



# Master Thesis Catalogue 2023

Department of Pharmacy



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## Preface

This thesis catalogue is intended to inspire you and help you complete the thesis that suits you best. In the next pages, you will find a description of each research group, together with examples of project titles and research areas. These descriptions should be viewed as tentative only, as future research results may alter the projects. Therefore, the final projects will be defined in agreement with the students immediately before the projects start.

What might not be written in the catalogue is that in addition to the projects performed in the facilities of the University of Copenhagen, most supervisors offer projects in collaboration with other institutions/industries in Denmark or abroad. Therefore, if you find an interesting project area, feel free ask for options as to where such a project can take place, also if you would like to know of options that are more theoretical e.g. projects that are not directly linked to practical laboratory work.

To make sure you have a positive experience, there might be expectations as to existing knowledge or grades, depending on the project placement, but please remember that grades are not everything, and that a good attitude will get you just as far as good grades.

NOTE: Groups do not all use the same procedure to recruit Master students. Look carefully at the section "Application procedure and dates" at the end of each group's presentation so as not to miss any deadline.

Good advice when contacting your potential thesis supervisor:

1. Study the research conducted in your potential supervisor's lab before you ask for a meeting
2. Don't send out generic emails – tailor your emails for each potential supervisor you contact
3. Tell your potential future supervisor why you find their specific area of research interesting
4. Tell something about yourself in the email – your academic background and your interests
5. Remember to be ready to answer questions about details about your study program, the timing of your thesis work, how many ECTS points, and remember to ask if the supervisor recommends any elective courses

Good luck and we hope to see many of you at the Department of Pharmacy in the near future.

## CNS Drug Delivery and Barrier Modelling

[www.pharmacy.ku.dk/research/cns-drug-delivery-barrier-modelling/](http://www.pharmacy.ku.dk/research/cns-drug-delivery-barrier-modelling/)



We investigate how we can overcome the barrier tissues in the body and deliver drug compounds at the site of action. The major focus is on transport of compounds through the blood- brain barrier.

The practical work includes design of novel peptide drug compounds, physicochemical studies of drug compounds, prodrugs and model drug compounds, ADME studies in cell models and *in vivo* and characterization of relevant membrane transport proteins. Special focus is on peptides. A number of peptide drugs for the treatment of brain diseases are available. However, to reach their target site of action, they must pass the blood-brain barrier (BBB). The capillary endothelium comprises the major physical barrier of the BBB and allows only passive permeation of molecules <400 Da. Brain delivery of the larger biopharmaceuticals, which today includes an increasing number of novel peptide-drug entities, is therefore restricted; both due to their large molecular size and hydrophilic nature. Thus, the development of peptide-drugs for the treatment of brain specific diseases requires a delivery strategy for overcoming the endothelial BBB in order to reach its final target within the brain.

The group consists of one professor, one assistant professor, one research scientist, as well as technicians, PhD-students and Masters students. We work in a cross-disciplinary fashion; have a large international network and an exciting work environment.

### Potential thesis supervisors

<p><b>Mie Kristensen</b> Assistant Professor mie.kristensen@sund.ku.dk <a href="#">Researcher Profile</a></p>	<p><b>Lasse Saaby</b> Research Scientist lasse.saaby@sund.ku.dk <a href="#">Researcher Profile</a></p>
<p><b>Birger Brodin</b> Professor birger.brodin@sund.ku.dk <a href="#">Researcher Profile</a></p>	

**Examples of projects**

<b><i>Cell models for screening of CNS drug compounds</i></b>
Industrial screening of CNS drug compound candidates involve the use of cell culture models. The project concerns characterization of drug transport in cell culture models developed by the group and investigation of their use in predicting blood-brain barrier permeability. The overall aim of the project is to generate predictive tools for CNS drug development.
<b>Supervisors:</b> Lasse Saaby & Birger Brodin. Max no of students: 3
<b><i>Drug delivery across the blood-brain barrier using shuttle peptides</i></b>
The shuttle peptides include cell-penetrating- and tight junction-modulating peptides. Subprojects count i) studies on the mechanism of barrier permeation at the cellular level, ii) effects of applying various labels to the shuttle peptide for detection and visualization purposes, and iii) pharmacokinetic evaluation in rodents including safety assessment.
<b>Supervisors:</b> Mie Kristensen. Max no of students: 2
<b><i>Nose-to-brain as pathway for pharmacological treatment of stroke-triggered brain tissue damage</i></b>
Subprojects count i) setting up and characterization of a state-of-the-art primary nasal epithelial cell culture model, ii) evaluate the potential of shuttle peptides to improve brain drug delivery <i>in vitro</i> and <i>in vivo</i> .
<b>Supervisors:</b> Mie Kristensen. Max no of students: 2

**Application procedure and dates**

If you are interested in writing your thesis with CNS Drug Delivery and Barrier Modelling, please write an email to one of the supervisors with more information about you. There is no deadline.

