International Pre-doctoral program 2026

Microcosm Earth Center:

Max Planck Institute for Terrestrial Microbiology (MPI-TM)

and

Philipps-Universität Marburg (UMR)

Project booklet

International Pre-doctoral program 2026

Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	UMR and MPI-TM
Name of host laboratory / group	Prof. Dr. Gert Bange and Dr. Patricia Bedrunka
Website of host laboratory / group	www.bangelab.org
Project title	Salt Stress and Microbial Adaptation: Unraveling Mechanisms of Environmental Resilience.
Project duration (3-6 months)	6 months
Prerequisites (educational)	Bachelor in natural or life sciences

Project proposal: description and expected outcomes of project (500 words max.):

Introduction and Background. Salinity is one of the most critical environmental stressors limiting microbial growth, ecosystem stability, and agricultural productivity. Microbes, as first responders to environmental fluctuations, have evolved intricate mechanisms to survive salt stress, including osmoprotectant synthesis, ion transport regulation, and stress signaling pathways. Among these, stress nucleotides such as guanosine tetraphosphate and pentaphosphate ((p)ppGpp) and diadenosine polyphosphates (e.g., Ap4N) play central roles as global regulators of cellular stress responses. These molecules act as “alarmones,” reprogramming transcription, translation, and metabolism under adverse conditions. However, their specific contributions to microbial adaptation under salinity stress remain poorly understood.

Research Objectives. This project aims to elucidate the role of stress nucleotides in microbial resilience to salt stress. Specifically, the study will:

- Investigate how (p)ppGpp and Ap4N are synthesized and regulated in microbes exposed to varying salt concentrations as well as different salts.
- Identify the downstream metabolic and transcriptional networks controlled by these nucleotides during salt stress adaptation.
- Explore the ecological implications of stress nucleotide-mediated adaptation in microbial communities under saline environments.

Methodology. This project will explore how stress nucleotides mediate microbial adaptation to salt stress using microbiology, enzymology, and structural biology. Salt-tolerant and sensitive strains (E. coli, B. subtilis, halophiles) will be exposed to graded NaCl to assess growth, viability, and morphology. Intracellular (p)ppGpp and Ap4N will be quantified by HPLC–MS, while mutants in RelA/SpoT and Ap4A-hydrolase will clarify genetic roles. Enzyme kinetics under salt conditions and structural analyses by X-ray crystallography and cryo-EM will reveal molecular mechanisms. RNA-seq and proteomics will define global networks, and soil microcosms will uncover community-level effects, linking molecular adaptation to ecosystem resilience.

Expected Outcomes. This research will provide mechanistic insights into how stress nucleotides orchestrate microbial adaptation to salt stress. The findings are expected to:

- Demonstrate differential accumulation of (p)ppGpp and Ap4N in microbes under salinity.
- Reveal novel regulatory pathways linking alarmone signaling to osmotic tolerance.
- Identify candidate microbial traits that could be harnessed for improving resilience in saline soils.

Significance. Understanding the molecular strategies by which microbes endure salinity stress will advance fundamental knowledge of stress biology and environmental microbiology. Furthermore, this work may contribute to applied solutions such as engineering stress-resilient microbial inoculants for sustainable agriculture and bioremediation of saline environments. By unraveling the interplay between stress nucleotides and microbial adaptation, this project aims to bridge molecular mechanisms with ecosystem resilience in the face of increasing soil salinization.

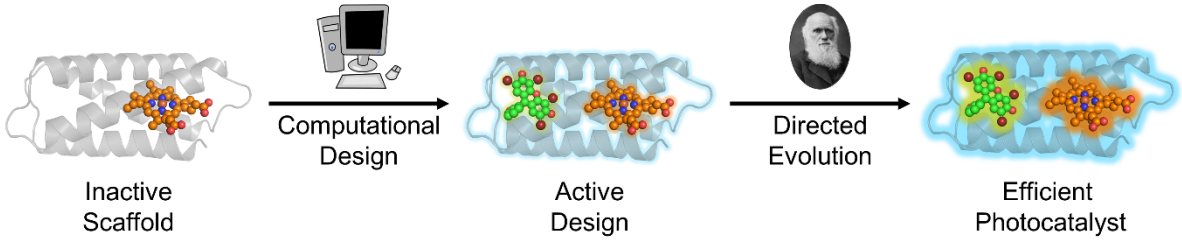
International Pre-doctoral program 2026

Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Max Planck Institute for Terrestrial Microbiology
Name of host laboratory / group	Bunzel
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/bunzel
Project title	Computational Design of Photoenzymes for Solar-Driven Carbon Capture
Project duration (3-6 months)	6 months
Prerequisites (educational)	**Necessary:** Basic biochemical experience in working with proteins Basic coding experience, such as Python **Desired:** Experience with protein design, structure prediction, or biomolecular simulations is helpful but not required. Experimental experience in protein engineering or photo-biocatalysis is helpful but not required.

Project proposal: description and expected outcomes of project (500 words max.):

Rising atmospheric CO_2 levels demand new solutions for carbon capture. Advances in computational protein design now allow us to engineer biology with unprecedented accuracy, enabling the construction of enzymes that would have been unimaginable only a few years ago. **The Bunzel group combines computational protein design and directed evolution to develop biocatalysts for solar-energy conversion.** In this project, you will computationally design photoenzymes that utilize sunlight to reduce CO_2, and experimentally validate the designed enzymes for photoactivity.



