Undegraduate project proposals

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Whether you choose one of the topics, have a project idea of your own, or are simply curious to see how our lab works, you are always welcome here! Reach out to us at Petr.Fatka@vscht.cz to arrange a guided tour of the entire laboratory.

Read more about the laboratory at https://chobotix.cz/.

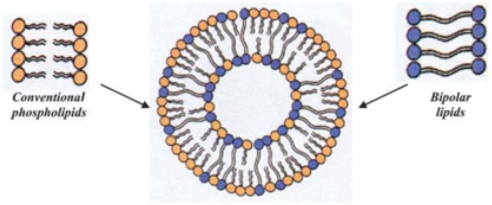
Nanoparticle Production and Drug Delivery Systems

Improving Liposome Stability for Oral Delivery Using GDGT

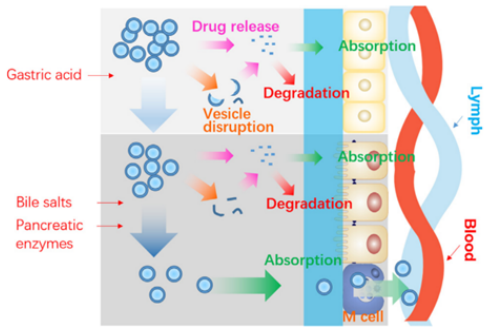
Project Type: Bc, Ing

Project Leader: Ing. Martin Roudný
Contact: Martin.Roudny@vscht.cz

Liposomes are spherical vesicles that mimic natural cell membranes, making them drug carriers. Due to their biocompatibility and ability to encapsulate both hydrophilic and hydrophobic substances, liposomes are promising for pharmaceutical applications. However, effective oral delivery of liposomes faces multiple challenges, especially their instability in the harsh gastrointestinal environment (Fig. (b)). Liposomes are exposed to acids, bile salts, and pancreatic enzymes, which disrupt their lipid bilayers and cause leakage of the encapsulated substance.



(a) Structure of a liposome composed of conventional and bipolar lipids



(b) Schematic presentation of the fate of liposomes following oral administration

He, Haisheng et al. "Adapting liposomes for oral drug delivery. *Acta pharmaceutica Sinica. B* vol. 9,1 (2019): 36-48. doi:10.1016/j.apsb.2018.06.005

This project will investigate the effect of the tetraether lipid Glycerol dialkyl glycerol tetraether (GDGT) on the stability of liposomes. In contrast to conventional phospholipids, GDGT is composed of two polar heads linked by 2 long carbonyl chains (Fig. 2) and is thus a potential ideal candidate for increasing the stability of liposomes in harsh environments. This work will aim to prepare liposomes containing GDGT and compare their properties with liposomes containing other stability enhancing elements (cholesterol, etc.). Subsequently, 5(6)-carboxyfluorescein will be encapsulated in the liposomes, the encapsulated amount will be determined and the leakage of the substance from the liposomes will be investigated.

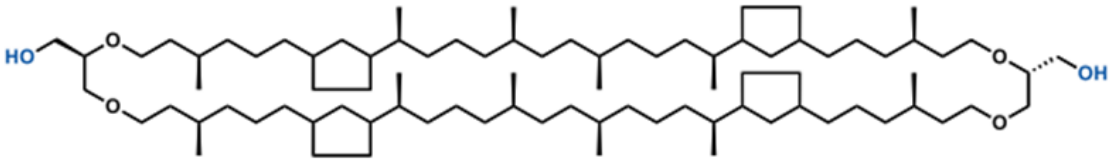


Figure 2: Molecular structure of GDGT

Stabilisation of Active Ingredients in Dosage Forms Using Wet and Dry Granulation

Project Type: Bc, Ing

Project Leader: Ing. Zuzana Hlavačková
Contact: Zuzana.Hlavackova@vscht.cz

This project focuses on developing stable pharmaceutical dosage forms using wet and dry granulation techniques, with the goal of stabilising the active ingredient and preventing impurity formation. The work involves preparing granules of the active ingredient with protective coatings, followed by detailed analysis using methods like Scanning Electron Microscopy (SEM) and X-Ray Powder Diffraction (XRPD). These granules will then be compressed into tablets, which will undergo stress and stability studies to evaluate their performance under various conditions.

The stability and purity of the active ingredient will be assessed using High-Performance Liquid Chromatography (HPLC), which will help to identify any impurities or degradation products formed over time. This project offers students practical experience in pharmaceutical formulation and stability analysis, ideal for those interested in applied pharmaceutical science.