## Copenhagen Centre for Regulatory Science

[www.cors.ku.dk](http://www.cors.ku.dk)

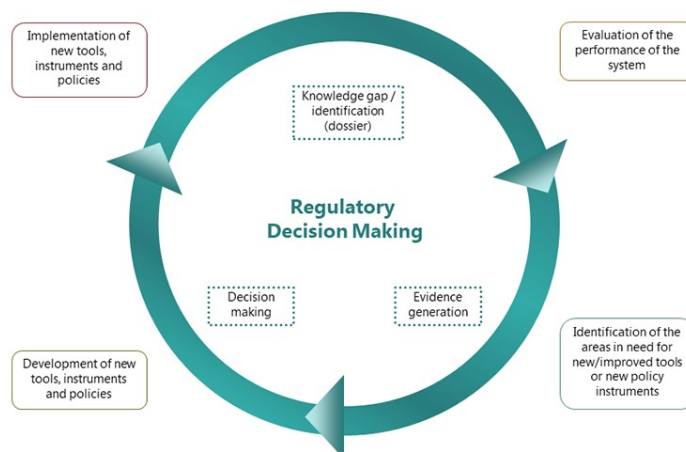


Medicines are important for our society, both to improve public health, but also for economic growth. At the same time, medicines are one of the most regulated products in our society.

Regulation is set in place to protect public health, while still fostering innovation that ensures that Europe continues to benefit from new medicines. However, regulating medicines is an increasingly complex issue. The structures of drug regulation that exist today have evolved over time, in an attempt to respond to an increasingly sophisticated pharmaceutical development, safety crises and needs and demands of the society.

The field of Regulatory Science seeks to study, evaluate and optimize drug regulatory systems in terms of their ability to ensure patient safety, enhance public health and stimulate innovation. This also includes the development of new methods, tools and instruments to assess the safety, effectiveness, quality, public health impact, or performance of medicines, thereby facilitating regulatory decision-making. Through improvement of the drug regulatory system, we aim to contribute to an improvement of the health of the society. Furthermore, we carry out research that produces evidence to be used in drug regulatory decision-making.

### Drug Regulatory Science ecosystem System approach





## Potential thesis supervisor



### Christine E. Hallgreen

Associate professor

cors@sund.ku.dk

[Researcher Profile](#)

Christine Erikstrup Hallgreen is an associate professor at the Copenhagen Centre for Regulatory Science. She has a background in engineering physics, and a PhD from Department of Physics at the Technical University of Denmark. In her professional career, she has been previously employed in the pharmaceutical industry (Novo Nordisk) and academia (Imperial College London). Christine has also conducted research at the National Institute of Health, Maryland, USA. In her research, she utilizes her quantitative and methodological training in the development and evaluation of drug regulatory tools and systems. Her research is motivated by a desire to describe and understand the functioning of the regulatory system and thereby optimize and improve the systems and regulatory tools set in place to promote public health. Her research includes development and evaluation of formal qualitative and quantitative methods to assess benefit-risk of pharmaceutical products, probabilistic methods to assess the effect of uncertainty in outcome data, and methods to collect preference values to support benefit-risk decisions.

## Examples of projects

### ***How best to protect public health: a comparative analysis of regulatory safety warnings on medicines in Australia, Canada the European Union and the United States.***



Medicines have important health benefits but can also lead to harm. When new safety concerns arise, national regulatory agencies issue warnings to health professionals and the public. These warnings differ between countries, but no research has compared the effectiveness of different approaches. This study compares safety advisories on medicines in Australia, Canada, the United States, and the European Union in order to identify how to best protect public health. Within the project several working groups will focus on different aspects: discordances in safety communication, regulatory policy analysis, qualitative analyses on HCP and patient perspectives, media analyses and pharmacoepidemiology to estimate health effects.

### ***Factors ensuring effective Direct to Healthcare Professional Communication of Risk Minimization***



Every day general practitioners receive all kinds of new information about new medicines and new research. But what do they need in their everyday practice in front of their patients? How can we secure that they receive vital information about newly discovered medicine risk? Normally physicians and HCPs receive this kind of information in a letter. But that mode of communication is not very beneficial to physicians nor patients. For those reasons this project sets out to understand how general practitioners prefer receiving this information and what is important for them to know about medicine. With this knowledge future communications may better support the decisions they make when prescribing medicine.

***The Impact of Paediatric Regulations on Drug Development in a Trans-Atlantic Perspective***

The objective of this project is to provide insights into the effectiveness of the EU and US paediatric regulations to promote access to medicines for children as well identifying potential barriers of the paediatric regulations to innovative drug development in general. Ultimately, these analyses should serve to provide recommendations for improvements to the global regulatory frameworks for paediatric medicines development with a focus on the US and the EU.

You can find examples of previous Master thesis projects at CORS on our website: [www.cors.ku.dk/education/](http://www.cors.ku.dk/education/)

**Application procedure and dates**

If you are interested in writing your thesis with CORS, please write an email [christine.hallgreen@sund.ku.dk](mailto:christine.hallgreen@sund.ku.dk) with a short motivation (250 words) describing why you are interested in Regulatory Science (deadline December 3, 2021).



