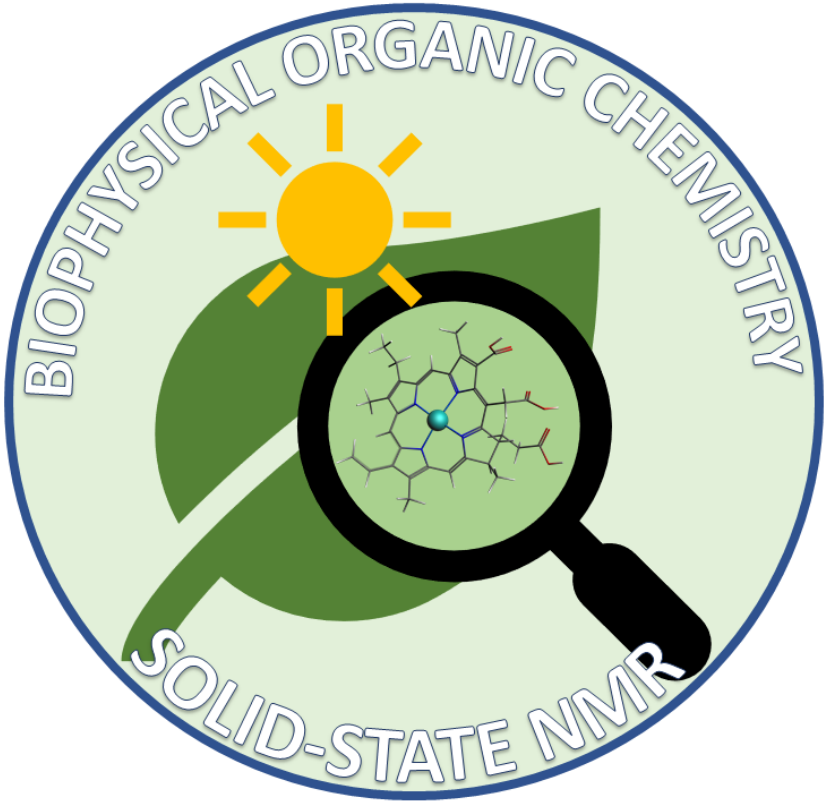
Biophysical Organic Chemistry

Student projects



QM/MM simulations to unravel glycosylation reaction mechanisms

PhD candidate: Bas Kreupeling

Contact: b.m.kreupeling@lic.leidenuniv.nl

Synthetic oligosaccharides are indispensable tools in chemical glycobiology, to unravel and manipulate the role of these important biomolecules in biological processes. However, the synthesis of oligosaccharides is an arduous and labor-intensive process, requiring a significant amount of time-consuming trial-and-error to optimize the reaction used to build the target oligosaccharide: the glycosylation reaction. Several reaction paths can be followed in the chemical union of two carbohydrate building blocks and these pathways determine the overall stereoselectivity of the glycosidic bond forming process.

We will here computationally investigate these pathways and determine what role they play in shaping the overall outcome of the glycosylation reactions at hand. We will make use of state-of-the art computational techniques, mainly DFT-based and hybrid (QM/MM) molecular dynamics simulations to capture the full complexity of the reaction systems, including dynamical and solvent effects explicitly. These simulations will make use of enhanced sampling methods (e.g., metadynamics) to accelerate the crossing of energy barriers.

I am looking forward to working with you!

Conformational ground state structural dynamics Investigated by NMR and sample preparation of the efficient light harvesting antennae chlorosomes

PhD candidate: Lolita D'Souza

Contact: l.a.dsouza@lic.leidenuniv.nl

Chlorosomes are the largest and the most efficient light harvesting antennae found in nature. They are found in Photosynthetic green bacteria. The attractive property of these chlorosomes is that they contain thousands of self-assembled bacteriochlorophyll *c,d,*or *e* as their principal light harvesting pigments. In comparison to other photosynthetic antennae where chlorophylls are tailored for the biological function by a protein environment, chlorosomes do not contain proteins in them which makes them less complicated and perfect system for studying the role of structural dynamics in energy transfer and resolve general principles that can serve in the development of mimics for artificial light harvesting systems.