Preparation of Nanocrystalline Formulations of Natural Substances for Food Supplements

Project Type: Bc, Ing

Project Leader: Ing. Stanislav Chvíla
Contact: Stanislav.Chvila@vscht.cz

The market of food supplements is undergoing a massive boom in the recent years, having led to the establishment of numerous companies and introducing dozens and dozens of novel supplements to the market, both natural and artificially synthesized. Many of these substances are already routinely used as dietary supplements and are often ascribed various beneficial effects on human health. Due to the regulatory status of food supplements, however, there is very little oversight as to the actual content and efficacy of these products. This project seeks to utilize nanosizing approaches to several already utilized compounds (e. g. rutin, hesperidin, curcumin) in order to devise an efficacious supplement form that would lead to the increase of their efficacy, keeping the possible commercial use in mind in terms of technology cost and scalability.

Lipids, Drugs, and Photons: Determining Membrane Bilayer Permeability Using Fluorescence Spectroscopy

Project Type: Bc, Ing, Semester project

Project Leader: Bc. Adam Tywoniak, M.Sc.
Contact: Adam.Tywoniak@vscht.cz

In this project, we aim to connect fundamental biophysical science with real-world pharmacology: The objective is to understand the effects of different pharmaceutical molecules on the properties of phospholipid membranes, as knowledge of these effects could explain some drug interactions in patients.

You will prepare liposomes (nanometer-sized bilayer structures composed of polar lipids) loaded with selected pharmaceuticals and measure the rate at which fluorescent dyes can cross such membranes.

What's in there for you: an opportunity to learn the techniques for preparation and characterization of liposomes, together with advanced analytical instrumentation. We can provide a fully equipped nano-engineering lab, and a great deal of supportive mentoring.

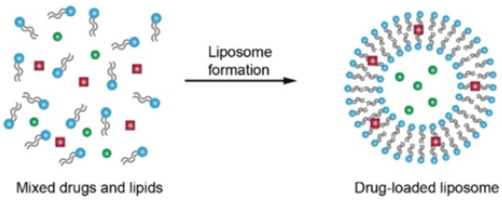
What you should bring: a willingness to learn and to try new techniques hands-on, and an open mind for curious questions and new hypotheses.

In-situ Precipitated Nanocrystals Using the Reverse Phase Evaporation

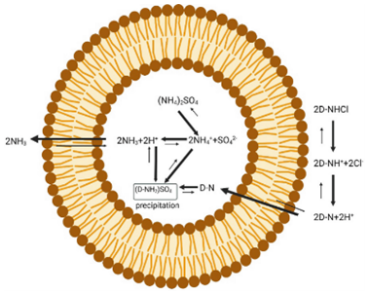
Project Type: Bc, Ing

Project Leader: Ing. Martin Roudný
Contact: Martin.Roudny@vscht.cz

Liposomes are an effective and biocompatible delivery system due to their ability to encapsulate hydrophilic and lipophilic drugs. However, the key limitation in the encapsulation of drugs in liposomes lies primarily in their capacity, which is limited primarily by the thermodynamic solubility of the active ingredient. This problem was overcome with the Doxil formulation by creating a pH gradient between the inner cavity of the liposomes and the outer buffer containing doxorubicin (Figure b). However, such a method of active loading and in-situ precipitation is only possible if the loaded substance has a functional group like an amine or carbonyl group.

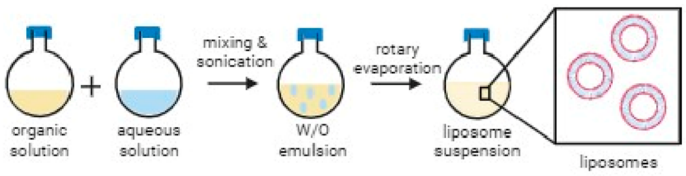


(a) Illustration of passive loading of liposomes



(b) Active loading of doxorubicin into liposomes

This project seeks to develop a general approach to encapsulation and precipitation of APIs for which the pH gradient loading method cannot be used, using the reverse phase evaporation method (REV). The REV method is based on the formation of a w/o emulsion where the organic phase contains dissolved phospholipids and API. By gradual evaporation of the organic phase, liposomes with in-situ precipitated nanocrystals can be formed. The first aim of the work will be to prepare pure liposomes by REV method, which will be characterized by dynamic light scattering and transmission electron microscopy. Subsequently, a suitable substance for in-situ precipitation by REV will be selected and liposomes containing nanocrystals will be prepared. The formed formulation will then be subjected to XRD and dissolution tests.