## Drug Delivery and Biophysics of Biopharmaceuticals





<https://pharmacy.ku.dk/research/drug-delivery-biophysics-biopharmaceuticals/>



Our research focus is the design and development of optimal drug formulations with a focus on biopharmaceuticals, specifically peptides and proteins, used for e.g. metabolic diseases or infections. Our research spans from advanced physicochemical analysis of stability/aggregation of biomolecules, and biomembrane interactions via design of advanced drug delivery systems, to assessment of the efficacy in cell culture models and animals. We aim to gain detailed, fundamental, and mechanistic understanding of the challenges associated with these molecules when administered via injectable and non-injectable routes.

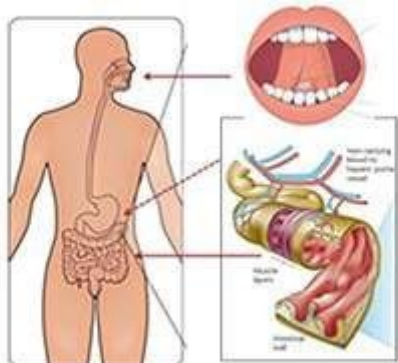
Please note, that the below described projects serves as examples. We are always open for suggestions and discussions to design a project based on your scientific interest.

### Potential thesis supervisors

	<p><b>Hanne Mørck Nielsen</b> Professor hanne.morck@sund.ku.dk <a href="#">Researcher profile</a> <b>Research focus:</b> Drug delivery of peptides and proteins (biopharmaceuticals) and antimicrobial drugs. Oral peptide delivery, drug delivery systems, nanogels, cell-penetrating peptides, biomembrane interactions, mucus, cell uptake and cell transport</p>		<p><b>Stine Harloff-Helleberg</b> Assistant Professor stine.harloff@sund.ku.dk <a href="#">Researcher profile</a> <b>Research focus:</b> oral drug delivery of biopharmaceuticals; intestinal mucosal barrier, interfacial science; biophysical characterization of barrier interactions; <i>in vitro</i> and <i>in vivo</i> models to further explore the barrier interactions.</p>
	<p><b>Marco van de Weert</b> Associate Professor marco.vandeweert@sund.ku.dk <a href="#">Researcher profile</a> <b>Research focus:</b> Peptide and protein formulation; biosimilars; analytical chemistry; fluorescence spectroscopy; peptide and protein aggregation.</p>		<p><b>Vito Foderà</b> Associate Professor vito.fodera@sund.ku.dk <a href="#">Researcher profile</a> <b>Research focus:</b> Protein science; neurodegenerative diseases; nanomaterials for drug delivery; X-ray and neutron science, microscopy and optical and IR spectroscopy; modelling of biological processes. If you want to look at my research focus, please visit: <a href="http://www.vitofodera.com/">www.vitofodera.com/</a></p>

## Examples of projects

### Novel dosage forms with permeation enhancers for oral delivery of peptides and proteins



Oral delivery of biopharmaceuticals is considered the Holy Grail of drug delivery. We will investigate new approaches to enhance uptake of biopharmaceuticals across oral mucosa by co-formulating the drug with permeation enhancers in novel solid dosage forms (e.g. micro-tablets, micro-containers, adhesive electrospun nanofiber patches, or expandable films). We will develop, characterize, and investigate *in vitro*, *ex vivo* and potentially *in vivo* how these increase oral peptide delivery.

**Supervisors:** Hanne Mørck Nielsen, PhD student Freja Fredholt, post doc, Jukka Rantanen; Stine Harloff-Helleberg and/or Mai Bay Stie. Collaboration with industrial partners possible.

### Overcoming biobarrier challenges in drug delivery by functional excipients in nanosystems



When studying drug delivery across epithelial barriers, e.g. the oromucosal or intestinal barrier, one of the key properties is the tightness of the epithelium due to the presence of epithelial cells as well as the tight junctions between the cells. This epithelial integrity is crucial for the normal function of the tissue, and tailored drug delivery systems are needed to enhance drug delivery.

In this project, we investigate the mechanisms of how tailored formulation can lead to improved drug delivery. Specific junction-modulating compounds or other permeation enhancers like cell-penetrating peptides will be formulated together with therapeutic peptides or proteins in nanoparticulate delivery system such as nanogels or polyelectrolyte complexes and thoroughly characterized. The drug delivery systems will be evaluated biophysically to understand the intermolecular interactions and biobarrier dynamics *in vitro* in cell

culture models.

**Supervisors:** Hanne Mørck Nielsen and PhD student Patrick Frøslev

### Hybrid drug delivery systems based on lipids and peptide self-assembled nanoparticles

Drug delivery systems based on well-characterized nanoparticles can be used to deliver various therapeutic compounds. In this project you will prepare and characterize nanoparticles and investigate their behavior *in vitro* using advanced characterization methods. Based on your interest, the project can be focused on the more fundamental biophysical characterization, on the production methods, or the interaction of these systems with cells and mucus, as well as their performance in terms of release and antibiotic activity.