You will work with state-of-the-art computational algorithms, including **AlphaFold3** for structure prediction, **ProteinMPNN** and **RosettaDesign** for protein design, and **MD simulations** to evaluate the success of your designs. These methods have recently been integrated into our **AI.zymes** enzyme design platform (Merlicek, Angew. Chem. Int. Ed. 2025), which provides a streamlined pipeline for enzyme design. **Using AI.zymes, you will design new binding pockets for small-molecule photosensitizers in enzymes that naturally reduce CO_2, enabling them to harvest sunlight for carbon capture.**

In the laboratory, you will **test hundreds of designed variants for photoactivity**. For this, you will employ high-throughput protein production and purification, and screen the resulting proteins for photosensitizer binding and light-driven CO_2 reduction. Promising candidates will then undergo more detailed characterization to uncover the structural and mechanistic factors that enable photoenzymatic function.

Through this project, you will gain hands-on training across the full design–build–test cycle: from **cutting-edge computational modeling** to classical laboratory techniques in **molecular biology and biochemistry**. This experience reflects the interdisciplinary nature of modern life sciences and will prepare you for future work at the interface of computation and experiment.

The Bunzel group is pioneering the development of photoenzymes for solar energy conversion. This project will demonstrate how computational protein design can be used to create enzymes that harness sunlight by integrating photosensitizers into protein scaffolds. Your work will directly contribute to these efforts and provide a foundation for directed evolution and next-generation designs of sustainable CO_2-reducing photoenzymes that address societally critical challenges.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	MPI for Terrestrial Microbiology
Name of host laboratory / group	Biophysics of environment sensing by motile microorganisms
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/colin
Project title	Metabolically entangled bacterial community under constraint
Project duration (3-6 months)	5-6 months
Prerequisites (educational)	Background in microbiology or physics

Project proposal: description and expected outcomes of project (500 words max.):

In labs, we typically study homogeneous populations of bacteria growing in well-mixed batch cultures. In contrast, natural bacterial populations present a wide diversity of phenotypes that interact with each other and live in highly structured environments, both physically and chemically (e.g. the soil). There, they are exposed to and they shape gradients of various environmental conditions, notably of nutrients, which they can navigate thanks to flagellated motility, coupled to the chemotaxis sensory pathway, to migrate towards more favorable conditions. In most microbial community, a fraction of the species is motile, the other not. Previous works from our lab have shown that the physical interactions between the two phenotypes lead to spatiotemporal organization patterns that are specific to such mixed populations. These patterns are also modulated by the environmental constraints that fluid flows and chemical gradients constitute. Natural microbial communities also often show metabolic entanglement, where a species produces metabolites needed by the other, while receiving some it needs in return. Chemotactic motility is hypothesized to facilitate the metabolic interaction, thanks to the navigation up the metabolite gradients, but evidences are scarce. We are currently developing a set of motile or non-motile and fluorescently tagged *Escherichia coli* mutant strains that are metabolically entangled due to complementary amino-acid auxotrophies.

We aim to understand which roles chemotactic motility plays in the maintenance of the metabolically entangled community under constraint. Depending on student's preference, two closely related projects could be undertaken. The first is interested in investigating the effect of motility and chemotaxis in the population response to the constraint of flow. Our lab develops microfluidics

devices, with which we submit bacterial population to well-controlled flows, which we combine with fluorescence microscopy and image analysis methods to study their behavior. During the project, we will study the effect of flow on the growth and self-organization of the metabolically entangled population, using both simple device and a microfluidic maze that mimic soil pore structure. We will focus on the role of motility and chemotaxis in the population response to flow. The second project is interested in generating motile and non-motile non-cooperator strains ("cheaters") that consume but do not produce the shared amino-acids, to investigate the role of motility during the invasion of an entangled cooperating community by cheaters. This investigation will again rely on biofilm formation assay, time-lapse fluorescence microscopy and image analysis. These projects aim at understanding to which extent is motility and chemotaxis facilitating metabolic interactions under two different environmental constraints.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Max Planck Institute for Terrestrial Microbiology
Name of host laboratory / group	Department of Biochemistry and Synthetic Metabolism
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/biochemistry-and-synthetic-metabolism
Project title	The Role of Lanthanides in Nitrogen Fixation by the Thermophilic Methanotroph 'Candidatus Methylocalor cossyra' CH1
Project duration (3-6 months)	6 months
Prerequisites (educational)	Bachelor or Master

Project proposal: description and expected outcomes of project (500 words max.):

Methanotrophs play an important role in methane mitigation and global carbon cycling by oxidizing methane as their sole carbon and energy source. '*Candidatus Methylocalor cossyra*' CH1, a thermophilic gammaproteobacterial methanotroph isolated from acidic geothermal soil, exhibits themetabolic capacity for both methane oxidation and atmospheric nitrogen fixation. This physiological versatility makes it a model system for studying how methane oxidation and nitrogen fixation are linked.

Previous work suggests a crucial role for lanthanides (Lns), a group of rare earth elements, in regulating nitrogen fixation in this strain. In chemostat culture experiments, under ammonium-supplemented conditions, the addition of 1 µM La^{3+} was sufficient to support growth, and lanthanide levels in the supernatant fell below the detection threshold (<25 pM), indicating effective uptake. However, under nitrogen-fixing conditions, this same concentration was insufficient to sustain growth in chemostat cultivation. Instead, 10 µM La^{3+} was required to support stable diazotrophic growth, with a residual concentration of 0.13 µM remaining in the culture supernatant. This substantial shift in lanthanide requirement under N_2-fixing conditions highlights a strong correlation between lanthanide availability and nitrogen fixation activity.

