted PSCs.

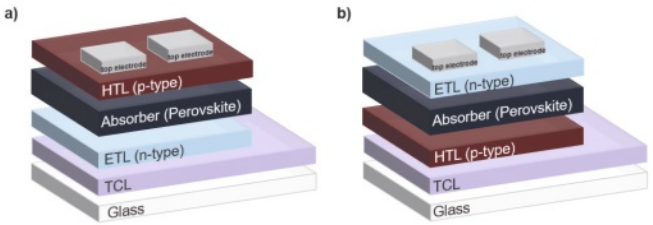

Fig. 1. Different PSCs device architectures, namely a) conventional (n-i-p) planar and b) inverted (p-i-n) planar.

Solar energy constitutes one of the most promising and abundant alternative energy sources, which can be harvested and transformed into electricity with solar cells. Solar cells based on hybrid organic-inorganic lead halide perovskites (PSCs) have become promising candidates for further scale-up, offering high efficiency and low fabrication cost. In a typical PSC, the semiconducting perovskite absorber is sandwiched between the charge transport layers (CTLs), namely the electron transport layer (ETL) and the hole transport layer (HTL), employed to extract the respective charge carrier from the perovskite (Fig. 1). Inverted (p-i-n) PSCs exhibit increased environmental stability compared to conventional (n-i-p) systems, but issues related to ion migration between the inorganic slabs and the operational stability of the devices are present, potentially inhibiting their commercialization.[1]

To further increase the stability of PSCs, there has been a shift from three-dimensional ABX_3 (3D) to two-dimensional (2D) perovskites. These low-dimensional (LD) perovskite phases are templated by the organic molecules (*i.e.* spacers), usually in the form of ammonium salts, between the inorganic perovskite slabs (Fig. 2). As a result, the hydrophobicity increases while the ionic migration between the inorganic slabs is suppressed. However, electronic conduction is also reduced due to the charge confinement within the inorganic framework of the LD phase, thus decreasing the efficiency of the devices.[2] Therefore, there is interest to develop semiconducting spacers with enhanced functionality that participate in determining the resulting optoelectronic properties, employed as interlayers on the perovskite-CTL interface. Various spacers have been employed as interlayers in highly efficient devices, such as 2-phenylethylammonium (PEA) and *n*-butylammonium (BA) on the p-side of n-i-p and propanediammonium (PDA) on the n-side of p-i-n PSCs, without facilitating charge extraction.[3]

The goal of this project was to develop materials as n-type interlayers in p-i-n PSCs, able to form LD perovskite phases but also exhibit appropriate energy alignment in such a way that they can conduct electrons from the perovskite to the ETL while simultaneously blocking the photogenerated holes. Towards this goal, spacers with semiconducting (electroactive) properties were designed and deposited on top of the perovskite absorber layer in PSCs. It was observed that the target devices achieved high but not champion efficiency, yet exhibited enhanced operational stability, thus providing a trade-off between these two performance parameters while providing insights for future material and device engineering.

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Future Plans

After successfully completing my MSc thesis in the Laboratory of Photonics and Interfaces at EPFL, I have started my PhD in Chemical Engineering at the University of Cambridge, under the supervision of Prof. Sam Stranks. I plan to continue my research on the fabrication of highly efficient and stable perovskite solar cells, while also developing ultrafast spectroscopy and multimodal microscopy techniques for their characterization and further optimizations. I would like to express my deepest gratitude to the Alfred Werner Scholarship Program of the Swiss Chemical Society Foundation for giving me the opportunity to carry out my studies in Switzerland.

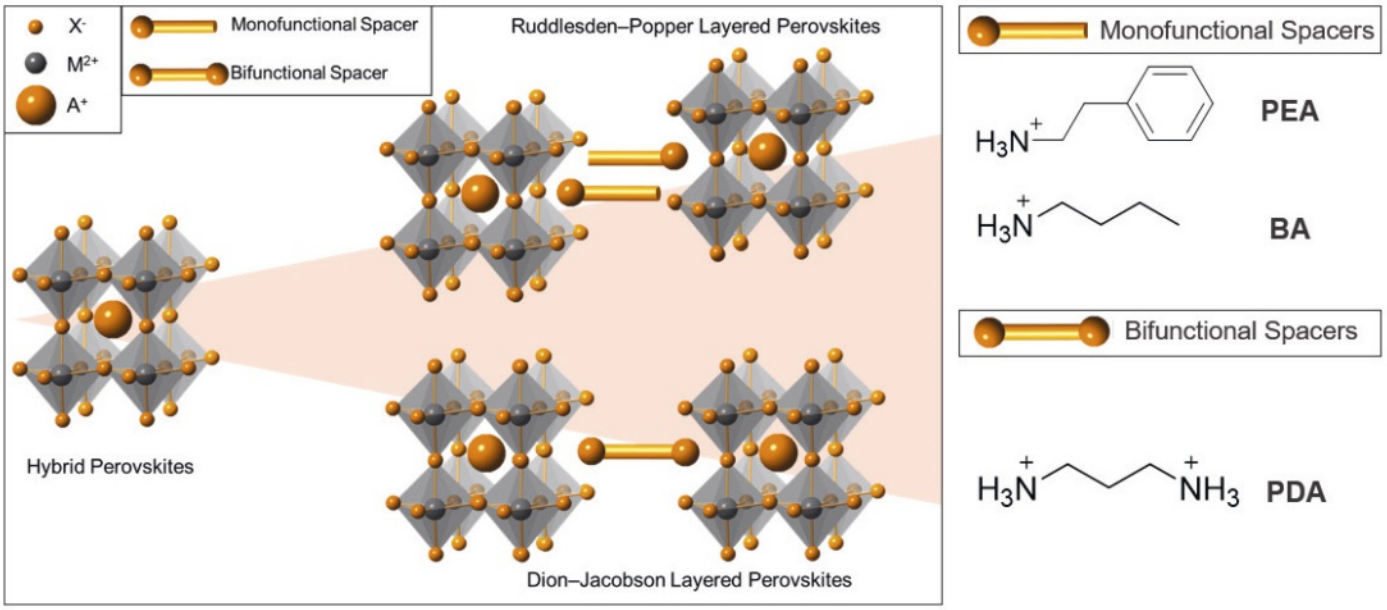

Fig. 2. Crystal structure of three-dimensional ABX_3 and two-dimensional perovskite phases (left). Structures of monofunctional and bifunctional spacers (right).

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Access to $ArCF_2SPh$ Compounds by Nickel-Catalyzed Cross-Coupling Reactions Using $PhSCF_2Br$

While various methods exist for synthesizing aryl-CF_3 compounds, most are unsuitable for incorporating ^{18}F into the molecule. The oxidative substitution of a thiophenyl group can efficiently introduce this label, but the availability of suitable starting materials is limited with current methods. We propose a novel approach to this class of compounds, utilizing $PhSCF_2Br$ as a coupling reagent in a Suzuki-Miyaura type reaction.

Incorporating fluorine into a molecule can greatly impact its pharmacokinetic and pharmacodynamic properties.[1] Around 20% of all approved small-molecule drugs contain fluorine. Approximately 15% of these compounds are aryl-CF_3 derivatives.[2] As a result, numerous methods have been developed to synthesize this functional group, employing nucleophilic (CF_3^-), electrophilic (CF_3^+), and radical ($CF_3^\bullet$) reagents.[3]

In the Schibli lab, a novel approach for synthesizing these compounds using the oxidative substitution of a thiophenyl group was developed. However, obtaining the necessary precursors for this transformation remains challenging.

Hence, the aim of the project was to develop a new approach for synthesizing $ArCF_2SPh$ compounds using readily available reagents. To achieve this, we decided to utilize aryl boronic acids as the starting material in a coupling reaction with $PhSCF_2Br$. While similar reactions have been established to some extent, having the electrophilic component with both thiophenyl and bromide groups on the same carbon remained challenging.[4]

Extensive screening of various reaction conditions was conducted, primarily using nickel catalysis. The conversion and yields of the reactions were monitored using ^{19}F NMR spectroscopy. Additionally, initial attempts were made to use aryl iodide with a reducing agent in reductive cross-coupling, instead of boronic acid. (Fig. 1).

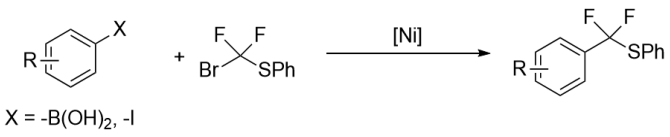

Fig. 1. Ni-catalyzed reaction of $PhSCF_2Br$ with aryl boronic acid and aryl iodide.

Preliminary mechanistic studies based on EPR and NMR suggest that the reaction proceeds *via* a Ni^{I}/Ni^{III} catalytic cycle, with oxidative addition to the C-Br bond occurring through a radical pathway.