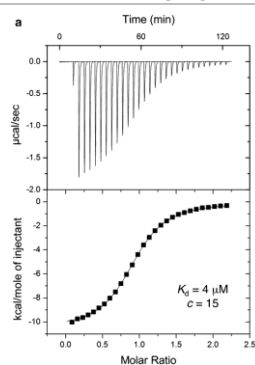
**Supervisors:** Hanne Mørck Nielsen and PhD student Yuan Yuan or PhD student Zheng Huang

### Coats for efficient drug delivery into the skin

Applying conventional dosage forms, such as creams and ointments for cutaneous therapies requires physical contact that may disrupt the sensitive skin and cause discomfort for the patients. The proposal aims to design and investigate the potential of a new topical formulation for easy application onto dry, cracked, compromised skin that occurs in many inflammatory skin diseases including atopic dermatitis.

**Supervisors:** Hanne Mørck Nielsen and PhD student

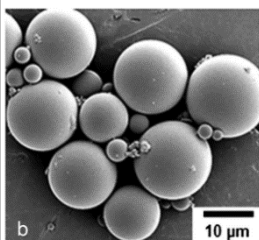
### **Characterizing ligand binding to proteins**



The pharmacological effect of drugs usually depends on their binding to a target protein and to plasma proteins. Protein binding can also be used to stabilize therapeutic proteins. It is therefore important to characterize this so-called ligand binding to proteins using a set of analytical methods. To do this characterization properly can be a challenge, however. In this project you will use several advanced analytical methods to characterize binding of model ligands to model proteins, and test different published approaches to analyze the data. You will thereby get a solid understanding of the advantages and limitations of various methods and learn how to critically assess the literature on this topic.

**Supervisors:** Marco van de Weert

### **Turning proteins into glass**



Proteins are often much more stable in dried formulations, but then need to be rehydrated to allow injection. However, by producing these dry proteins as glassy microbeads, these formulations can be suspended in an oily phase and directly injected without the need for rehydration. This would simplify the administration of unstable proteins considerably. In this project you will prepare and characterize these protein-containing glassy microbeads in terms of size, protein structure, and suspendability in oily phases, using both advanced protein characterization methods and rheology.

**Supervisors:** Marco van de Weert

### **Physical instability of peptides/proteins**

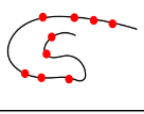
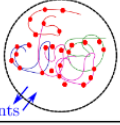
Therapeutic peptides offer many advantages, but their instability is often a major formulation challenge. Many peptides tend to aggregate into long fibrillar structures. Preventing this fibrillation is a major challenge. Within this area you can go into some fundamental aspects of peptide (or protein) fibrillation, and study how the fibrillation process is changed by using heavy water (D<sub>2</sub>O).


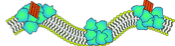
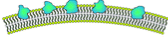
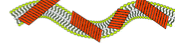
A second, more practically oriented project is to study the impact of various excipients on the instability of some model compounds. This project may be performed at, or in collaboration with, a local company.

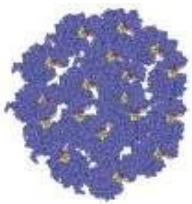
In both projects you will use a panel of advanced analytical techniques to study the aggregation process.


**Supervisors:** Marco van de Weert + Vito Foderà or company supervisor


### **Liquid-liquid phase separation in amyloid systems**


<p><b>Liquid dilute phase</b></p>  <p>● interaction region</p>	<p><b>Liquid dense phase</b></p> <p>Δ protein concentration Δ interaction strength Δ crowders</p> <p>↔ Exchange of components</p>  <p>○ Protein dense-phase</p>	<p><b>Aggregate phase</b></p> <p>Irreversible aggregation</p> <p>✗ Misfunctioning disease state</p> <p>■ Irreversible protein aggregate</p>	<p>Protein-protein interactions are regulated by the physico chemical properties of the solution. Co-solvents (e.g. alcohols), pH and mechanical stress strongly affect such interactions having as a final result the modification of the stability of a protein solution. This generates phase separation and eventually aggregation. With this project, we want to investigate what is the effect of different parameters on both the kinetics of formation and the structure of supramolecular aggregates. There is the possibility to perform part of the research abroad.</p>
<p><b>Supervisors:</b> Vito Foderà and Marco van de Weert + Postdoc</p>			