This project will explore how lanthanides support nitrogen fixation in 'Ca. M. cossyra' CH1. We will grow this strain CH1 under both ammonium and nitrogen-fixing conditions, using different concentrations of La^{3+} (0–20 µM). We will measure growth, nitrogenase activity (via acetylene

reduction), and La^{3+} uptake to determine how much lanthanide is needed and how it affects nitrogen fixation.

In parallel, we will aslo perform proteomic analyses to identify genes and proteins that respond to lanthanide availability. These may include nitrogenase components, regulatory proteins, and lanthanide-binding proteins. Furthermore, the role of XoxF-type methanol dehydrogenases—known to be lanthanide-dependent—will be explored beyond C_1 metabolism, considering their potential involvement in nitrogen fixation regulation.

Expected outcomes include:

1. A quantitative model of lanthanide requirements for nitrogen fixation and methanotrophic growth in strain 'Ca. M. cossyra' CH1;
2. Identification of lanthanide-dependent gene and protein complexes associated with nitrogen metabolism;
3. Insights into the regulation and stabilization of nitrogenase activity by lanthanides;
4. Discovery of novel lanthanide-binding proteins potentially involved in nitrogen metabolism and regulatory pathways.
5. If necessary, targeted gene knockouts will be performed using genetic tools (e.g., conjugation-based gene disruption) to confirm the specific roles of candidate genes involved in lanthanide-dependent nitrogen fixation.

This study will provide important new knowledge about the role of lanthanides in microbial nitrogen fixation, particularly in extreme environments. It will also help us understand how rare earth elements influence key microbial processes, with possible applications in environmental biotechnology and sustainable agriculture.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Max Planck Institute for Terrestrial Microbiology
Name of host laboratory / group	Erb group
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/erb
Project title	Directed evolution of a formaldehyde-activating enzyme
Project duration (3-6 months)	6 months
Prerequisites (educational)	Biochemistry, molecular biology, microbiology

Project proposal: description and expected outcomes of project (500 words max.):

Our current fossil-based industry is largely a linear process, requiring unsustainable fossil resources and emitting large amount wastes. Being one of the major waste, carbon dioxide (CO2) can also serve as a useful resource. CO2-derived one-carbon (C1) substrates, such as methanol or formate, are attractive feedstocks for a circular bioeconomy, where C1 feedstocks are utilized by (microbial) cell factories and transformed into valuable products. In such processes, formaldehyde serves as the core intermediate bridges the abiotic C1 world and the biological world.

We have successfully employed several aldolases as key enzymes in synthetic formaldehyde/C1-assimilation metabolic pathway designs. Leveraging their promiscuous enzyme activities, we have demonstrated the proof-of-concept of the artificial pathways. While these enzymes have significant formaldehyde-condensing activities, their low promiscuous activities are still major bottleneck of the metabolic pathways.

In this project, we will focus on one of the key enzymes, use different approaches, iterative saturated mutagenesis, hyper-mutagenesis, metabolic selection, and structural biology, to engineer the target aldolase for better activity and selectivity of using formaldehyde as a substrate. An outline of the project would be:

Months 1 – 2: Molecular cloning, recombinant protein production, and enzyme kinetic assay method development

Months 2 – 4: High-throughput screen method development, iterative saturated mutagenesis

Months 3 – 5: Hyper-mutagenesis

Months 5 – 6: Kinetic characterizations

The outcomes of the project will be method establishments of kinetic assay, high-throughput screen, and hyper-mutagenesis, as well as in the end a significantly improved version of the target enzyme. The enzyme will be used in establishing multiple (published and unpublished) C1-assimilation pathways.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Philipps-Universität Marburg (UMR)
Name of host laboratory / group	Höfer Laboratory / Bacterial Epitranscriptomics
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/mprg/katharina-hoefer - Uni page will be also added soon
Project title	Regulation of redox cofactor-capped RNAs in algae
Project duration (3-6 months)	6 months
Prerequisites (educational)	Biochemistry, Biology

Project proposal: description and expected outcomes of project (500 words max.):

CapCarbon – RNA Caps in Carbon Fixation

RNA is a dynamic and highly regulated molecule whose diversity extends far beyond the canonical bases A, U, C, and G. More than 170 chemical modifications are currently known, many of which influence RNA stability, translation, and gene regulation. In addition to these base modifications, several redox cofactors, including nicotinamide adenine dinucleotide (NAD), flavin adenine dinucleotide (FAD), and 3'-dephospho-coenzyme A (dpCoA), have recently been identified as 5'-RNA caps across all kingdoms of life. These discoveries opened a new research field connecting redox biology with RNA biology.

The Höfer lab is a leader in studying NAD-capped RNAs, having developed NAD captureSeq (Höfer et al., 2015) to identify and quantify NAD-RNAs in living systems. The group aims to unravel how redox cofactors, when attached to RNA, influence gene expression and physiology. A groundbreaking finding from the lab was the discovery of RNAylation, the enzymatic linkage of NAD-RNA to proteins, revealing a new layer of RNA–protein interplay (Wolfram-Schauerte et al., 2023). Yet, the broader functions of NAD- and other cofactor-capped RNAs remain largely unexplored.