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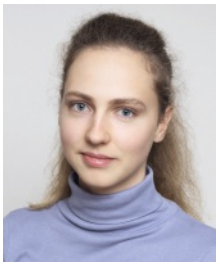
Future Plans

I am grateful to the Alfred Werner Foundation for enabling my studies at ETH Zürich. After successfully completing my Master's degree, I continued my studies and research at ETH Zürich as a PhD student in the Morandi group. In the coming years, my research interests will include, but are not limited to, reversible reactions in organic chemistry using transition metal catalysis.



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Thiazole-based Donor-acceptor Conjugated Polymers *via* Suzuki Catalyst Transfer Polymerization

In this work, we developed a novel synthetic route for thiazole-based conjugated polymers, successfully achieving high molecular weights and controlled dispersity via Suzuki Catalyst Transfer Polymerization (SCTP). This study expands the versatility of SCTP towards the synthesis of narrow band gap donor-acceptor polymers.

The synthesis of π-conjugated polymers (CPs) has gained significant attention primarily due to their affordability, flexibility, and ease of processing. These polymers, especially donor-acceptor CPs, show great potential for applications in organic photovoltaics, field-effect transistors, and light-emitting diodes.[1] However, traditional synthesis methods, such as transition-metal-catalyzed cross-coupling, often result in CPs with poor molecular weight control and broad dispersity, limiting their reproducibility and applicability in devices.[2,3] To address these limitations, living chain-growth polymerization techniques have been developed to offer more precise control over molecular weight and dispersity, although the scope of the monomer remains limited.[4]

In my thesis, three main tasks were successfully completed: developing the donor-acceptor monomer, conducting its controlled polymerization, and studying the degradation processes of the resulting polymer. The synthesis process began with the preparation of monomers through a multi-step synthetic route from commercially available reagents. The desired solubility of the polymer was achieved by introducing octyldodecyl side chains. The optimized polymerization conditions led to the formation of polymers with molecular weights up to 50 kDa and dispersity (Đ) values ranging from 1.2 to 1.3.

The living character of the polymerization was supported by end-group analysis through MALDI-ToF and ^1H NMR analysis. The UV-Vis absorption spectra showed the expected lowering of the energy gap, indicating efficient charge transfer interactions and strong light absorption potential in optoelectronic applications. Additionally, the degradation behavior of the polymers under oxidative conditions was explored. The polymer demonstrated high stability towards traditional chemical oxidation reagents, while significant breakdown was observed under UV irradiation in an oxygen atmosphere. This photo-oxidative degradation pro-

cess reduced the polymer's molecular weight to < 1kDa from 50kDa, indicating a potential pathway for the environmental degradation of these materials.

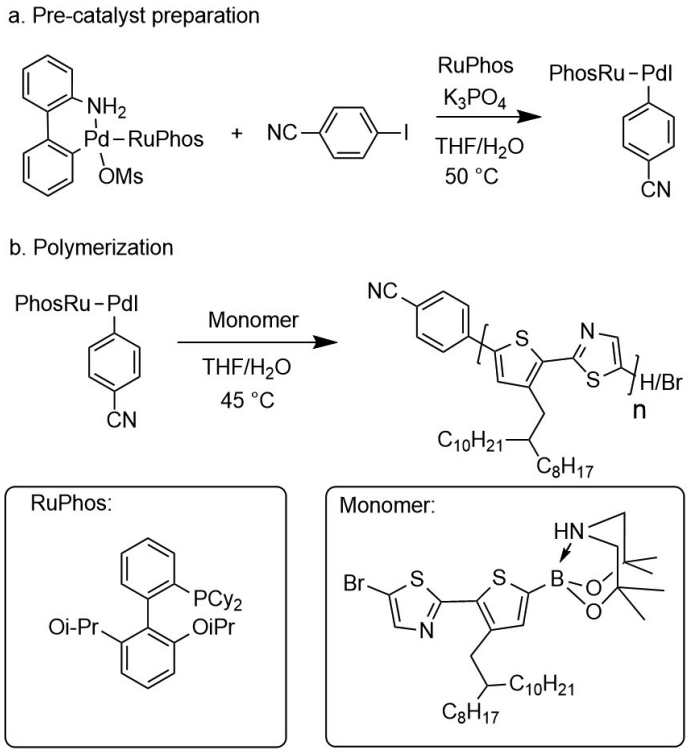

Fig. 1 The synthesis of thiazole-based degradable donor-acceptor conjugated polymers.

In conclusion, a new degradable conjugated polymer was synthesized in a controlled manner, expanding the versatility of SCTP polymerization to thiazole-based monomers.

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[2] J. Sakamoto, M. Rehahn, G. Wegner, A. D. Schluter, *Macromol. Rapid Commun.* **2009**, *30*, 653, https://doi.org/10.1002/marc.200900063[2] J. Sakamoto, M. Rehahn, G. Wegner, A. D. Schluter, *Macromol. Rapid Commun.* **2009**, *30*, 653, https://doi.org/10.1002/marc.200900063.
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Future Plans

After graduation, I will start a PhD in the field of elastomer-based sensors at EMPA and EPFL. This would not have been possible without the help of Alfred Werner Scholarship Program of the SCS Foundation, to whom I am deeply grateful.

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Master at: *ETHZ*
Master thesis supervisor: *Prof. Maksym Kovalenko*

Design of Novel Ligands for Perovskite Nanocrystals

Lead halide perovskite nanocrystals (LHP NCs) exhibit instability due to the dynamic and labile nature of both their inorganic core and the organic-inorganic interface, adversely impacting their optical and electronic properties. Surface ligand engineering, thus, remains an imminent research topic. It was shown that the new sulfonium ligands are an excellent alternative to ammonium-containing cationic ligands for the $CsPbBr_3$ NCs. In addition, the formation of NC-PMMA composites induced by novel polymerization ligands has shown promising results for the stabilisation of $CsPbBr_3$ in various solvents.

The quest for novel capping ligands has not stopped, rather contrary,[1] given the ever-expanding expectations for LHP NCs' deployment as classical and quantum light sources.[2,3] We hypothesized that the facile molecular engineering of novel cationic ligands enables highly customized surface chemistries for LHP NCs.

First, we synthesized a small library of new X-type ligands (namely, DDSB, OSB, br-ISB, DMST), *i.e.* organic sulfonium salts, for high-efficiency $CsPbBr_3$ perovskite nanocrystals (PNCs). $CsPbBr_3$ NCs capped with sulfonium bromides exhibit photoluminescence quantum yields exceeding 90% in colloids and enhanced durability in the typical purification processes. Two ligands, DDAB and DDSB, were also compared using *ab initio* MD simulations. Also, Molecular dynamics simulations indicated that DDSB exhibits equal or greater affinity to $CsPbBr_3$ surfaces compared to their broadly studied ammonium counterpart DDAB.

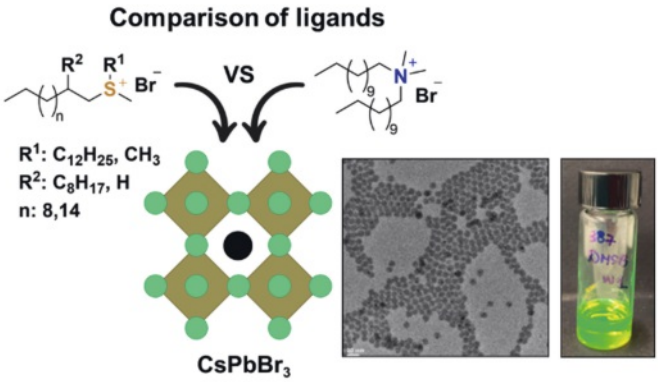

Fig 1. Comparison synthesized Sulfonium ligands (DDSB, br-ISB, OSB) with DDAB.

As another approach of modification for perovskite nanocrystals, we synthesized polymerizable ligand (Z)-*N*,*N*-dimethyl-*N*-(4-vinylbenzyl)octadec-9-en-1-ammonium bromide. $CsPbBr_3$ nanoparticles capped with this ligand formed stable composite nanoparticles-polymethylmethacrylate *via* photoinduced polymerization of methyl methacrylate (MMA) without any initiator. Increasing QY, saving shape, and spatial separation of nanoparticles after polymerization were observed. Increasing stability *via* the formation of PMMA (polymethylmethacrylate)-NCs composite showed optimistic results. A new polymerizable ligand was synthesized and capped on $CsPbBr_3$ nanoparticles, which NMR confirmed. Polymerized particles are well distributed in polymer and chemically bonded to the PMMA matrix. Besides that, saving form and shape of nanoparticles, increasing QY (up to 82%) and stability in polar solvents (EtOAc, Acetone, $CHCl_3$, THF) were observed. Related to this, we planned to conduct mechanistic experiments to understand intermediates of polymerization, using other monomers in the polymerization reaction and increasing the stability of perovskite SPLs *via* this approach.