<p><b>Amyloidogenic protein interaction with biological interfaces</b></p>		<p>The formation of amyloid fibrils is considered to play a key role in the development of pathologies such as Parkinson's and Alzheimer's diseases. New view supports the concept that the interactions of amyloidogenic proteins with biological interfaces are a key factor in regulating related toxicity mechanisms. Aim of this project is to directly observe the progression of amyloid fibril formation in the presence of interfaces both in synthetic model systems and in living cells. There is the possibility to perform part of the research abroad.</p>
<p><b>Bare GUVs</b> Bending Modulus 27.2 k<sub>B</sub>T</p> 	<p><b>Prefibrillar Species</b> Bending Modulus 11.3 k<sub>B</sub>T</p> 	
<p><b>Partially Unfolded Proteins</b> Bending Modulus 21.5 - 23.6 k<sub>B</sub>T</p> 	<p><b>Amyloid-Like Fibrils</b> Bending Modulus 14.5 k<sub>B</sub>T</p> 	
<p><b>Supervisor:</b> Vito Foderà + Postdoc</p>		

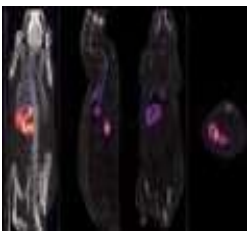
<p><b>Enzyme-like activity of protein amyloid superstructures</b></p>	
	<p>Protein aggregation and fibrillation are associated with numerous neurodegenerative diseases such as Alzheimer's and Parkinson's. In addition to their pathological role, these amyloid materials have also been identified as functional biological materials <i>in vivo</i> and in many technological applications. Therefore, it is crucial to investigate the biological activities of amyloid materials. Aim of the project will be to study the enzyme activity in amyloid superstructures of the model proteins and investigate whether the morphology and conformation affect the antibacterial activity.</p>
<p><b>Supervisors:</b> Marco van de Weert, Hanne Mørck Nielsen &amp; Vito Foderà</p>	

<p><b>Green and sustainable protein materials for drug delivery</b></p>	
	<p>A new frontier in protein self-assembly is represented by the analysis of protein structures in terms of their mechanical/structural properties. This is pivotal for the use of protein aggregates as sustainable materials for drug delivery. Aim of this project is to produce green protein nano- and micro- materials via electrospinning techniques, bulk methods and microfluidic chips and use them for the delivery of active compounds in <i>in vitro</i> and <i>in vivo</i> models.</p>
<p><b>Supervisors:</b> Vito Foderà, Postdoc Mai Bay Stie and PhD student Kleopatra Kalouta</p>	

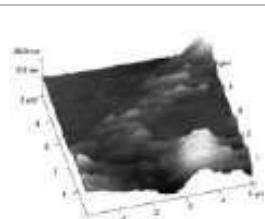
<b>Protein stability in pharmaceutical formulations</b>	
	<p>The presence of protein aggregates in protein drug products is a major concern in pharmaceutical industry. These particles may alter the efficacy of the product. Consequently, it is of great relevance to isolate and characterize each of these types of particles and evaluate their risk profile. Aim of this project is to produce and analyze homogeneous populations of protein aggregates, their features and stability.</p>
<p><b>Supervisor:</b> Vito Foderà and Marco van de Weert+ company supervisor</p>	

<b>Improving biopharmaceutical stability using lipids</b>	
	<p>Formation of aggregates in biopharmaceutical formulation continues to be one of the major quality concerns in biotherapeutics development. The presence of large quantities of aggregates is believed to be one of the causes of unwanted immunogenic responses. Protein particulates can form in a wide range of sizes and shapes. Lipids can generally bind on proteins and peptides, which could lead to improved stability. Aim of this project is to inhibit the protein aggregation in presence of medium-chain fatty acids and lipids.</p>
<p><b>Supervisors:</b> Marco van de Weert &amp; Vito Foderà</p>	

<b>Biophysical characterization of mucosal cross-talk: biopharmaceuticals and their excipients</b>	
	<p>This proposed project aims to uncover the interaction between delivery system encapsulating a biopharmaceutical and mucus at molecular level allowing for novel and innovative biomedical approaches to overcome the challenges of mucosal drug delivery. Relevant techniques would be X-ray scattering, rheology, calorimetry (DSC &amp; ITC), microscopy (CLSM; SEM; PLM) and spectroscopy. Moreover, <i>in vitro</i> models could be included to evaluate the effect of the developed delivery systems on permeability and cell integrity.</p>
<p><b>Supervisor:</b> Stine Harloff-Helleberg Master thesis projects can be carried out both at Department of Pharmacy, in collaboration with researchers at DTU, KU-SCIENCE or internationally.</p>	

<b>Understanding mucosal barrier interactions in vivo</b>	
	<p>Exploring orally administered biopharmaceuticals such as insulin <i>in vivo</i>. Depending on your interest, the project could focus on optimization of delivery system or excipients and the effect hereof on bioavailability, intestinal integrity and mucosal interaction. Please note that this project requires 60 ETCS credits and elective course in Laboratory Animal Science (SVEK17001U).</p>
<p><b>Supervisors:</b> PhD student, Stine Harloff-Helleberg &amp; Hanne Mørck Nielsen</p>	

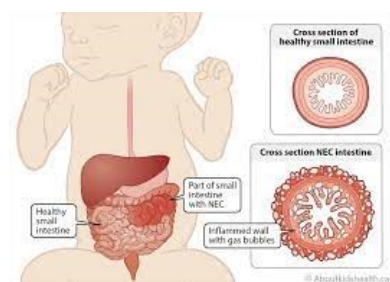
### ***Mucosal interaction studied using in situ ellipsometry and atomic force microscopy***



This project aims to develop a model to explore molecular interaction and surface morphology alterations between excipients (used in drug delivery systems intended for oral administration of biopharmaceuticals) and mucin (the main component of mucus) using *in situ* ellipsometry and atomic force microscopy. Please note that this project requires laboratory work both at Malmö University and University of Copenhagen.