Liposome preparation via reverse phase evaporation

Downsizing the Production of Pharmaceutical Nanosuspensions and Prediction of Their Colloidal Stability

Project Type: Bc, Ing

Project Leader: Ing. Stanislav Chvíla
Contact: Stanislav.Chvila@vscht.cz

The field of pharmaceutical research has undergone significant progress in recent years. These advances, however, come at the cost of substantial losses due to failed drug products. This often occurs even after candidate drugs prove their efficacy in the initial stages of cell tests with solubilising agents, such as cyclodextrins. It would therefore be beneficial to establish a reliable platform for efficacy tests of novel drugs that utilises a consistent formulation approach across all stages of drug development and clinical trials.

As proof of concept, the Chobotix lab has focused on the production of phospholipid-stabilised drug nanocrystals. These have so far been prepared by wet-stirred milling with zirconium oxide beads at scales of dozens of milligrams per batch. Despite the advances made, the capabilities of small-scale milling are still limited due to loss of drug during milling and relatively long milling times in comparison to commercial apparatuses. This issue becomes even more glaring if there is only a small amount of drug available, which is common during mass synthesis screenings. Therefore, great progress can still be made in terms of improving the milling procedure. The work package can be adapted to a bachelor or to a master thesis. No previous knowledge of lab practices is necessary (while still an advantage). Some manual dexterity will be considered beneficial, as well as knowledge and application of basic principles of physics and chemical engineering.

Interaction of Glucan particles with macrophages

Project Type: Bc, Ing

Project Leader: Ing. Petr Fatka
Contact: Petr.Fatka@vscht.cz

Yeast-derived glucan particles (GPs) are porous polysaccharide shells, which can be used for encapsulation of different kinds of molecules including pharmaceutically relevant ones (known as APIs – active pharmaceutical ingredients). They have also been reported to be phagocyted by macrophages in the intestine. This makes them interesting as a drug delivery system, as the macrophage uptake could help transfer the encapsulated molecules through the intestinal wall and further to the human body. This macrophage uptake is an interesting subject of interest. This study focuses on understanding of this phenomenon and what parameters are affecting it.

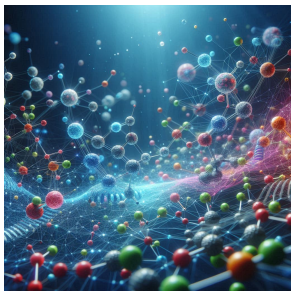
- Study of Glucan particles macrophage uptake its extent kinetics
- Study of effect of surface modifications of GPs on their macrophage uptake
- Investigation of encapsulated APIs effect on the uptake

Computational and AI Techniques in Drug Analysis

Computational Study of Binary Interactions between Common Drugs for Permeation Analysis

Project Type: Bc, Ing

Project Leader: Ing. Terezie Císařová
Contact: Terezie.Cisarova@vscht.cz



The passive permeation of small molecules through cell membranes is not only a crucial biological process but also a primary pathway for delivering active pharmaceutical ingredients (APIs) into living cells. Historically, the permeation rate was determined by the molecular composition of the phospholipid bilayer and the permeant itself. However, recent studies indicate that introducing a second permeant can significantly alter the permeability of the first, suggesting that interactions between drug molecules may have an important role in modulating permeability.
(https://doi.org/10.1021/acs.molpharmaceut.3c00766)

This study will explore these binary interactions using molecular dynamics (MD) simulations, a globally recognised tool in the development of quantitative structure-activity relationship (QSAR) models. In this project, you will gain practical experience with the MD software Gromacs to simulate binary systems of commonly used drugs in aqueous environments. The insights gathered will help deepen our understanding of drug-drug interactions and their implications for permeability in biological systems.

Automation and AI in Drug Delivery: Optimising Self-Emulsifying Systems with Robotics and Neural Networks - 3 projects

Project Type: Bc, Ing

Project Leader: Ing. Martin Krov
Contact: Martin.Krov@vscht.cz

One of the approaches to work around low solubility of active pharmaceutical compounds are self-emulsifying drug delivery systems comprising a lipid carrier and surfactants. Development of such systems is largely empirical, and therefore, automation of the process is currently being explored with a robotic pipetting system. Moreover, AI assistance could be beneficial to reduce the amount of required experimental work.