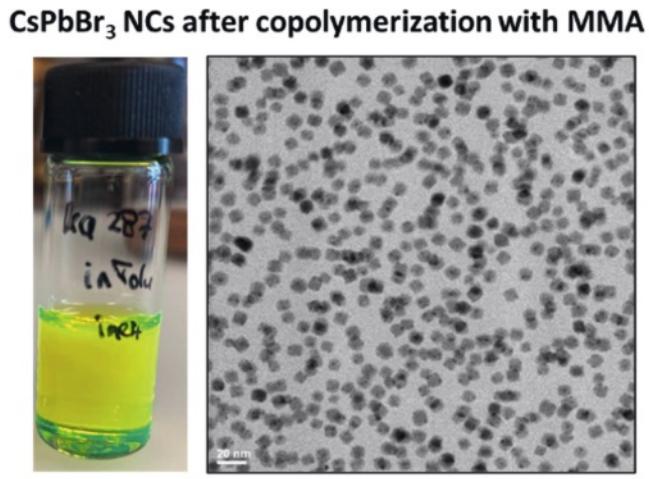

Fig 2. Polymerized composite of $CsPbBr_3$ nanoparticles capped with polymerizable ligand and PMMA.

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Future Plans

Following this project, I started my PhD in Professor Maksym Kovalenko's group to continue my work in ligand design and NCs surface modification. I would like to express my gratitude to the Swiss Chemical Society Foundation and the Alfred Werner Scholarship Program for their support during my Master's program.

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Master thesis supervisor: *Prof. Dr. Jeffrey Bode*

Synthesis of C–Terminal Amides and Esters of Peptides

Peptides are widely recognized as biologically active molecules. Modifying the C-terminus of peptides can enhance their physicochemical properties and enable peptide ligations. Consequently, the development of efficient methods for C-terminal modifications that yield diverse products is crucial. In this work, we developed protocols for functionalizing the C-terminus of peptides with amides and esters in a parallel manner. Additionally, we address the current limitations of these methods and propose potential solutions.

C-terminally functionalized peptides form a highly diverse group of peptide derivatives, each with distinct properties. These range from C-terminal peptide esters used in subtiligase ligation[1] to the critical role of C-terminal amides in certain hormones, such as oxytocin.[2] Subtiligase is a rationally designed cysteine-peptide ligase that is currently widely used for peptide ligation, total protein synthesis, thioesters preparation, and peptide cyclization (Fig. 1).[1] All these applications demand robust, versatile methods for synthesizing C-terminal peptide esters. From the other side, *N*-alkyl amides of peptides offer valuable advantages such as enhanced stability up to full resistance towards peptidases,[3] increased activity by reducing the negative charge at the C-terminus or altering the isoelectric point,[4-6] and improved membrane penetration.[7] These features make *N*-alkyl amides highly attractive for peptide modification.

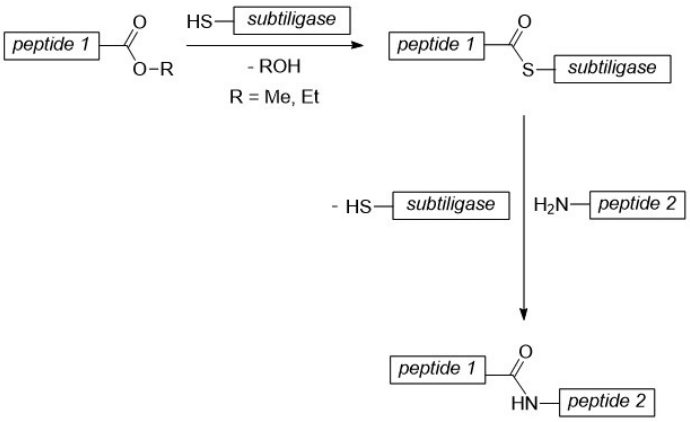

Fig. 1. Subtiligase ligation.

The goal of my project was to establish optimized conditions for the parallel synthesis of C-terminally modified peptide esters and amides from a common precursor. We began by systematically optimizing reaction conditions using model small-molecule substrates, eventually moving toward more complex systems ending up with protected pentapeptides. Through this stepwise approach, we successfully synthesized and isolated both peptide esters and amides, confirming their compositions using high-resolution mass spectrometry (HRMS).

During the project, we also identified certain amino acids that were incompatible with the transformation, partially defining the scope of this method. These findings were valuable in understanding which amino acids side chains posed challenges and helped shape the future application of this approach as well as optimize conditions for the transformation. Although the reactions were generally successful, yields were consistently low to moderate, prompting further investigation into potential causes.

To address these limitations, we developed a hypothesis suggesting side product interference and proposed several strategies to improve the process. These included modifying reaction pathways, adjusting reagents, and refining work-up techniques. Overall, while the project achieved significant progress in the synthesis of C-terminally modified peptides, further refinement is necessary to improve yields and broaden the method's applicability.

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Future Plans

I would like to express my heartfelt gratitude to the Alfred Werner Scholarship Program and the Swiss Chemical Society Foundation for providing me with the opportunity to pursue my Master's studies at ETH Zurich. This experience has allowed me to deepen my understanding of chemistry and related fields while enhancing my research skills. I am excited to continue my scientific route at ETH Zurich as a doctoral student in the group of Prof. Dr. Kathrin Lang.

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The Development of a Novel Macrocyclic DNA Encoded Chemical Library

In the following work we investigated the development of a novel macrocyclic DNA Encoded Library (DEL). The project focused on the on-DNA construction of a macrocyclic derivative with the Inverse Electron Demand Diels Alder (IEDDA) reaction as one of the key macrocyclization steps. For this purpose, various multi-step strategies were investigated. The results obtained demonstrate the potential of these synthetic approaches for the development of an original macrocyclic DEL.

DNA Encoded Libraries (DELs) are collections of molecules each tagged with their unique encoding DNA sequence.[1] The discovery of novel pharmaceutical hits *via* this biochemical tool has been largely focused on small molecules. In the recent years however, there has been an increasing interest towards macrocyclic derivatives because of their beneficial drug-like properties such as the higher target specificity compared to their acyclic analogues.[2]

In this context, peptide-like macrocyclic DELs have been the most vastly explored due to their ease of preparation.[3,4] On the other hand, libraries characterized by macrocycles with alternative backbone structures have been far less investigated.

The goal of our project was to validate a synthetic strategy for the preparation of a macrocyclic DEL based on an original macrocyclization step. For this purpose, the Inverse Electron Demand Diels Alder (IEDDA) reaction between a 1,2,4,5-tetrazine core and a dienophile was selected.[5]

The thesis was specifically centered around the design of a macrocyclic two Diversity Element (DE) library with the IEDDA as one of the key-steps to achieve macrocyclization. The tetrazine derivative could have potentially served for a third DE. Cyanuric chloride (TCT) was employed as the trifunctional core to 'direct' the introduction of the Building Blocks (BBs) *via* Nucleophilic Aromatic Substitution (S_NAr). A PolyEthyleneGlycole (PEG) linker was added to TCT through an off-DNA S_NAr. Next, the PEG-substituted TCT was ligated to a 5'-DiBenzoCycloOctyne (DBCO)-modified DNA template *via* Cu-free click reaction (Fig. 1).

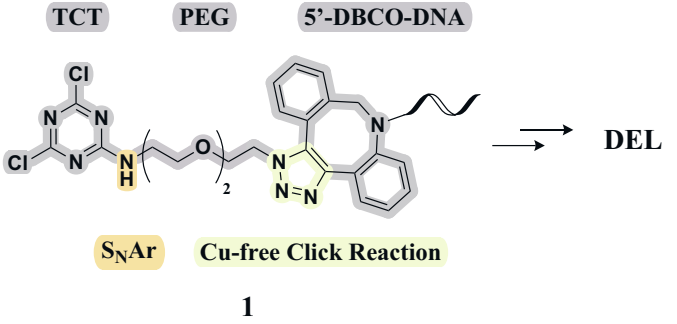

Fig. 1. Design of intermediate **1** for DEL synthesis.

Starting from the resulting intermediate **1**, three distinct multi-step syntheses were then explored to assess the optimal synthetic design of the desired DEL.

The strategy characterized by a IEDDA and an intramolecular amide coupling as final macrocyclization steps, could be fully explored and minor amounts of the desired product were obtained (Fig. 2).

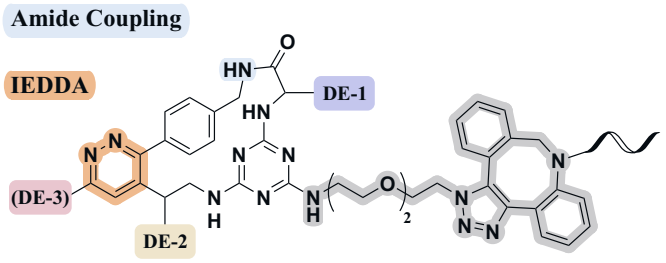

Fig. 2. Successfully detected macrocycle.