Supervisors: Stine Harloff-Helleberg & Professor Marité Cárdenas (Malmö University)

### ***Understanding the impact of intestinal diseases on barrier properties and drug permeation***



We have shown, that intestinal diseases such as necrotizing enterocolitis (NEC) occurring in pre-term infants significantly affects the barrier properties of the intestinal barrier. In this project, we aim to further explore those findings by linking presence of inflammatory markers and microbiome to drug permeation.

Supervisors: Stine Harloff-Helleberg & Assoc. Prof. Duc Ninh Nguyen (Frb. Campus)

### ***From laboratory to the clinic***



In collaboration with Herlev Sygehusapotek, we are working on projects related to the clinical use of medicines. Aspects such as biophysical compatibility, stability in biologically relevant fluids and other related areas.

Supervisors: Stine Harloff-Helleberg & Herlev Sygehusapotek

### ***Theoretical projects in the field of protein biophysics and protein delivery***



We also offer the possibility to students interested in protein science and protein drug development, but not willing to do experiments in the lab, to perform theoretical thesis in our group. We have a broad range of aspects that would be interesting to focus on, going from an in-depth literature review of emerging topics in the field, to the collection of already published data for further analysis. We can design the project based on the interests of the students.

Supervisors: Vito Foderà, Hanne Mørck Nielsen, Marco van de Weert, Stine Harloff-Helleberg

### ***Projects in industry or at international universities***



The group has many collaborations in industry (e.g. Ferring Pharmaceuticals, Novo Nordisk, Zealand Pharma, Leo Pharma) as well as abroad. Industrial collaborations will deal with peptide and protein stability and/or formulation and delivery, whereas at projects at other universities will depend on their focus of interest. Contact us for more details if interested. Be aware that these projects require an independent attitude and overall good grades

**Supervisors:** Hanne Mørck Nielsen, Vito Foderà, Marco van de Weert

### **Application procedure and dates**

If you are interested in writing your thesis with Drug Delivery and Biophysics of Biopharmaceuticals, please contact us for more details on our projects and possibilities.



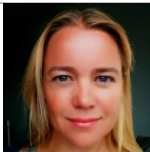
## LEO Foundation Center for Cutaneous Drug Delivery

[www.pharmacy.ku.dk/research/lfccdd/](http://www.pharmacy.ku.dk/research/lfccdd/)



The aim of the center is to contribute to an integrating knowledge on skin as a barrier for drug absorption, and key properties of drugs and excipients for cutaneous drug delivery. Based on a predominantly physicochemical approach, we aim to develop methods for the rational development of novel drug delivery systems for cutaneous and transcutaneous delivery of both small and large molecules, ranging from wounds to intact skin.

### Potential thesis supervisors

 <p><b>Martin Malmsten</b> Professor Martin.malmsten@sund.ku.dk <a href="#">Researcher profile</a></p> <p><b>Research focus:</b> Microgels, nanoparticles for drug delivery, and host defence peptides for combatting infection and inflammation</p>	
 <p><b>Andrea Heinz</b> Associate Professor Andrea.Heinz@sund.ku.dk <a href="#">Researcher profile</a></p> <p><b>Research focus:</b> Drug delivery, electrospinning, wound healing</p>	 <p><b>Mariena van der Plas</b> Associate Professor mariena.van_der_plas@sund.ku.dk <a href="#">Researcher profile</a></p> <p><b>Research focus:</b> Skin and wound infections, inflammation, innate immunity, membrane vesicles, host defence peptides, peptide delivery systems, and peptidomics</p>

### Examples of projects

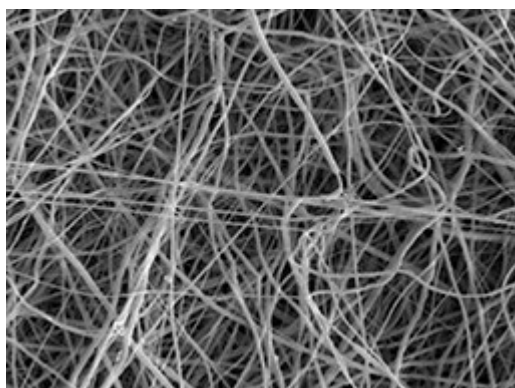
**Oxidative stress on lipid membranes as a new tool for developing new antimicrobial agents**