1. One Bc. or Ing. student project would be focused on developing a neural network aimed at predicting the optimal composition of a self-emulsifying drug delivery system for a given active compound, machine learning on a dataset created by the robotic pipetting system.
2. Another Bc. or Ing. project would be aimed on optimizing the robotic pipetting system, automating the existing screening process further with the use of a robotic arm, and exploring the influence of the active pharmaceutical ingredient on the emulsification properties.
3. A third potential project for a Bc. student would explore the use of particle-stabilized (Pickering) emulsions in pharmaceutical drug development. The main envisioned steps are identification of suitable materials, preparing emulsions, drying the emulsions and assessing their redispersibility, and exploring mass transfer between the encapsulated liquid and the surrounding continuous phase.

Study of Crystallisation in Continuous and Semi-Batch Systems with Non-Ideal Mixing

Project Type: Bc, Ing

Project Leader: Ing. Jan Trnka
Contact: Jan.Trnka@vscht.cz

Crystallisation is the most significant separation and purification process in the production of solid substances, widely used in fields such as pharmaceuticals, food production, and agriculture. In addition to classic crystallisation techniques, such as evaporative and cooling crystallisation, crystals can also be generated by methods that involve mixing fluids of differing compositions. These methods include continuous and semi-batch processes, where supersaturation is induced either by chemical reaction or by altering solubility through the addition of an antisolvent. This project focuses on investigating these specific processes.

The main issue is that the modelling of such systems generally assumes ideal mixing, which can often lead to significant inaccuracies. Literature indicates that, as mixing intensity increases, crystal size may increase, decrease, or reach a maximum or minimum, yet the underlying reasons for these phenomena remain unclear. This project aims to address these gaps. We will work with an existing crystallisation model that accounts for non-ideal mixing. The objective is to conduct experimental parametric studies on various crystalline substances, both inorganic and organic, across different types of crystallisers. Based on these data, we will validate, and if necessary, extend the crystallisation model to explore the interaction between mixing and crystallisation through simulations.

Pharmaceutical Production Methods

Detailed Kinetic Study of Wet Milling of Drug Particles

Project Type: Bc, Ing

Project Leader: Ing. Stanislav Chvíla
Contact: Stanislav.Chvila@vscht.cz

Particle milling and comminution is a useful step in drug production, leading to an increase in dissolution speed of the milled substance. Wet milling allows for pushing the limit of particle size beyond microscale to nanoscale, utilizing the addition of surfactants to prevent their agglomeration. In practice, however, the milling process may be prone to particle aggregation or production of colloidally stable Pickering foams, leading to massive increases in medium viscosity and therefore to reduced efficacy of milling, or halting thereof. The purpose of this project is to identify process parameters which lead to greatest risk of process destabilization and to test for the potential risk in smaller scales of milling. All suspensions will be also described in terms of temporal colloidal and chemical stability and purity.

Permeability Measurement of Pharmaceutically Relevant Substances and Developing Cutting-edge Methodologies for IVIVC - 2 projects

Project Type: Bc, Ing

Project Leader: Ing. David Zůza
Contact: David.Zuza@vscht.cz

This projects aims to advance methodologies for permeability measurement in pharmaceutical applications using an in-house, custom-developed device capable of simultaneous dissolution and permeation assessment. There are two main areas of focus:

1. Engineering and Application Development The first aspect concentrates on engineering the device and exploring its applications, specifically investigating how permeability is influenced by factors such as pH, hydrodynamic conditions, and molecular size. The goal is to gain insight into how these variables affect permeability measurements and improve the reliability of in vitro-in vivo correlation (IVIVC) predictions.
2. Bio-membrane Development and Alternative Permeability Measurement Approaches The second part of the project focuses on bio-membrane innovation, exploring advanced methodologies such as measuring permeability using living cell cultures. This research aims to better replicate biological conditions, improving the relevance and accuracy of permeability measurements in a pharmaceutical context.

Both parts of this project demand interdisciplinary collaboration and innovative, out-of-the-box thinking. The outcome is expected to significantly impact the understanding and prediction of permeability behaviours, contributing to enhanced drug development processes.

Development of a Streamlined, Scalable Approach for Yeast-derived Glucan Particle Production

Project Type: Bc

Project Leader: Gabriela Ruphuy Chan, M.Sc., Ph.D.