The detection of the desired macrocycle may be considered as a first promising result for the development of an original macrocyclic DEL. However, alternative approaches to bypass the issues faced in achieving full conversion should be taken into consideration. In these regards, BBs of longer lengths could render the macrocyclization energetically more favored offering a potential solution to the encountered challenges.

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Future Plans

Following graduation at Universität Basel, I will explore my career opportunities through an internship at Roche. I deeply thank the Swiss Chemical Society for the opportunity I have been given as an Alfred Werner scholar.

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Synthesis and Investigation of Small Molecule Interleukin-6 Unfolding Agents

Targeted protein degradation is an emerging strategy for targeting classically 'undruggable' proteins, such as cytokines. We demonstrated a method of a direct unfolding of the cytokine interleukin-6, the dysregulation of which is implicated in a variety of diseases. We introduced a new concept of targeted protein unfold-

ing agents that consist of protein binders carrying reactive warheads.

Human interleukin-6 (IL-6) is a small protein that plays a crucial role in regulating the immune system and inflammatory responses in the body. Despite the variety of important biological functions of IL-6, dysregulation of its production occurs in a plethora of various diseases[1] such as rheumatoid arthritis, Alzheimer's disease, Crohn's disease, multiple sclerosis, and cancer. While certain humanized monoclonal antibodies such as tocilizumab[2] are being used clinically, their usage is restricted due to high costs, only parenteral administration (by injection or infusion), and potential immunogenic effect. As a result, there is a demand for the development of small molecule *anti*-IL-6 therapeutics.

We investigated a method of a direct unfolding of IL-6. For this, we introduced a new concept of protein unfolding agents that consist of a recognition element and a reactive warhead (Fig. 1).

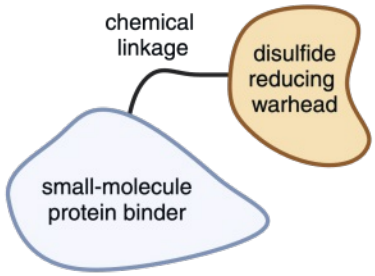

Fig. 1. Generalized structure of protein unfolding agent.

The recognition element is a small molecule protein binder which provides proximity-induced selectivity.

Different reducing agents can be used as warheads to disrupt disulfide bonds within a protein, potentially leading to its unfolding[3] and loss of biological activity.

The synthesis of several unfolding agents for IL-6 was an essential part of the project. We synthesized several IL-6 small-molecule binder analogues that bear groups like NH_2 and COOH as reactive handles. They allowed us to chemically attach different disulfide-reducing warheads to a core of small molecule IL-6 binder.

Then we studied the effect of synthesized compounds on IL-6 stability and folding state. The nanoDSF technique was used to define the relative folding state of the protein after the incubation in the presence of unfolding agents at various concentrations.

It was shown that one of the synthesized IL-6 unfolding agents causes IL-6 unfolding in a dose-dependent manner (Fig. 2). C_{50} was determined to be 14.6 μM. It was also confirmed that neither the reducing warhead nor the small-molecule binder alone caused the same effect.

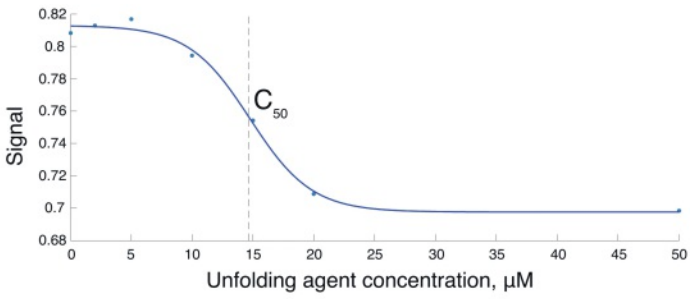

Fig. 2. Dose-response curve.

Therefore, the introduced concept of targeted protein unfolding agents could result in a new paradigm for the development of small molecule therapeutics for classically 'undruggable' proteins.

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Future Plans

In August 2024 I finished a 1-year Roche Internship in Medicinal Chemistry (RiCH) Program in Basel. After completing my Master's Studies at ETH Zurich in January 2025 I plan to continue my career path in the pharmaceutical industry in Switzerland.

I would like to express my deepest gratitude to the Alfred Werner Scholarship Program and the SCS Foundation for the incredible opportunity to complete my Master's Studies and pursue my further career in Switzerland.

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Electron Tomography of Beam-sensitive Functional Materials

Electron tomography makes it possible to observe the three-dimensional structure of materials. However, data acquisition for this method involves large cumulative electron doses, which can be detrimental to beam-sensitive materials.

In my thesis, electron tomography of beam-sensitive materials was carried out, while investigating ways of minimizing the detrimental effect of the electron beam on the samples. Valuable insights were gained on lead halide perovskite-based materials. In particular, we found that carbon embedding improves the stability of lead halide perovskite nanorods and reduces the formation of lead particles on their surfaces. This approach may also be extended to other beam-sensitive samples.

Electron microscopy is a powerful technique for the characterization of specimens down to the atomic level thanks to the shorter wavelength of the electrons. The images in Fig. 1, can provide valuable structural and chemical information, but are only two-dimensional projections of an object, which can be non-informative or even misleading in evaluating the sample's true structure. One way of obtaining three-dimensional information is by utilizing electron tomography. The images recorded at different orientations are used to reconstruct the three-dimensional model of the object and provide a better understanding of the sample properties.

In this work, the $CsPbBr_3$ nanorods and $CsPbBr_3$-$CsPbBr_3$ and $CsPbBr_3$-Au superlattices were investigated. However, the investigation of such samples posed a challenge – when lead halide perovskites (LHP) are irradiated with an electron beam of high intensity, small lead crystals start to form on the surface of the $CsPbBr_3$ particles,[1] while during the tilt series acquisition the accumulated dose may reach ~10^3–10^6 $e^-Å^{-2}$.[2,3] Electron beam irradiation also renders the corners of nanocrystals round and the edges amorphous. To avoid this detrimental effect on the samples, the microscope parameters were optimized to achieve a balance between a reasonable signal-to-noise ratio and a lower total accumulated electron dose. Also, different sample preparation methods were tested to study their response to beam damage.

We found that a higher ligand coverage on the surface of the nanocrystals improves the stability of the nanorods to the electron beam. However, the formation of lead particles on the nanorod

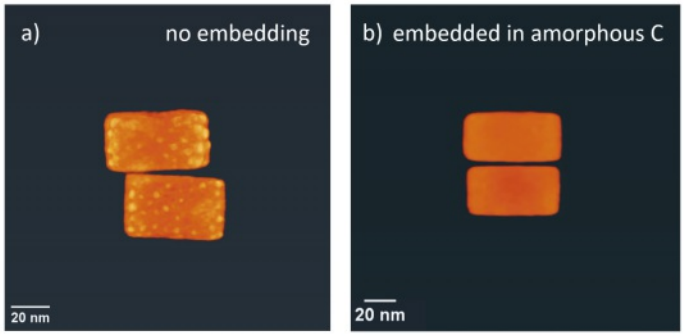
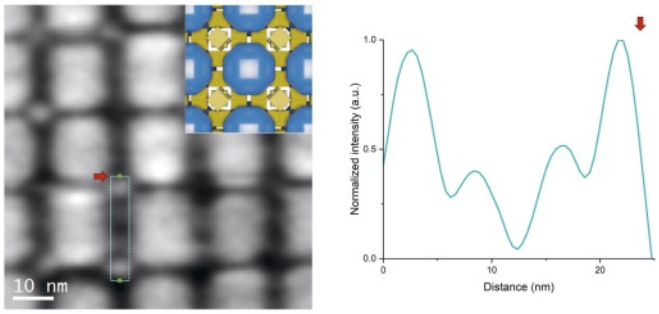


Fig. 1. Volren representation of the reconstructed volume. Electron damage is evident in the sample in the picture a) by the bright dots on the surface of the nanorods. These bright dots consist of lead particles. No lead particles are formed on the surface of the sample in the picture b), which was embedded in thick layer of amorphous carbon.

surface could not be completely avoided. Instead, we found that embedding the nanorods in carbon substantially improves their stability (Fig. 1). Strikingly, we did not observe electron beam damage in any of the superlattice samples despite the smaller size of the constituent particles. We suspect that these samples contain carbon species on their surfaces that protect them from degradation under the electron beam. Thus, for beam-sensitive materials, coating the specimen with a thick conducting film such as carbon may provide an effective solution to mitigate the electron beam damage.