This project will investigate the regulatory potential of redox cofactor caps in carbon fixation by the model alga *Chlamydomonas reinhardtii*. We hypothesize that NAD-, FAD-, and dpCoA-capped RNAs contribute to the regulation of photosynthesis and CO_2 assimilation, potentially linking RNA modification status to light responses. C. reinhardtii is ideally suited for this study because it can be

grown under defined light/dark cycles, thereby enabling synchronous comparisons of cap levels across different phases of the light/dark cycle.

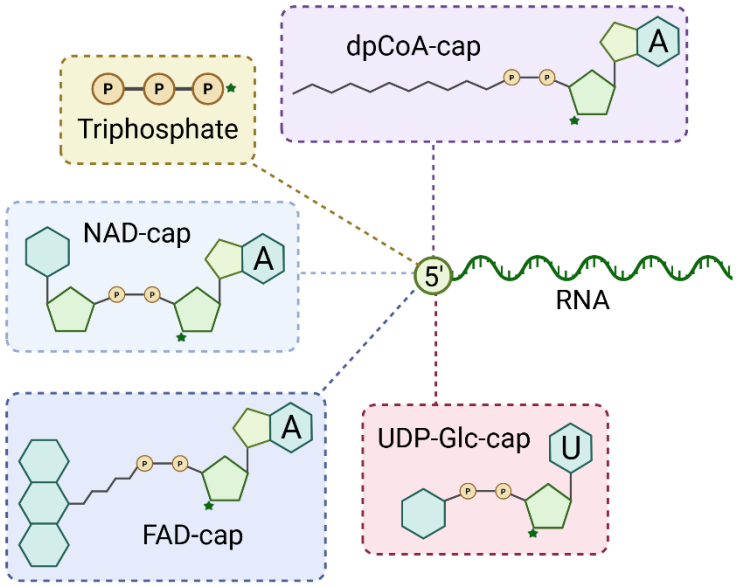

Figure 1: Examples of 5'-RNA caps with the location of the RNA chain indicated by a green star. UDP-Glc is uridine diphosphate-glucose.

Objective 1: Establish an *in vitro* assay for cofactor-capped RNAs

NAD-, FAD-, and dpCoA-capped RNAs will be generated by in vitro transcription (IVT). Enzymes required for cap removal (e.g., NudC) and for subsequent cap conversion with ATP (e.g., NadR) will be cloned, expressed in *E. coli*, and purified. The IVT-derived capped RNAs will then be incubated with these enzymes in the presence of radiolabeled ATP. Separation and detection of the released cofactors will be accomplished through a thin-layer chromatography (TLC)-based method.

Objective 2: Quantify cofactor-capped RNAs in *C. reinhardtii*

After validation with IVT-derived RNAs, the assay will be applied to native RNA. *C. reinhardtii* will be cultured under light/dark cycles, and RNA will be isolated at defined time points. RNA integrity will be verified using urea-PAGE and Bioanalyzer analysis. Samples will then be analyzed with the established assay, with IVT-generated RNAs serving as quantification standards. This approach will allow systematic comparison of NAD-, FAD-, and dpCoA-cap levels across different phases of the light/dark cycle.

Expected Outcomes and Training:

The project will establish a robust assay for rapid quantification of redox cofactor-capped RNAs, enabling comparisons across biological samples and conditions. For the student, this project provides comprehensive training in RNA biochemistry, including RNA isolation, *in vitro* transcription of capped RNAs, protein cloning and purification, and enzymatic assay development. Beyond advancing methodological expertise, the work will contribute a broadly applicable tool to the scientific community and generate new insights into the regulatory role of RNA modifications in photosynthetic organisms.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Microcosm Earth Center	
Name of host laboratory / group	Klatt Lab	
Website of host laboratory / group	https://www.uni-marburg.de/en/microcosm-earth/wg-klatt	
Project title	Light vs. Life: Photochemical vs. Biological Pathways of Fe(II) Oxidation in the ancient oceans	
Project duration (3-6 months)	6 months	
Prerequisites (educational)	End of M.Sc. or already graduated	

Project proposal: description and expected outcomes of project (500 words max.):

The oxygenation of Earth's atmosphere was a transformative event that ultimately enabled the rise of complex life. Yet, the processes that drove the earliest oxygenation and their timing remain poorly understood. Banded Iron Formations (BIFs) provide one of the clearest records of this transition. These deposits, consisting of alternating layers of iron oxides and silica, document the large-scale removal of dissolved Fe(II) from Archean oceans between 4.0 and 2.5 billion years ago. The sheer volume of iron oxidized and deposited in BIFs makes them central to debates about how Earth first became oxygenated.

Traditionally, BIFs were seen as evidence for oxygenic photosynthesis by cyanobacteria, with the O_2 they produced driving Fe(II) oxidation. Yet, this view has been challenged. Anoxygenic phototrophs may have used Fe(II) directly as an electron donor, a metabolism known as photoferrotrophy. Intense ultraviolet radiation from the young Sun could also have promoted purely abiotic Fe(II) oxidation, yielding Fe(III) minerals and molecular hydrogen. Finally, Fe(II) may not have been oxidized in the water column at all. Instead, it could have been stabilized by high concentrations of silica, bicarbonate, or CO_2 and deposited as minerals such as greenalite or siderite, with Fe(III) phases forming later through diagenetic alteration.