Contact: ruphuycg@vscht.cz

Glucan particles (GPs) derived from baker's yeast (*Saccharomyces cerevisiae*) have shown promise as vaccine adjuvants and bioactive carriers for targeted drug delivery. However, the current preparation method is restricted to laboratory-scale production, involving batch processing; a high volume of organic solvents relative to the GPs produced, and limited output. These constraints pose challenges to the industrial scalability of GPs. In this project, we seek to examine the current GP preparation method and develop a more efficient and scalable process that supports continuous production. For that, we aim to develop an innovative process based on centrifugation with filtration technology. We will be testing the new equipment and developing the necessary modifications with the help of 3D printing.

Design and Testing of a Custom Spray Drying Nozzle for In-situ Antisolvent Precipitation (Bc/Mgr)

Project Type: Bc, Ing

Project Leader: Ing. Filip Zavřel
Contact: Filip.Zavrel@vscht.cz

In this project, you would join a team already developing a technology for continuous antisolvent precipitation and spray drying of drug nanoformulations. The aim of the technology is to transfer the standard state-of-the-art batch processes into a more efficient and controllable continuous setting. You will research, build and test a custom spray drying nozzle that would enable the antisolvent precipitation near-immediately before spray drying. This way, the smallest possible nanoparticles could be obtained in a controllable manner, improving the potential of the technology. At your disposal, there would be some know-how, a 3D printing paradise and a lot of encouragement.

Fluid Bed Workup of Pharmaceutical Nanosuspensions for Tailored Release Profiles

Project Type: Bc, Ing

Project Leader: Ing. Stanislav Chvíla
Contact: Stanislav.Chvila@vscht.cz

Fluid bed technology is an expanding and fashionable technology in the pharmaceutical industry. This process involves fluidization of particles which are being sprayed upon at increased temperature, leading to drying of the sprayed solution, and in consequence, agglomeration or coating of the fluidized particles. This technology can be used in conjunction with drug nanosuspensions which combine the benefits of dissolution rate increase due to very small particle size, leading to possible increase in drug dissolution and in vivo absorption. This project will build on previous research experience in the Chobotix laboratory in order to develop clear plans on how to regulate drug dissolution and absorption via adjustment of coating composition, spraying rate, drying rate etc., in order to achieve flexible and adjustable drug absorption profiles.

CHOBOTIX
CHEMICAL ROBOTICS

Vanluchene Lab (Laboratory of Chemical Engineering for Green Chemistry)

My research is focusing on sustainable advancements in fine chemical synthesis by integrating chemical engineering with heterogeneous photocatalysis and photochemistry. We prioritize using earth-abundant, metal-free catalysts, such as graphitic carbon nitride (g-C_3N_4), and visible light as an energy source to drive eco-friendly, cost-effective chemical processes. Due to limited light penetration, this approach cannot be used in traditional batch setups, which is why we are focusing on developing novel photo microreactors.

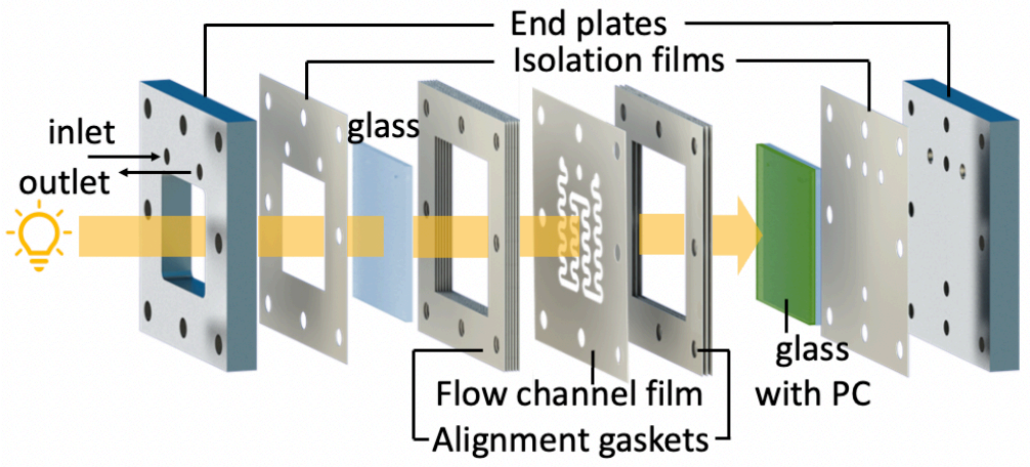
By overcoming challenges like light penetration and solid handling in microflow reactors, we aim to revolutionize the production of active pharmaceutical ingredients and fine chemicals, achieving better sustainability, competitiveness, and reduced foreign dependency in these productions. We focus from synthesis of various graphitic carbon nitrides, development of different microreactors (microfluidic chips, flow cells) to study mass transport phenomena in these type of reactors.