Also, information about the structure and the number of stacked layers was obtained for all superlattice samples (Fig. 2).[4]



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Future Plans

After graduating, I started a PhD at ETH Zürich. I will continue researching lead halide perovskites in the Functional Inorganic Materials group under the supervision of Prof. Dr. Maksym Kovalenko. I want to express my gratitude to the Swiss Chemical Society Foundation for awarding me the prestigious Alfred Werner Scholarship, which made my studies at ETH Zürich possible in the first place.

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Liquid Crystal Elastomer-based Soft Multimaterial Fiber Actuators

The interplay between materials chemistry, processing, alignment, and stimuli response is fundamental to liquid crystal elastomer (LCE) research. Key variables such as crosslinking degree, mesogen connectivity, domain orientation, and phase have been identified to establish robust composition and structure-property correlations. LCEs are renowned for their large deformations (up to 400% strain) triggered by stimuli like heat, and their nonlinear mechanical response, termed soft elasticity. Mesogen alignment in LCEs is vital for their actuation capabilities, which are suitable for applications in soft robotics, adaptive optics, and smart textiles.[1] However, achieving uniform and consistent mesogen alignment with a large aspect ratio is challenging. Existing methods, including mechanical stretching, magnetic or electric field alignment, and extrusion, often lack precise control and consistency. Mechanical stretching can cause uneven stress distribution and material damage, while magnetic and electric field-induced alignments require high field strengths, energy density, and complex setups, limiting practicality.

My thesis explores thermal drawing as a novel materials and processing technique to address mesogen alignment challenges in LCEs. By precisely controlling temperature gradients and mechanical forces during fabrication, this method achieves more uniform mesogen alignment throughout the LCE matrix. Macroscopic preforms are processed in a custom-built, three-zone vertical tube furnace, where a controlled thermal environment aligns the mesogens as the material is drawn through the furnace. The preforms are introduced at a speed of 1 mm/min with take-up speeds ranging from 100 to 900 mm/min, resulting in diameter scale-down ratios of 10 to 30.[2] These parameters are optimized for optimal mesogen alignment. Tensile testing of the thermally drawn fibers revealed significant improvements in uniformity and performance compared to other methods.

We engineered LCE-based soft fibers, comprising LCE within a thermoplastic elastomer (TPE) cladding, combining mechanical stretchability with thermoplastic processability using a tailored thermal drawing process, providing a scalable and reproducible method for fabricating high-performance multilateral LCE fiber actuators. Various fiber architectures are explored, and their potential with heat as the stimulus is assessed by monitoring fiber mechanical deformation based on the mesogenic content. My thesis, along with the insights gained in the domain of multimateral, soft LCE fiber actuators, lays the foundation for further soft fiber science research.

The high aspect ratio achieved through thermal drawing is particularly advantageous for applications requiring long, continuous fibers with uniform properties. Additionally, the ability to integrate multiple layers within a single fiber structure opens new possibilities for combining different functional materials and creating highly specialized fibers.[4] This multifaceted approach not only improves the performance and functionality of LCE fibers but also expands their potential applications, paving the way for the development of next-generation smart materials and devices. For example, in biomedical engineering, LCE fibers could be used to

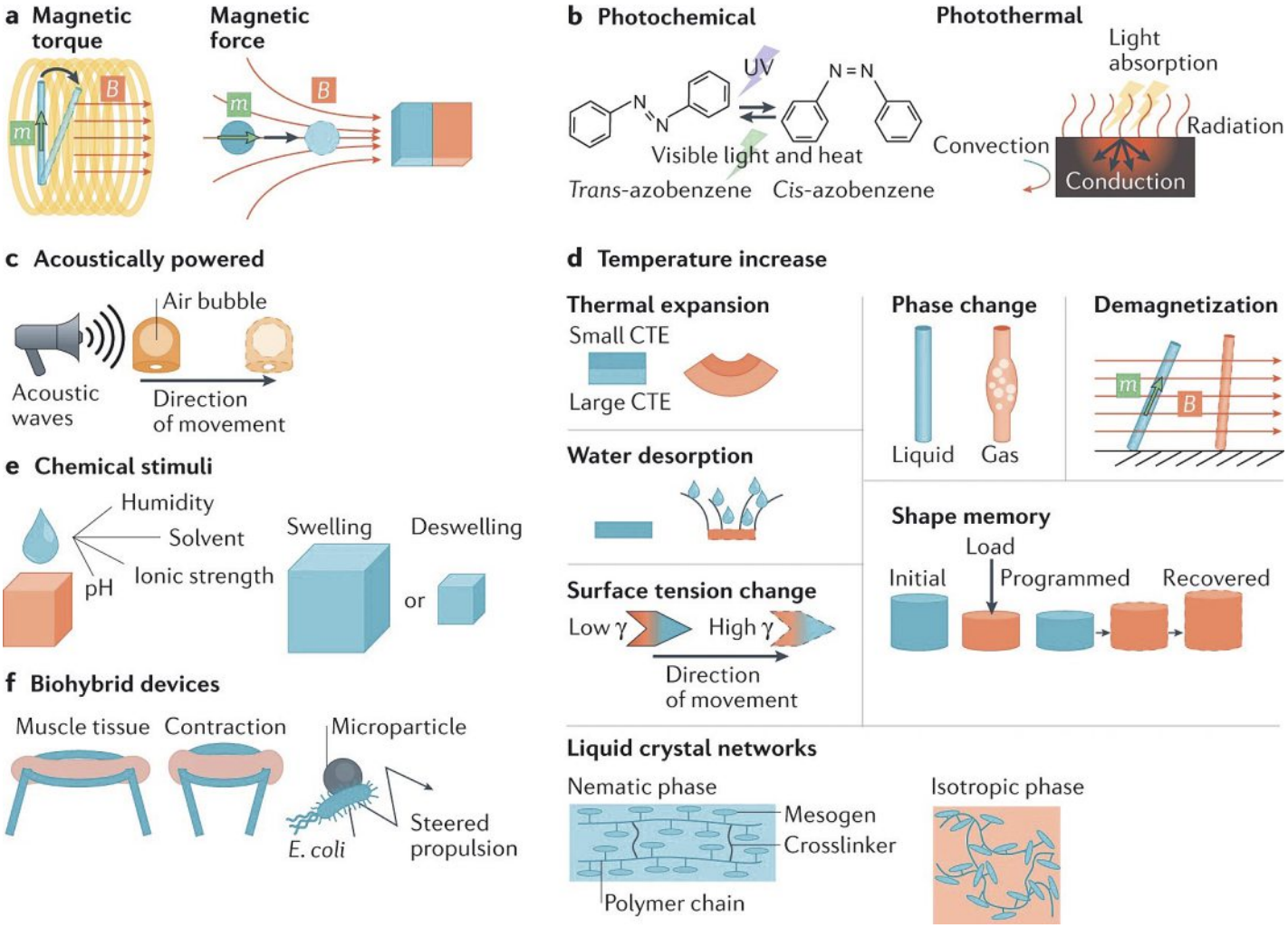

Fig. 1. Overview of stimuli-responsive functional materials and their working principles for untethered soft actuators applications. Concept adapted from ref [3].

create advanced prosthetics and implants that adapt to the body's movements and conditions.

In summary, our thermal drawing approach, inspired by the optical fiber industry, offers a groundbreaking platform for the production of high-performance integrated LCE fiber actuators. Its ability to achieve continuous, high-speed, and uniform fabrication with well-defined liquid crystal orientation sets it apart from existing methods. This advancement holds significant potential to drive innovation across a wide range of applications, heralding a new era in materials science and engineering.

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Future Plans

I would like to extend my heartfelt gratitude to the Alfred Werner Scholarship for funding my Master studies in Switzerland. After graduating, I started my PhD in Materials Science and Engineering at Northwestern University, Illinois, USA. Here, I plan to continue my research in design and fabrication of soft materials for applications in healthcare.

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Overcoming Ligand Lability in Iron(II) Complexes with Chelating Scaffolds for Catalytic Asymmetric C–H Amination

Intramolecular C–H amination using alkylazides is an atom economic method of forming N-heterocycle building blocks relevant for pharmaceuticals among other products. We demonstrate for the first time that chiral iron complexes catalyze the asymmetric reaction, while also uncovering the kinetic lability of once thought to be strongly bound carbene phenolate chelate ligands and the direct consequences this imposes when designing iron complexes for catalytic applications.