In this project, we will experimentally simulate Archean ocean conditions to evaluate the relative contribution of the competing pathways of Fe(II) oxidation and BIF formation:

1. Oxygenic photosynthesis: oxidation of Fe(II) by O_2 released from cyanobacteria.
2. Photoferrotrophy: direct microbial oxidation of Fe(II) by anoxygenic phototrophs.

3. Photochemical oxidation: abiotic Fe(II) oxidation driven by intense Archean UV radiation.
4. Fe(II) stabilization and diagenesis: deposition of Fe(II)-bearing minerals such as greenalite or siderite, with Fe(III) phases arising later through diagenetic processes.

Depending on the candidate's background, the project may emphasize (i) mineralogy of Fe-bearing precipitates, (ii) aqueous geochemistry and oxidation kinetics, or (iii) microbial physiology of cyanobacteria and photoferrotrophs.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Microcosm Earth Center	
Name of host laboratory / group	Klatt Lab	
Website of host laboratory / group	https://www.uni-marburg.de/en/microcosm-earth/wg-klatt	
Project title	Silica-coated spores as natural redox nanoreactors in early oceans	
Project duration (3-6 months)	6 months	
Prerequisites (educational)	End of M.Sc. or already graduated	

Project proposal: description and expected outcomes of project (500 words max.):

Background

Precambrian oceans were saturated with dissolved silica, creating conditions where microbes were constantly exposed to high Si levels. While diatoms much later evolved elaborate silica frustules, earlier microbes likely interacted with silica in more opportunistic ways. In particular, dormant stages such as cyanobacterial akinetes or bacterial endospores often became coated with amorphous silica. This process provided durable mineral armor and enhanced fossilization in cherts, but it may also have had environmental implications. Silica surfaces are chemically active: silanol groups bind metals, stabilize organic molecules, and catalyze redox processes. Modern biotechnology has rediscovered this principle by engineering silica-coated spores as "nanoreactors."

Hypothesis

Silicified spores were not only survivors but also portable catalytic microenvironments that influenced local geochemistry where they accumulated, for example by mediating redox transformations at the sediment–water interface in the Precambrian, and perhaps still today in silica-rich habitats.

Aims

This project will explore whether silica-encrusted spores could have functioned as natural redox nanoreactors, bridging microbiology, geochemistry, and evolution. It links Precambrian ocean chemistry with microbial adaptation strategies, and revisits an ancient phenomenon that modern biotechnology already exploits.

Depending on the candidate's background and interests, possible directions include:

1. Induce resting stage formation in model microbes (e.g. cyanobacteria) under silica-rich conditions.
2. Characterize silica encrustation of spores (microscopy, spectroscopy).
3. Test redox activity of silicified spores in simulated sediment settings (Fe, Mn, and organic substrates).
4. Model environmental impact: simulate how spores "rained down" on ancient sediments and acted as catalytic grains in biogeochemical cycling.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	MPI-TM
Name of host laboratory / group	Research Group Synthetic Cofactors and Orthogonal Metabolism/ Dr. Maren Nattermann
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/1484346/Maren-Nattermann
Project title	Enzyme engineering for orthogonal metabolic pathways
Project duration (3-6 months)	6 months
Prerequisites (educational)	For this project, we are looking for a highly motivated student with a background in natural sciences. Previous laboratory experience is a bonus, but not required. The main language in our lab is English, therefore good English proficiency (B2-C1) is important.

Project proposal: description and expected outcomes of project (500 words max.):

The reduction of atmospheric CO_2 is one of the most pressing challenges of the 21st century. In recent years, many synthetic pathways for the efficient use of CO_2 by engineered organisms have been developed. These routes are more efficient than those evolved by nature and can be coupled to biological production pathways for bulk and fine chemicals, providing a large toolbox for biotechnological CO_2 re-capture and upcycling.

However, the implementation of synthetic pathways is challenging due to the delicate balance required between growth and product generation. This matter is particularly pressing in organisms relying on low-energy feedstocks such as CO_2. Here, any energy spent on off-pathway products or futile cycles can impede the implementation of a pathway: key cellular resources like ATP or NADPH may be drained or important metabolite pools such as acetyl-CoA disrupted, rendering the organism incapable of growth. In pathway engineering, a lot of effort is placed on minimizing these interactions. This concept is referred to as pathway orthogonality, where synthetic pathways interact with core metabolism as little as possible, allowing for a better allocation of cellular resources and a higher likelihood of successful implementation in vivo.

This project will focus on generating short orthogonal cascades for the production of chemicals. Mainly, the synthetic enzymes required for efficient catalysis will be developed. Here, you will purify


enzymatic candidates, compare their activities, develop high-throughput screens and screen mutant libraries to find improved variants. Towards the end of the project, the variants generated will be characterized biochemically via kinetic assays based on UV-Vis, fluorescence or HPLC-MS analytical methods.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	MEC; MPI-Marburg
Name of host laboratory / group	Geochemical Protoenzymes / AGPreiner
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/martina-preiner
Project title	Exploring the catalytic properties of metal-organic complexes
Project duration (3-6 months)	6 months
Prerequisites (educational)	Master degree Chemistry or Biochemistry

Project proposal: description and expected outcomes of project (500 words max.):

Nucleotides and amino acids coordinate with metal ions through their charged moieties, which can produce catalytically active complexes. In enzymes, metals such as Magnesium and Zinc are more often stabilizers and activators, while others like Iron and Molybdenum are catalytic [1]. On their own, they can still be active[2, 3], but both life and chemists have found that it is worth developing metal-organic complexes for catalysis.