Inorganic nanoparticles are very attractive as antimicrobial agents ('nanobiotics'), notably due to the increasing resistance development against conventional antibiotics. Apart from scalability and versatility, such materials offer advantages related to responsiveness of antimicrobial and anti-inflammatory effects and the possibility of controlling them by a range of triggering factors. For instance, oxidative stress is known to be behind the antimicrobial activities of TiO<sub>2</sub> nanoparticles when activated by UV light. However, studies on the mechanisms underlying these activities remain scarce. Based on previous work done by our group on the oxidative destabilization of lipid membranes, and using different biophysical and surface-chemical techniques such as fluorescence spectroscopy,

QCM-D, FTIR-ATR, and DLS, the present project will focus on the effects of TiO<sub>2</sub> nanoparticle-induced oxidation of lipid membranes, lipid degradation, and their consequences for membrane structure and stability. Any potential membrane selectivity that could allow more efficient antimicrobial activities along with reduced side effects will be also explored, for instance the combination with cationic peptide coatings. In a wider perspective, this project will contribute to the mechanistic foundation for the use of photocatalytic nanomaterials as triggerable antimicrobial agents.

**Supervisor:** Martin Malmsten

### ***Development of peptide-based electrospun wound dressings***



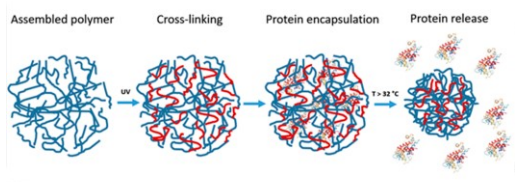
Wound healing is a major burden to healthcare systems worldwide, and there is a clinical need for dressings that can be used to treat partial thickness burn wounds that affect the epidermal and dermal layers of the skin. Requirements for ideal wound dressings include the ability to prevent infection and maintain skin hydration. The wound dressing should further be non-toxic, non-immunogenic and should enhance tissue regeneration. Peptide-based electrospun wound dressings fulfil these criteria.

This project focuses on the development of an electrospinning method to produce peptide-based wound dressings.

The peptide will either be electrospun in a mixture with a polymer or co-axially electrospun (peptide core surrounded by polymer mantle). The electrospun fibers will then be comprehensively characterized by a range of analytical techniques, including scanning electron microscopy, X-ray powder diffraction and differential scanning calorimetry. The release of the peptide from the fibers will also be determined.

**Supervisor:** Andrea Heinz

### ***Development of peptide-based nano- and microgels for the treatment of Ichthyosis vulgaris***



Ichthyosis vulgaris (IV) is a relatively common skin condition that causes dry skin and strongly increases the risk of atopic dermatitis (AD). Individuals with IV have a flaky and dry skin and increased occurrence of hair follicle plugging on the upper arms and shoulders. As the disorder is caused by a loss-of-function mutation in the filaggrin (FLG) gene, replacement of the protein FLG shows great potential for relieving symptoms of IV and significantly improving the quality of life of IV patients.

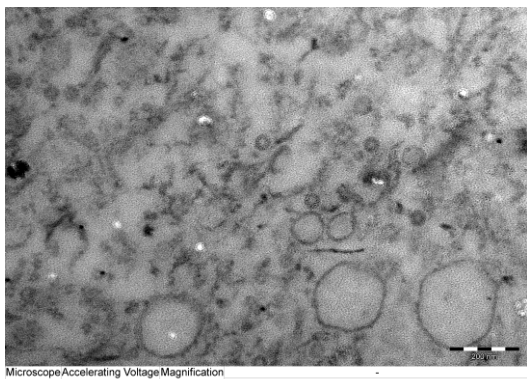
This project will develop nanogel formulations containing FLG peptides for the treatment of IV and AD. The nanogel formulations contain a novel class of polyethylene glycol-based excipients. Systematic investigation of the physicochemical properties of the nanogel formulations with and without peptides will allow optimizing the systems with respect to their (a) physical stability during storage and sterilization, (b) protein release, (c) biocompatibility and (d) pharmaceutical performance with respect to treatment of IV.

**Supervisor:** Andrea Heinz

**2D and 3D skin models for atopic dermatitis**

The goal of this project is to develop skin infection models for studying drug delivery systems in atopic dermatitis. The work will consist of techniques within the fields of immunology and microbiology (including cell and bacterial cultures, analysis of inflammatory markers and signalling pathways, cytotoxicity, and histology), as well as skin penetration studies of various drug delivery systems and penetration enhancers.