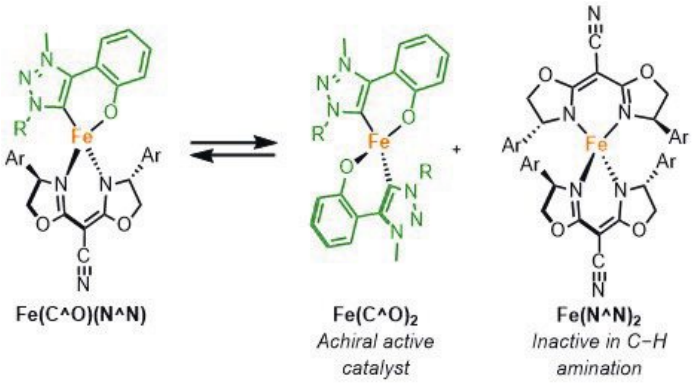
Nitrogen-heterocycles are prominently featured in natural products, pharmaceuticals, and agrochemicals. With approximately 60% of all FDA approved drugs containing *N*-heterocycles, this highlights the importance of developing efficient, economic and sustainable methods for their synthesis.[1] Chiral pyrrolidines are especially common motifs in active pharmaceutical ingredients and natural products and exhibit diverse bioactivities.[2] To synthesize these compounds the formation of C–N bonds is not only a key step, but also often a challenging step, which typically relies

on functional group exchange, thereby resulting in the production of stoichiometric waste.

In 2013, Betley introduced intramolecular C–H amination of aliphatic azides as a highly atom-efficient method for forming these 5-membered rings, producing only nitrogen gas as a by-product (Fig. 1a).[3] Since then, many catalysts have been developed, primarily focusing on improving robustness and catalytic efficiency, but only a few have concentrated on enantioselectivity. Due to the abundance and low costs of iron, as well as the superior activity of iron catalysts in achiral intramolecular C—H amination, we aimed to develop an iron catalyst that performs this transformation enantioselectively.

Our group has previously developed a highly active iron catalyst for C–H amination using chelating phenolate-carbene (C^O) ligands.[4] To render this catalyst chiral, a heteroleptic iron(II) complex, Fe(C^O)(N^N), was synthesized combining the same highly active C^O ligand with a chiral monoanionic bisoxazoline (N^N) ligand that has previously afforded enantioselectivity in this transformation.[5] Although these heteroleptic Fe(C^O)(N^N) catalysts showed activity for C–H amination of pro-chiral alkylazides, they afforded the corresponding pyrrolidine product as a racemic mixture.

To probe the origin of the lack of enantioselectivity, stability studies of the Fe(C^O)(N^N) complexes were performed by ^{1}H NMR spectroscopy. These studies revealed an unexpected ligand redistribution reaction taking place, resulting in the formation of the corresponding homoleptic chiral, yet catalytically inactive Fe(N^N)$_2$ complex and an achiral and catalytically highly competent Fe(C^O)$_2$ complex (Scheme 1).[6] Chelation has long been considered a suitable methodology for supporting the labile first row metal-carbene M–C bond through introduction of a strongly coordinating donor site.[7] This discovery, however, demonstrated that even chelating phenolate-carbene ligands are kinetically labile in iron(II) complexes with direct consequences when designing iron complexes for asymmetric catalytic applications.



Scheme 1. Observed ligand rearrangement of the heteroleptic Fe(C^O)(N^N) complex to the two homoleptic Fe(C^O)$_2$ and Fe(N^N)$_2$ complexes.

One strategy to embrace the substitutional lability of iron complexes uses homoleptic complexes in which ligand exchange processes do not alter the catalytic species (Fig. 1b). Along these lines, we developed a series of iron complexes bearing known chiral salicyloxazoline (Salox) ligands,[8] that are active for the enantioselective intramolecular C–H amination with alkylazides. A substrate scope revealed moderate to high enantiomeric excess (*ee*) for the amination of benzylic bonds, outperforming other first row transition metal catalysts in this transformation. These Fe(Salox)$_2$ catalysts were also the first to achieve asymmetric amination of aliphatic C–H bonds, although with reduced *ee* in comparison to benzylic substrates. Furthermore, primary aliphatic C–H bonds, which are typically challenging even for achiral catalysts, could also be activated to induce remote chirality with moderate *ee*.

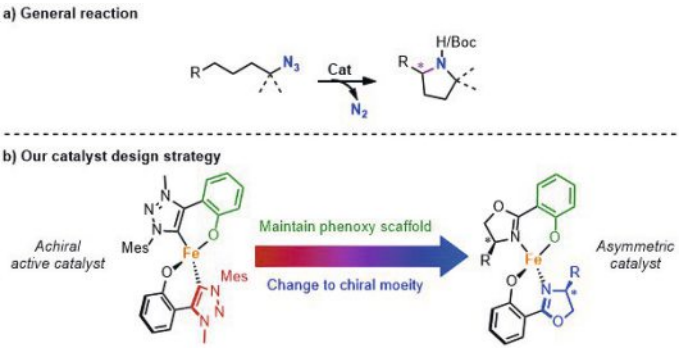


Fig. 1. (a) General reaction scheme for the asymmetric intramolecular C–H amination using aliphatic azides. (b) our strategy towards homogeneous iron-catalyzed asymmetric C–H amination.

In conclusion, we demonstrate for the first time that chiral iron complexes catalyze the asymmetric intramolecular C–H amination of alkylazides by development of a catalytically active homoleptic chiral complex, which is not compromised by ligand exchange.

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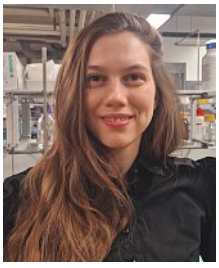
Future Plans

I would like to express my gratitude to the Alfred Werner Scholarship Program, whose support made it possible for me to pursue my master's in Switzerland. After completing my master's, I started my PhD studies at ETH Zürich in the Morandi group, where I continue to explore the synthesis and reactivity of Earth-abundant first-row transition metals and develop novel catalytic methods utilizing these metals.



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Master at: *ETH Zurich*
Master thesis supervisor: *Prof. Dr. Shana J. Sturla*

Development of a Fluorescence-based Method to Quantify *O*^{6}-carboxymethyl-2'-deoxyguanosine in Biological Samples

The investigation of DNA mutations is a crucial step in understanding the processes of mutagenesis, carcinogenesis, and

other related biological events. Among various DNA lesions, O^6-carboxymethyl-2'-deoxyguanosine (O^6-CMdG) has been detected in colon tumor samples, with its presence ranging from 5 to 68 O^6-CMdG adducts per 10^9 nucleotides.[1] Additionally, individuals on a processed meat diet have higher O^6-CMdG levels in colon cells compared to those on a vegetarian diet,[2] suggesting that processed meat consumption may contribute to the formation of these DNA lesions. However, further research is needed to clarify this connection, underscoring the importance of establishing robust analytical methods for accurately detecting and quantifying carboxymethylated DNA adducts induced by mutagens and carcinogens in human cells and biological samples. In this study, we developed a fluorescent labeling approach using azaserine-treated naked calf thymus DNA (ctDNA) as a model analyte to detect the formation of O^6-CMdG and reliably quantify it.

Mutational hotspots in colon cancer frequently include G>A point mutations in the KRAS, APC, and p53 genes, with KRAS also showing G>T and G>C mutations.[3] Carboxymethylation of guanosine impairs hydrogen bonding in the G:C Watson-Crick base pair resulting in a reversed wobble O^6-CMdG:C pair or canonical-like A:T interaction as O^6-CMdG:T[4] (Fig. 1). In human cells, O^6-CMdG lesions were moderately bypassed by DNA polymerases (Pol) κ or ζ, with exclusively G>A mutations due to Pol ι.[5] Replication of a plasmid containing O^6-CMdG resulted in misinsertions closely resembling p53 mutations in tumors.[6] These findings suggest that O^6-CMdG-induced mutations may contribute to the mutational patterns observed in colon cancer. Therefore, developing the approach for tracking O^6-CMdG abundance in human cells is crucial for understanding the link between O^6-CMdG formation and cancer development, potentially offering insights into cancer initiation and progression.

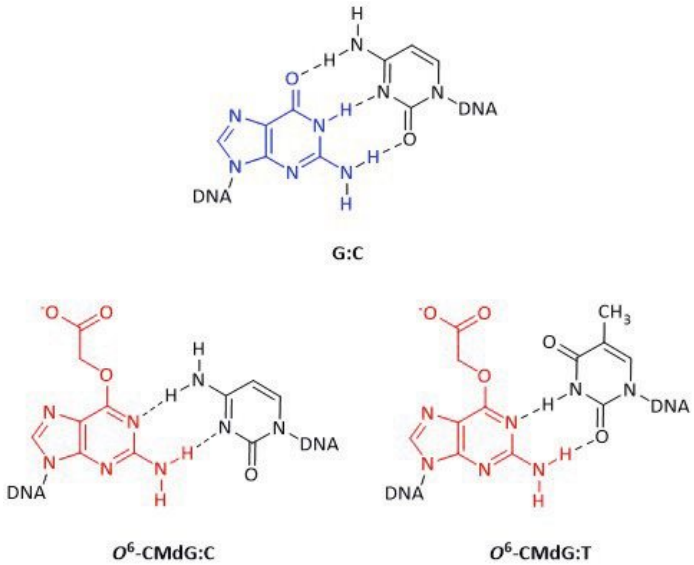

Fig. 1. Hydrogen bonds between G:C, the reversed wobble pair O^6-CMdG:C and the Watson-Crick base pair O^6-CMdG:T.