From an origin of life perspective, natural minerals and metal ions are hypothesized as the first catalysts that served to transform inorganic material into the first organic molecules [4]. In this project, we plan to explore the next step of these catalytic systems by testing the properties of complexes that can form in a mixture of metal and building blocks, or other small organic molecules that could have existed long before life itself.

The student should be able to screen a variety of different conditions and complexes through chromatography, which should expand our understanding of how proto-metabolic systems could have formed before life.

1. Andreini C, Bertini I, Cavallaro G, et al (2008) Metal ions in biological catalysis: from enzyme databases to general principles. JBIC J Biol Inorg Chem 13:1205–1218. https://doi.org/10.1007/s00775-008-0404-5
2. Kandemir T, Schuster ME, Senyshyn A, et al (2013) The Haber–Bosch process revisited: On the real structure and stability of "ammonia iron" under working conditions. Angew Chem Int Ed 52:12723–12726. https://doi.org/10.1002/anie.201305812
3. Liu L, Corma A (2018) Metal catalysts for heterogeneous catalysis: from single atoms to nanoclusters and nanoparticles. Chem Rev 118:4981–5079. https://doi.org/10.1021/acs.chemrev.7b00776
4. Belmonte L, Mansy SS (2016) Metal catalysts and the origin of life. Elements 12:413–418. https://doi.org/10.2113/gselements.12.6.413

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Max Planck Institute for Terrestrial Microbiology
Name of host laboratory / group	AG Preiner
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/martina-preiner
Project title	Silica as preprotein matrix for cofactors at the origins of life
Project duration (3-6 months)	3-5
Prerequisites (educational)	Masters in bio- or geochemistry

Project proposal: description and expected outcomes of project (500 words max.):

Active sites of enzymes often have small organic molecules or transition metal ions as cofactors to drive biochemical reactions. While they can function independently of their surrounding protein scaffold, their efficiency, stability, and fine tunable reactions would dwindle. At the origins of life, simple organic molecules, such as coenzymes, could have been present while more complex protein scaffolds were unlikely to come by. If a similar substitute would have been present, life could have utilized that to harness the cofactors better.

Porous silica structures were abundant in potential environments that could have been central to the origins of life, such as hydrothermal vents or shallow tidal pools. Silica surfaces are known to adsorb and concentrate reactants, and in some cases catalyze chemical transformations. What remains unclear is whether porous silica structures could have interacted with cofactors or coenzymes that could have also been present at life's emergence.

The goal of this project is to investigate the potential prebiotic role of silica and its biochemical interactions with cofactors (metal ions, porphyrins, flavins), and whether it could enhance or modulate prebiotic reactions like an early protein matrix.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Max Planck for Terrestrial Microbiology
Name of host laboratory / group	AG Sourjik
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/sourjik
Project title	Investigating biofilm formation by pathogenic *Escherichia coli* strains
Project duration (3-6 months)	6 months
Prerequisites (educational)	Molecular biology, microbiology, bioinformatics (plus)

Project proposal: description and expected outcomes of project (500 words max.):

Biofilm formation is an important virulence factor when considering nosocomial infections, increasing bacterial resistance to chemical treatments and antibiotics. There is a complex network involved in biofilm regulation and development that is poorly understood for diverse non-pathogenic and pathogenic isolates of *E. coli*. In this project, we aim to identify differences and commonalities in biofilm formation and presence of biofilm-related genes in genomes of different *E. coli* strains, with a primary focus on pathogenic isolates. We will compare biofilm development for a collection of *E. coli* pathogenic strains under several different conditions, using staining and gene expression analysis. Selected strains will be analyzed for their genome composition, including presence or absence of known biofilm-related genes and sequence of their promoters. We will also compare the proteome profiles of the strains in liquid and solid growth. These approaches will offer insights into the diversity of biofilm forming abilities of natural *E. coli* isolates and identify genes associated with different capacity or types of biofilm formation, which might be useful as targets for drug development in the future.

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Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	MPI-TM
Name of host laboratory / group	Treuner-Lange
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/anke-treunerlange
Project title	Expression, purification and mutagenesis of bacterial PilY1 adhesins for elucidation of function and structure
Project duration (3-6 months)	6 month
Prerequisites (educational)	Basic knowledge of microbiology, biochemistry, molecular biology, structural biology

Project proposal: description and expected outcomes of project (500 words max.):

Motility is important for adaptation and colonization of various habitats and overall fitness by directing cells towards nutrients and away from toxins and predators. The most widespread form of bacterial surface-associated motility is twitching motility, which is mediated by Type IV pili (T4P). T4P are built from thousands of copies of the major pilin subunit and tipped by a complex composed of minor pilins and in some systems also a PilY1 adhesin. PilY1 proteins are large, multidomain proteins that play central roles in the assembly, function, and signaling of T4P in various bacterial species. They act as tip-associated adhesins, contribute to pilus-mediated twitching motility, and are essential for host cell attachment and mechanosensing. While the structure of the C-terminal domain of *Pseudomonas aeruginosa* PilY1 was resolved in 2010 (PDB: 3HX6), structural information on the N-terminal domains and full-length PilY1 proteins has remained elusive.

Excitingly, recent high-confidence AlphaFold models suggest that PilY1 proteins interact with minor pilins, connecting to one of them through a process called β-strand addition—an interaction known for its exceptional structural stability. Building on this, we are planning to express and purify three different Strep-tagged myxobacterial PilY1 proteins along with one or more minor pilins, in hopes of producing stable PilY1 complexes suitable for detailed studies.