If you have an interest in any of my research topics or would like to learn more about the laboratory, please feel free to contact Ing. Anna Vanluchene, Ph.D. at Anna.Vanluchene@vscht.cz.

Project topics

Singlet Oxygen Oxidations in the Microflow Cell Photocatalysed by g-C_3N_4(Bc./Ing.)

Direct oxygenation of C – H bonds is atom-economical but limited by oxygen's low reactivity under mild conditions. Singlet oxygen, being more reactive, is valuable for pharmaceutical synthesis, yet batch processes suffer from poor irradiation and short singlet oxygen lifespans. Flow reactors address this limitation, and using metal-free g-C_3N_4 photocatalysts adds a sustainable dimension. This project will focus on (i) immobilizing g-C_3N_4 on glass, (ii) constructing a microflow cell, and (iii) evaluating singlet oxygen generation efficiency via anthracene dipropionic acid oxidation, monitored by UV/VIS spectrophotometry.



- Immobilisation of photocatalyst g-C_3N_4 on glass.
- Construction of a microflow cell for enhanced photochemical processes.
- Evaluation of singlet oxygen generation efficiency using UV/VIS.

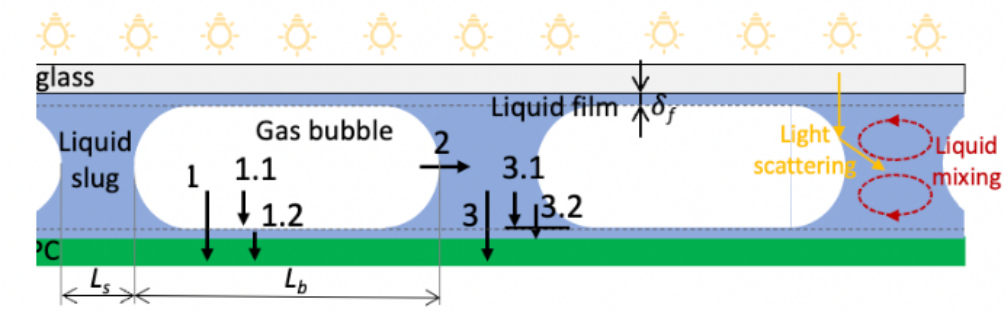
Advancing Photocatalytic Materials: From Doped Carbon Nitride to Plasma-Treated Thin Layers (Bc./Ing.)

Graphitic carbon nitride (g-C_3N_4) is an inexpensive, metal-free photocatalyst with activity in the visible light spectrum. This project aims to synthesize and thoroughly characterize different types of carbon nitride and investigate the effects of doping with nanoparticles, such as Fe_2O_3. The synthesized materials will be fully characterized, and their photocatalytic activity will be tested. Thin layers of the doped carbon nitride will be prepared and evaluated for their photocatalytic performance. Additionally, the impact of plasma treatment on the surface of these thin layers and its influence on photocatalytic efficiency and stability will be explored.

- Synthesis and characterization of various photocatalysts.
- Preparation of thin layers of photocatalyst and evaluation of their photocatalytic activity.
- Exploration of plasma treatment effects on surface properties, photocatalytic efficiency, and stability of thin layers.

Designing Microreactors for Enhanced Photon Utilization in Flow Photocatalysis (Bc./Ing.)

Graphitic carbon nitride (g-C_3N_4) is a visible-light-active, metal-free photocatalyst with strong potential for advancing sustainable green chemistry. However, current reactors often suffer from poor light utilization and limited performance. Transitioning from batch to flow systems in microfluidic chips can improve light utilization and mass transfer, enhancing the efficiency of photochemical processes. This thesis will focus on preparing and immobilizing g-C_3N_4 in microfluidic chips and fabricating these chips using soft lithography in various configurations to optimize mass transfer and photon utilization.



- Immobilisation of photocatalyst g-C_3N_4 in microfluidic chips.
- Fabrication of microfluidic chips using soft lithography as a 4-phase reactor (gas/liquid/solid/photons).
- Optimization of mass transfer and photon utilization in the microfluidic chip.