Liquid chromatography with tandem mass spectrometry (LC-MS/MS) methods are a gold standard for DNA adduct analysis, and it has been used widely to detect O^6-CMdG.[7,8] Although fluorescence-based approaches are more accessible and cost-effective for widespread analysis of biological samples, there is a notable lack of reliable fluorescent labelling methods for detecting and quantifying O^6-CMdG. Therefore, the main aim of this research project was the establishment of such a method. To achieve this, we mimicked O^6-CMdG adduct formation using azaserine treatment, followed by comparing the result from LC-MS/MS analysis with the fluorescence-based approach to confirm its applicability.

The work carried out in this project consisted of fluorescent labeling procedure elaboration on naked calf thymus DNA, followed by its stepwise transition to biologically relevant samples, such as DNA extracted from cells and donors' blood samples. We developed a two-step chemical labeling method to modify O^6-CMdG based on an amine ligation and copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) click reaction. The purified O^6-alkynyl-modified oligonucleotide was used in the following CuAAC click reaction to attach a fluorophore-azide (Fig. 2). Since a fluorophore was successfully attached to O^6-CMdG, we observed a dose-dependent increase in the fluorescent signal in samples treated with a range of azaserine concentrations. These results were compared with results obtained from O^6-CMdG detection by multiple reaction monitoring (MRM) in positive mode on a triple quadrupole mass spectrometer with an electrospray ionization source.[9] This comparison allowed us to convert the relative abundance of O^6-CMdG measured by fluorescence into the number of nucleotides and consequently to evaluate the limit of detection for the fluorescence-based method.

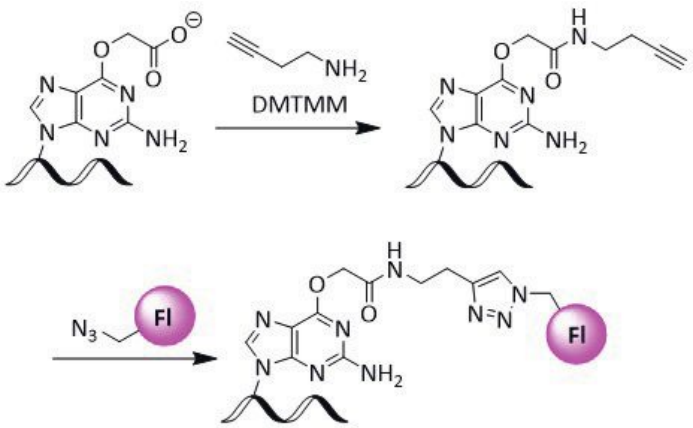

Fig. 2. Amine-click ligation scheme. Fl = fluorophore.

Therefore, we concluded that by using this approach, we are able to quantify O^6-CMdG in ctDNA samples in the fmol range. Further research is needed to expand the current procedure for quantification of O^6-CMdG in DNA extracted from cultured cells, blood, and tissue biopsies. This will require additional steps and the avoidance of contaminants that could interfere with fluorescence measurements and optimize the capacity to detect the DNA adduct at even lower levels. Aside from quantitation purposes, the amine-click ligation could be envisioned for damage enrichment from complex biological samples for further analysis such as by adduct sequencing.[10]

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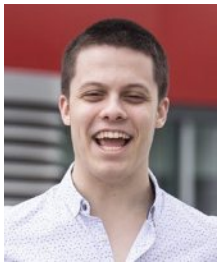
Future Plans

First, I would like to thank the Alfred Werner Scholarship Program and the Swiss Chemical Society for giving me the opportunity to pursue my master's studies at the ETH Zurich. Through this experience, I not only expanded my knowledge and scientific skills, but also gained a broader perspective of the scientific community. I have completed my Master's degree and have been doing PhD studies at the ETH Zürich since November 2023. I stayed in the same scientific group because I value the high level of expertise and the strong relationships within the team here. My current research focuses on studying the metabolism of food-related compounds by human gut microbiota and involves the application of LC-MS/MS analysis. After completing my PhD, I will pursue a scientific career either in academia or industry. Most importantly, my future work should involve a high level of innovation and continuous development at the intersection of organic chemistry, analytical chemistry, and biochemistry.



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N_2O Synthesis *via* Ammonia Oxidation Over Mn/CeO_2 Catalysts in Technical Form

In recent years, single-atom Mn/CeO_2 emerged as a highly active and selective heterogeneous catalytic system in the direct synthesis of nitrous oxide (N_2O) via ammonia oxidation. Its outstanding activity, N_2O selectivity and stability, as well as its relative synthetic simplicity, singled it out as an attractive candidate for attempting the transition from powder to technical form. This thesis was thus concerned with investigating and demonstrating the challenges that arise in the development of Mn/CeO_2-based extrudates able to selectively yield N_2O. A first formulation was successfully developed and an initial understanding of the extrusion of CeO_2-based bodies was gained. Nevertheless, further investigations into the interplay between the factors affecting the structural properties and catalytic performance of such materials are warranted.

Nowadays, nitrous oxide (N_2O) is an established chemical for its niche uses in areas such as the semiconductor, food or aerospace industries, as well as in the medical sector as an anesthetic.[1] Moreover, considering the need of the chemical industry for an oxidant able to selectively perform oxidations, it has also emerged as a clean, atom-efficient, single oxygen atom donor.[2] Nevertheless, since virtually all N_2O synthesized today comes from the thermal decomposition of ammonium nitrate, its production through this route is prohibitively expensive (*ca.* 4000 $\$\bullet t^{-1}$), thus limiting the scale of its industrial production. On the other hand, by adapting the process of ammonia oxidation to selectively produce N_2O, it is expected that the costs associated with its synthesis can be lowered to *ca.* 600 $\$\bullet t^{-1}$ and the necessity of downstream purification can be eliminated.[1,2]

With this purpose in mind, researchers at the Boreskov Institute of Catalysis (BIC) first developed a catalyst for this process, namely a Mn-Bi mixed oxide supported on α-Al_2O_3.[3] However, it operated in an excess of O_2 and suffered from key issues such as deactivation and insufficient N_2O selectivity.[3,4] The field ultimately experienced a revival in the last few years with the development of a series of three CeO_2-based ammonia oxidation catalysts: Au nanoparticles supported on CeO_2;[1] low-valent Mn atoms supported on CeO_2;[2] and Cr atoms incorporated into CeO_2 as $CrCeO_x$.[4] All three systems proved able to work under stoichiometric amounts of NH_3 and O_2, as well as produce N_2O with high selectivities (*ca.* 80 % or above).[1,2,4] However, to this date, no technical catalysts have been successfully developed for the direct synthesis of N_2O *via* ammonia oxidation. The only documented attempts of running this process on a pilot scale were made by researchers at the BIC employing the same Mn-Bi-O/α-Al_2O_3 catalytic system, but again under large oxygen excess.[5,6]

The aim of this thesis work was to explore and assess the challenges arising in the production of a technical formulation starting from the state-of-the-art Mn/CeO_2 powder catalyst developed by Surin *et al.*[2] Although other highly selective catalytic systems have been reported by the Pérez-Ramírez group for the direct oxidation of ammonia, such as Au/CeO_2[1] or $CrCeO_x$,[4] Mn/CeO_2 stood out for its ability to fully preserve its outstanding N_2O selectivity while entailing a much simpler preparation protocol compared to the other two catalysts (Fig. 1).

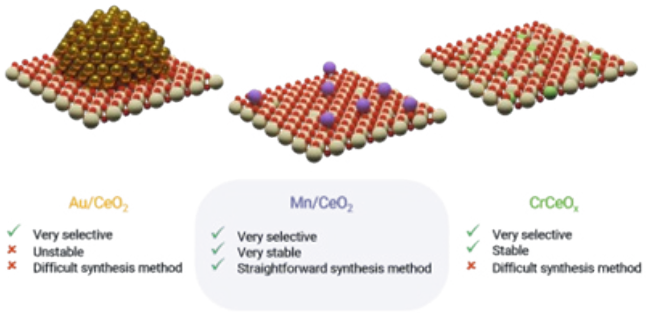

Fig. 1. Comparative view of the three ceria-based catalytic systems developed for the direct synthesis of nitrous oxide.