PilY1 proteins also contain conserved calcium-binding motifs, making calcium critical for their structural stability and biological activity. In addition, they are rich in cysteine residues. Evidence points to disulfide bridges within PilY1, which may enable force-triggered shape changes essential for the protein's role in surface sensing and mechanosensitive adhesion. By using site-directed mutagenesis to alter specific key residues in the three myxobacterial PilY1 proteins, we aim to uncover the precise contributions these features make to PilY1's function.

International Pre-doctoral program 2026

Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Marburg University
Name of host laboratory / group	Olallalab / Vázquez lab
Website of host laboratory / group	https://olallalab.org
Project title	Expanding the antimicrobial peptide toolbox with unnatural amino acids
Project duration (3-6 months)	6 months
Prerequisites (educational)	Chemistry with specialization in organic chemistry (ideally in both theory and experimental)

Project proposal: description and expected outcomes of project (500 words max.):

The rise of antibiotic-resistant bacteria has created an urgent need for new antimicrobial agents. Antimicrobial peptides (AMPs) have emerged as promising alternatives to traditional antibiotics due to their broad-spectrum activity. However, AMPs are limited by susceptibility to protease degradation and, consequently, poor stability. Non-canonical amino acids can address this limitation while they also offer additional advantages, such as enhanced specificity, improved activity, conditional control, and the ability to confer optical properties. In this context, we will synthesise new unnatural amino acids and incorporate them into AMP, with the ultimate goal of creating potent antimicrobials against both Gram-negative and Gram-positive bacteria.

Methodology

The project will consist on:

- Unnatural Amino Acid Synthesis: Design and chemically synthesize a novel amino acid. The amino acid will be prepared via organic synthesis and protected (e.g., with an Fmoc group) for compatibility with peptide solid phase
- Solid Phase Peptide Synthesis (SPPS): Incorporate unnatural amino acids into peptide sequences using Fmoc-based solid-phase peptide synthesis. After assembly and cleavage from the resin, the peptides will be purified by HPLC and characterized

- Antimicrobial Testing: Evaluate the new peptides against *E. Coli* and *B. subtilis*. Determine their minimum inhibitory concentrations (MICs) and compare their antimicrobial efficacy to our previous results.
- Mode of Action and Stability: Assess the stability of the most promising candidaties as well the preliminary mode of action.

Preliminary Results

We count on preliminary results of novel AMP containing unnatural amino acids, which showed strong antimicrobial activity against in several organisms.

Expected Outcomes

By the conclusion of the project, we expect to achieve:

1. Synthesis of the Unnatural Amino Acid: The novel amino acid will be obtained in good yield and purity, ready for use in peptide synthesis.
2. Successful Peptide Incorporation: Efficient integration of the unnatural amino acid into antimicrobial peptide sequences via SPPS, producing stable peptide products.
3. Demonstrated Antimicrobial Efficacy: The resulting peptides will exhibit potent antimicrobial activity (low MIC values against E. coli and B. subtilis) and enhanced proteolytic stability, confirming the benefits of the unnatural residue.
4. Exploration of Mode of Action

International Pre-doctoral program 2026

Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Marburg University
Name of host laboratory / group	Olallalab / Vázquez lab
Website of host laboratory / group	https://olallalab.org
Project title	Fluorescent turn-on probes for bacteria labeling
Project duration (3-6 months)	6 months
Prerequisites (educational)	Chemistry with specialization in organic chemistry (ideally in both theory and experimental)

Project proposal: description and expected outcomes of project (500 words max.):

Fluorescence is invaluable for detecting microorganisms in complex environments. Conventional probes often suffer from high background, limited specificity, or poor selectivity. Turn-on probes, which are triggered by a specific stimulus, provide a powerful alternative by ensuring high signal-to-noise ratios and enabling selective target visualization. Enzyme-responsive turn-on probes offer a particularly attractive strategy by exploiting enzymatic activities that are exclusive to bacteria but absent in mammalian cells.

Among the wide array of bacterial enzymes, many families remain underexplored for probe development. For example, dimethyl sulfoxide reductases (DMSORs) represent a family of molybdenum-containing enzymes present in bacteria and archaea but absent in eukaryotes. While DMSORs have not been studied in the context of fluorescent labelling, they provide an excellent proof-of-concept target for enzyme-activated probes. Indeed, we already have promising preliminary results using DMSOR-responsive probes, validating the overall concept.

In this project, we will focus on continuing our work on BODIPY-based probes for DMSORs labelling, as well as exploring novel turn-on probes. The general design involves the modification of the fluorophore with an enzyme-cleavable masking group. This strategy ensures fluorescence is only observed in the presence of active bacterial enzymes, yielding highly selective bacterial labelling.

Methodology

The project will consist on:

- Synthesis of Masked Fluorophores – Chemical synthesis of fluorescent-based probes with different masking groups designed to respond to bacterial enzymes. This includes groups that mimic natural substrates of reductases, hydrolases, or other bacterial-specific enzymes.
- Photochemical Characterization and Enzymatic Testing – *In vitro* evaluation of probe fluorescence and activation with(out) bacterial lysates (or purified bacterial enzymes, if possible).
- Biological Application – Application of the probes to live bacterial cultures using flow cytometry and microscopy.