The project mainly deals with chlorosome sample preparations which includes various steps such as culturing and labelling *C.tepidum* bacteria followed by purification of the labelled cultures which includes steps such as centrifugation, French press, ultracentrifugation, sucrose density gradient, dialysis and concentration steps.

Finally, the obtained chlorosome sample is investigated mainly using NMR. Apart from NMR we also use techniques such as UV-VIS, HPLC and mass spectrometry. We have a fancy growth cabinet for culturing bacteria and many more interesting things for you to discover in the lab.

I am looking forward to work with you!

Biosynthesis of advance biofuel by Engineered Cupriavidus necator

PhD candidate: Chuang Wang

Contact: c.w.chuang.wang@lic.leidenuniv.nl

C. necator H16 is a Gram-negative lithoautotrophic bacterium, being capable of subsisting on H_2 and CO_2 as its sole source of energy and carbon, beside gluconate, fructose and N-acetylglucosamine. Which makes it possible to realize the conversion and utilization of CO_2 resources into production of target chemicals and fuels with *C. necator* as a chassis cell.

Here, we will construct the biosynthesis pathway to produce acrylic acid, 1,3-propandiol, malonic acid, biodegradable polyesters, and other valuable chemicals based 3-hydroxypropionic acid intermidate in *C. necator.* In order to achieve this goal, several methods and tools will be used like patehway design, engineering, and optimization. And what you can learn like Pathway design tools, Pathway construction tools, Pathway optimization tools (gene expression an d Protein activity). If you are interested and want to get into this research, I will appreciate it. Looking forward to your joining.

Cu_xO catalyst combined with $BiVO_4$

PhD candidate: Suzanne Assen

Contact: s.m.e.assen@lic.leidenuniv.nl

Cu_xO is a promising catalyst for water oxidation with a low onset potential (roughly around 1.6V vs RHE), as measured by our Autolab electrochemical work station. We can make the nanoleaf shape of the Cu_xO catalyst ourselves, either using the potentiostat or by immersing copper foil into a very alkaline solution that is almost boiling. This specific shape of the Cu_xO is thought to introduce some chirality into the system giving rise to a nonadiabatic conversion process, making it possible to oxidize water very efficiently.

We would also like to combine the Cu_xO as a cocatalyst to a $BiVO_4$ solar cell (bandgap 2.4 eV) to form a novel photoanode. The combination should work really well, as the relevant energy levels of $BiVO_4$ and Cu_xO are well aligned which should promote charge separation on the interface and overcome the low carrier mobility of $BiVO_4$. With the unique shape of the nanoleaves, we should be able to see a very early water oxidation onset when the sample is illuminated and a similar onset to normal Cu_xO in the dark. This would make it a step closer to a cheap solution to start producing solar fuels.

In this project, you will look for different ways to make Cu_xO nanoleaves and how to combine them with $BiVO_4$ without damaging either of them. When you have found a nice combination, you can characterize it illuminated with potentiostat and with the scanning electron microscope.

I am looking forward to working with you!

Constitution and structure determination of an artificial light-harvesting antenna complex

Phd candidate: Padmaja Kar (p.kar@lic.leidenuniv.nl)