Through this thesis, an initial technical formulation of the powder Mn/CeO_2 system was produced and tested in the synthesis of N_2O. Besides attempting to understand how to best extrude a CeO_2-containing support, aspects such as the optimal way of depositing the active phase, the maximum achievable N_2O selectivity and the stability of the developed catalytic system were investigated. The study was concluded by testing the developed catalyst on an ammonia oxidation pilot plant – this provided an indication of the suitability of this system for further scale-up studies. Successful runs demonstrated the potential of this system in N_2O production, but certain challenges remain when attempting to make the transition from laboratory to pilot scale, especially the management of the considerable amounts of generated heat. In all, the development of a technical form of the Mn/CeO_2 powder catalyst appears promising. However, further investigations are required to develop strategies to address the challenges identified over the course of this thesis. Namely, aspects such as the mechanical stability of the bodies, the efficient dissipa-

tion of heat, and the minimization of mass transfer limitations are all challenges associated with the transition from powder to extrudate form.

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Future Plans

I would first like to acknowledge the invaluable help and opportunity offered by the Alfred Werner Scholarship of the Swiss Chemical Society Foundation through their support of my MSc studies at ETH Zürich. Following the conclusion of my MSc studies in the near future, I am looking to pursue a PhD degree in Catalysis and Sustainable Chemistry.

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Modeling the Nutrient Limitation of Deep Ocean Picoheterotrophs and their Role in Biogeochemistry

Deep ocean picoheterotrophs play a critical role in recycling organic matter into inorganic nutrients, thereby influencing the Earth's biogeochemical cycles. Despite their importance, the nutrient limitation regime governing their growth has been largely unexplored, particularly regarding potential iron limitation in deep ocean environments. By introducing a mechanistic modeling framework, this research investigates the relationships between picoheterotrophs, the marine iron cycle, and carbon cycle. It sheds light on potential iron limitation in the deep ocean and provides a starting point for the inclusion of picoheterotrophs in broader biogeochemical models.

Understanding how marine systems react to environmental changes constitutes one major challenge in Earth Science. This is especially true for processes involving the micronutrient iron, whose short oceanic residence time renders it particularly susceptible to rapid changes driven by oceanic and atmospheric processes, including those caused by anthropogenic activity.[1-3] Changes in the input of iron to the surface ocean have been linked to major shifts in productivity of iron-limited phytoplankton species in the Soutern Ocean with effects on the whole Earth system, such as glacial-interglacial variations in atmospheric CO_2.[4] The primary determinant of the amount of dissolved iron present in sea water is the size of a diverse pool of organic Fe-binding ligands[5] that effectively prevent the removal of dissolved iron through precipitation or scavenging and hence influence the limitation regime of marine organisms.[6] Heterotrophic prokaryotes – also known as picoheterotrophs due to their small size – form an integral part of marine (eco-)systems. They convert dissolved organic carbon (DOC) into biomass and dissolved inorganic carbon (DIC). Their growth influences the marine carbon cycle and is subject to iron limitation in certain parts of the ocean surface, much like phytoplankton – this is largely attributed to the high iron requirements associated with their respiratory chain.[7,8] In addition, their interaction with biogeochemical cycles in deep ocean environments affects the properties of sea water that is transported from the deep back to the ocean surface, indirectly influencing primary productivity and potentially climate.

Here, we investigate whether deep ocean iron limitation of picoheterotrophs is plausible given our current understanding of the marine iron and carbon cycle and deep ocean conditions. We develop a model that links the growth of deep ocean picoheterotrophs with the marine iron, organic carbon, and ligand pools, including the dominant processes influencing the deep ocean dissolved iron pool: complexation by Fe-binding ligands and removal by scavenging.[9] A schematic representation of the modeled processes is shown in Fig. 1. DOC and iron are supplied by the dissolution of sinking particles (including particulate organic carbon (POC)). The DOC pool is further divided into a labile – *e.g.* bioavailable – and a refractory pool (LDOC and RDOC, respectively). Accurately estimating the relevant parameters of all modeled processes is challenging, due to limited deep ocean observations.

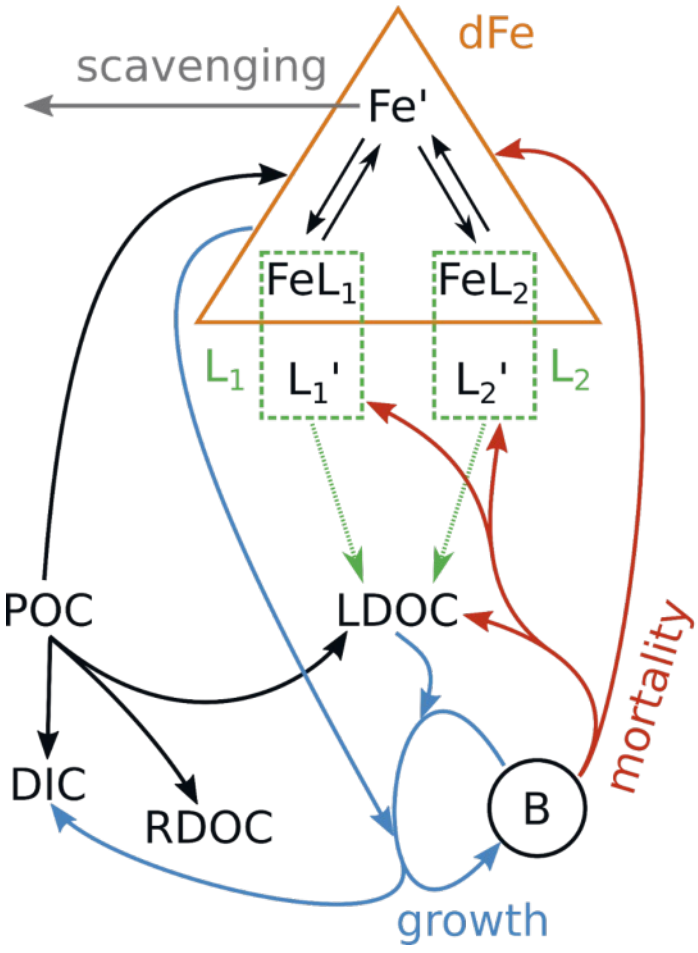

Fig. 1: Simplified representation of the quantities and processes represented in the developed model: **B**: picoheterotrophic biomass; **POC**: particulate organic carbon; **LDOC**: labile DOC; **RDOC**: refractory DOC; **DIC**: dissolved inorganic carbon; **dFe**: dissolved iron. Arrows indicate the flow of quantities in the dynmiac model.

Even so, due to the comparatively low complexity of the developed modeling framework, it is possible to obtain a closed-form steady-state solution for a 0-dimensional (globally integrated) case. By constraining the analytical solution of the model with available deep ocean observations and applying a repeated random sampling procedure, we are able to refine the ranges of certain model parameters and demonstrate that iron limitation is unlikely given observational data, while limitation by DOC appears more plausible. Going one step further, the developed modeling framework is integrated into an existing dynamic 3-box model of the ocean (Fig. 2).[10] By coupling the deep ocean ligand sink to the growth of picoheterotrophs, simulations with this 3-box ocean model can reproduce observed nutrient concentrations, limitation regimes, and key characteristics of the oceanic ligand pool. An extensive ensemble of simulations also supports the hypothesis that the availability of Fe-binding ligands strongly influences the global state of the ocean. The adapted 3-box model further provides a platform for investigating the broader biogeochemical impact of picoheterotrophs and may guide future research in this area.

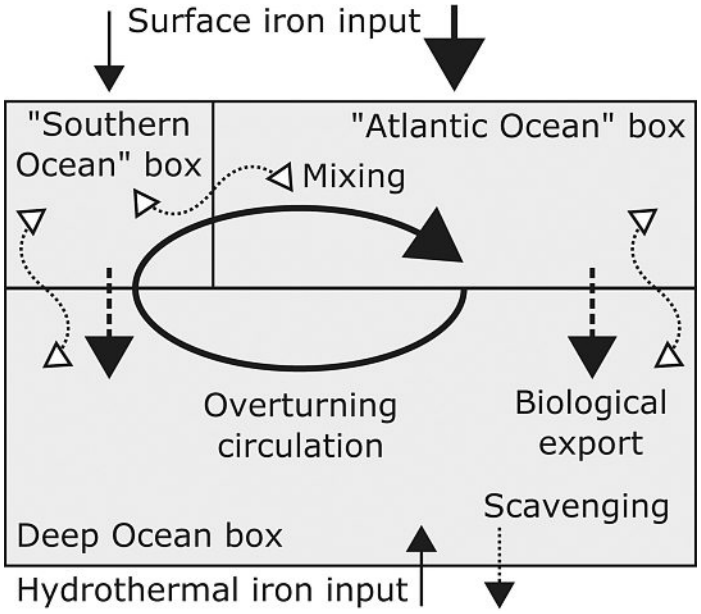

Fig. 2: Schematic illustration of the 3-box model taken from ref [10].

Future Plans

After completing my master's thesis in the US, I returned to Zürich, where I recently began a PhD in climate science in Prof. Reto Knutti's group. I am excited to tackle new problems at the intersection of science and policy. With the generous support of the Alfred Werner Foundation, I was able to gain international research experience and identify a research area I am truly passionate about.

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