Preliminary Results

We count on preliminary results with a DMSOR-targeting probes based on BODIPY chemistry.

Expected Outcomes

1. Successful synthesis of a library of BODIPY-based fluorogenic probes for DMSORs
2. Demonstration of enzyme-triggered turn-on fluorescence in vitro.
3. Selective bacterial labeling in live cultures, with minimal interference from mammalian cells.
4. Exploration of bacterial enzymes beyond DMSOR by the synthesis and characterization of novel masked fluorophores

International Pre-doctoral program 2026

Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Max Planck Institute for Terrestrial Microbiology
Name of host laboratory / group	RG Yuan
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/systems-and-synthetic-microbiology/jingyuan
Project title	Investigate the impact of microbial community on UPEC gut colonization
Project duration (3-6 months)	6 months
Prerequisites (educational)	B.S. or M.S.

Project proposal: description and expected outcomes of project (500 words max.):

Uropathogenic *Escherichia coli* (UPEC) is the leading cause of urinary tract infections (UTIs), responsible for over 150 million cases globally each year. UPEC typically resides harmlessly in the human gut, forming a reservoir. Through fecal shedding, UPEC cells spread to the periurethral area or vagina, where they enter the urethra, ascend the urinary tract, and trigger infections in the bladder and kidneys. In case of recurrent UTIs, the abundance of intestinal UPEC contributes to the infection and correlates with changes in gut microbiota composition. These findings suggest strong connections between UPEC and gut microbiota, underlining the critical role of gut colonization in the development and persistence of these infections. Gaining a deeper understanding of this colonization process may help in preventing UTIs and reducing the reliance on antibiotics for treatment.

Bacteroides is a genus of Gram-negative, obligate anaerobic bacteria. *Bacteroides* species are prominent members of the human gut microbiota, responsible for converting dietary fibers and host-derived glycan to fermentable sugars and the production of short chain fatty acids. The abundance and diversity of Bacteroides species directly determine the dynamics of a microbiota. However, their impact on UPEC colonization have not been explored.

During the six-month fellowship, the student will introduce a UPEC strain into two model systems: (i) a defined consortium of one to four Bacteroides strains and (ii) a miniature gut-microbial community comprising nine species, including the same Bacteroides isolates. UPEC growth within these communities will be evaluated under fiber-rich and glycan-rich nutrient conditions to assess how diet-derived substrates influence UPEC persistence in the community. In parallel, the student will monitor UPEC interactions with mammalian cells, both in isolation and in the presence of the microbial consortia. By the end of the fellowship, this work is expected to provide new insights into how gut microbial communities—particularly Bacteroides—affect UPEC growth and adhesion to host cells, thereby clarifying the ecological factors that shape UPEC colonization potential.

International Pre-doctoral program 2026

Microcosm Earth Center: Max Planck Institute for Terrestrial Microbiology (MPI-TM) and Philipps-Universität Marburg (UMR)

Name of Institution	Max Planck Institute for Terrestrial Microbiology
Name of host laboratory / group	RG Yuan
Website of host laboratory / group	https://www.mpi-marburg.mpg.de/systems-and-synthetic-microbiology/jingyuan
Project title	The sweet tooth of *Bacteroides thetaiotaomicron*
Project duration (3-6 months)	6 months
Prerequisites (educational)	B.S. or M.S.

Project proposal: description and expected outcomes of project (500 words max.):

Gut microbiota plays a pivotal role in human health by breaking down non-digestible dietary fibers, providing essential nutrients, and acting as barriers against pathogen colonization. *Bacteroides thetaiotaomicron*, a prominent member of the human gut microbiota, resides in the colon and encodes a large array of polysaccharide utilization loci (PULs) for breaking down dietary polysaccharides and host-derived glycan into fermentable sugars. This primary energy acquisition strategy is essential for supporting the growth of other microbes, modulating the complex structure of gut microbiota, and indirectly boosting the defense against pathogens. A typical PUL in *B. thetaiotaomicron* is a cluster of co-regulated genes encoding a collection of proteins for the extracellular binding, initial breakdown, periplasmic import, and final digestion of specific complex polysaccharides.

A unique two-component system (TCS) is central to controlling this highly coordinated process. It acts as a sensor for polysaccharides and a transcription regulator for the expression of the PUL gene cluster in *Bacteroides.* Divergent from the canonical TCS, which consists of two proteins in charge of signal sensing and transcription regulation separately, the TCS regulating PUL has only one polypeptide chain with both proteins fused together via a highly charged linker, namely a hybrid two-component system (HTCS). HTCS shows relaxed specificity between the cognate protein pair due to the covalent linkage. But how does it work? The transcription factor needs to bind to a specific DNA region to initiate

transcription, while in HTCS, it is linked to the membrane-inserted sensor kinase. Would there be a protease activity that releases the transcription factor upon activation? Or the DNA would be brought into proximity to the membrane to enable HTCS-regulated transcription and translation?

We use a build-to-understand approach to answer these questions. During the six-month fellowship period, the student will reconstruct and follow the activity of a *Bacteroides* HTCS in *E. coli*. The unique sigma factor from Bacteroides will be introduced to *E. coli* to help HTCS expression. Tagging HTCS with mNeonGreen allows further investigations using fluorescence microscopy as well as single-molecule tracking. By the end of the fellowship, we expect to have established a functional recombinant HTCS in *E. coli* and gained insights into the requirements for its proper expression and regulatory function.