Artificial photosynthesis is aimed at converting solar power into chemical fuel, for sustainable energy production and storage. Photosynthesis requires three fundamental actions performed in order; light harvesting, charge-separation, and redox catalysis. These actions span different timescales and require the integration of varied functional architectures. In this project, we would build a photoexcitable assembly between a chromophore (Zinc protoporphyrin IX(ZnPP)) and a novel peptide. Here we investigate a peptide construct, tCsmA, with functional helical segments of the CsmA, BchlA binding protein of *C. tepidum*. CsmA is an important membrane protein of the chlorosome organelle of *C. tepidum* and forms baseplate with BChlA which efficiently transfers excitonic energy from the chlorosomes to the reaction center, the FMO protein complex at very low light intensities. (Pedersen et al)

tCsmA can be expressed in E.coli through recombinant expression with autoprotease 'EDDIE' fusion tag and also via solid-phase Fmoc-based chemistry. The peptide is amphiphilic with the histidine binding pocket buried in the hydrophobic region of the helix.We use the chemically robust zinc-protoporphyrin IX (ZnPP), as a cofactor, found in red blood cells that is often used in artificial light harvesting studies, to replace BChl a. Upon complexation with the co-factor ZnPP it forms fibrils that are paracrystalline and show excellent charge transfer properties. (Z. Sun thesis 2019)

The student would be involved in 13C and 15N labeled peptide sample preparation, perform binding assays, and fast magic angle spinning NMR experiments at the 750MHz on 13C and 15N labeled and unlabelled samples.Interested, feel free to reach out ^^

Vibronic coupling in Catalyst-Dye complexes for water oxidation

PhD candidate: Titus de Haas

Contact: t.de.haas@lic.leidenuniv.nl

Dye-sensitized photoelectrochemical cells (DS-PECs) for solar fuel production are a promising tool for reducing greenhouse gas emissions. At the heart of the DS-PEC lays the process of photoinduced water splitting. In the last decades, a combination of spectroscopic, electrochemical and theoretical efforts have contributed significantly to the understanding of the proton coupled electron transfer (PCET) steps in both natural and artificial photosynthesis.[1,2] Recently, ab initio molecular dynamics (AIMD) simulations have shown that specific nuclear vibrational modes can affect the PCET reactions in water oxidation.[3,4] It is thus of critical importance to take advantage of the vibrational coupling between reactant and product states in order to design DS-PECs with a high yield solar to fuel conversion.

In this research you as a student will learn to work with quantum chemical simulation methods, such as semi-empirical tight binding approaches and density functional theory. Using ab-initio molecular dynamics simulations, the student will investigate vibronic coherences in systems that are relevant for DS-PECS.

If this sounds interesting to you, please don't hesitate to contact me. We are also open to your input and encourage creative new ideas!

References

[1] Pannwitz, A.; Wenger, O. S. *Dalton Trans*. **2019**, *48* (18), 5861–5868.
[2] Warburton, R. E.; Soudackov, A. V.; Hammes-Schiffer, S. *Chem. Rev*. **2022**, 52.
[3] Goings, J. J.; Hammes-Schiffer, S. *ACS Central Science*. **2020**, *6* (9), 1594–1601.
[4] Shao, Y.; Groot, H. J. M. D.; Buda, F. *ChemSusChem*. **2020**, *13*, 1–9

Biosensor design with Evolutionary Molecular Dynamics

PhD candidate: Art Hoti

Contact: a.hoti@lic.leidenuniv.nl

Single walled carbon nanotubes (SWCNTs) are biosensor scaffolds which possess optimal optoelectronic properties for use in medical imaging. In this project you will employ our evolutionary molecular dynamics platform (Evo-MD) to develop biosensing peptides that can functionalize SWCNTs for the highly specific recognition of neurotransmitter molecules. From a fundamental perspective, you will address whether ligand recognition in intrinsically disordered proteins must rely on classical enzyme-like binding modes or whether such a recognition can be alternatively based on highly transient and dynamic interactions. Developed biosensors will be synthesized and tested by our experimental collaborators (Sebastian Kruss lab – Bochum University).

During the project you will gain extensive experience in both atomistic and coarse-grained molecular dynamics simulations, with direct applications to biosensor design and the modelling of intrinsically disordered proteins. You will also strengthen multiple computational skills including software development in python and high-performance computing.

Please feel free to reach out if this project sounds interesting! I look forward to working with you.