**Supervisors:** Mariena van der Plas

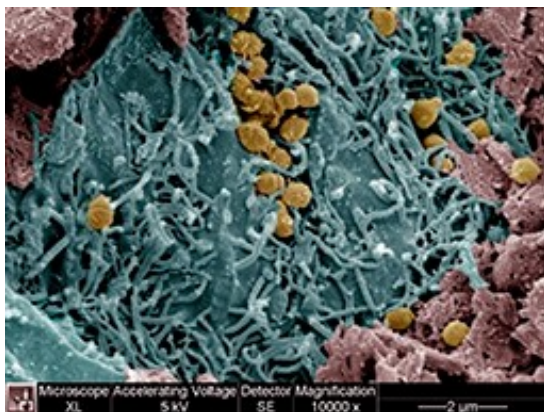
**Membrane vesicles for targeted drug delivery**

Microscope Accelerating Voltage Magnification  
CM 80 kV 92000 x

— 200 nm —

Antibiotic resistance development is one of the biggest challenges of our time. Antimicrobial host defence peptides are promising alternatives to antibiotics, as they kill a broad spectrum of microbes, including multi-resistant strains. As both human and microbial membrane vesicles play essential roles during infection, the purpose of this project is to investigate the potential of membrane vesicles as nanoparticles for targeted delivery of antimicrobial peptides. The work will include techniques within the fields of microbiology, cell biology, molecular biology, physical chemistry and drug formulation and characterization.

**Supervisors:** Mariena van der Plas

**Peptide-based drug delivery systems for atopic dermatitis skin infections**

Microscope Accelerating Voltage Detector Magnification  
XL 5 kV SE 10000 x

— 2 μm —

Atopic dermatitis (AD) is a multifactorial relapsing inflammatory skin disease affecting 1 out of 5 Danish children. As decreased levels of antimicrobial peptides are a popular explanation for the increased susceptibility to infection in these patients, antimicrobial and immunosuppressing peptides have great therapeutic potential in AD.

The goal of this project is the development of potent and safe peptide delivery systems for treatment of AD lesions. The work will comprise optimisation and characterization of delivery systems, *in vitro* antimicrobial assays, biofilm assays and cell assays. Several students can work on this project independently.

**Supervisor:** Mariena van der Plas & Martin Malmsten

**Application procedure and dates**

If you are interested in writing your thesis with the LEO Foundation Center for Cutaneous Drug Delivery, please write an email to one of the supervisors with more information about you. There is no deadline.

## Manufacturing and Materials

[www.pharmacy.ku.dk/research/manufacturing-materials/](http://www.pharmacy.ku.dk/research/manufacturing-materials/)



The Manufacturing and Materials group is focusing on processing and material sciences around solid state and semisolid pharmaceuticals. This international group has over 20 PhD students, postdocs and associate professors. The section is aiming for understanding the chemical and physical properties of the active pharmaceutical ingredients, both small molecules and bio-macromolecules, and excipients in relation to their processing behaviour. Further, the group aims to optimize stability and bioavailability of the final dosage form. The research is focusing on facilitating the future implementation of Quality by Design (QbD) principles for drug development processes, as well as implementation of process analytical technologies (PAT) for industrially relevant applications.

We focus on processing of small-molecule and protein/peptide-based medicinal products. Our goal is to understand the properties of active pharmaceutical ingredients and excipients in relation to their processing behaviour, and further, in relation to the optimal bioavailability of the final dosage form.

### Potential thesis supervisors



**Lene Jørgensen**

Associate Professor

[lene.jorgensen@sund.ku.dk](mailto:lene.jorgensen@sund.ku.dk)

[Researcher Profile](#)

**Research focus:** Protein stability, protein formulation, adsorption to surfaces, manufacturing and processing of protein pharmaceuticals, excipients design and requirements, quality of pharmaceutical products, regulatory aspects of manufacturing pharmaceuticals.



**Natalja Genina**



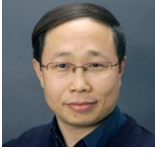

Associate Professor

[natalja.genina@sund.ku.dk](mailto:natalja.genina@sund.ku.dk)

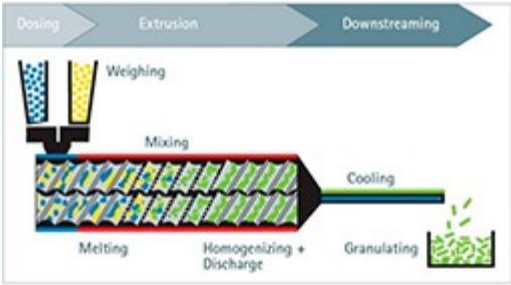
[Researcher Profile](#)

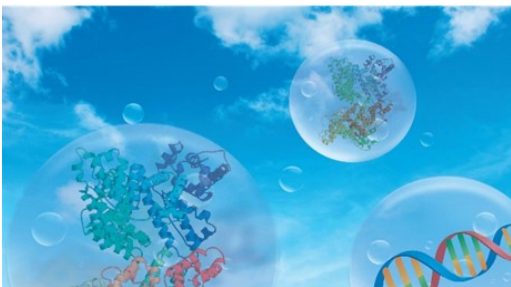
**Research focus:** 2D printing/inkjet printing, 3D printing/additive manufacturing, personalized medicine, physicochemical characterization of innovative product, innovative manufacturing, spectroscopy.



 <p><b>Johan Peter Bøtker</b> Associate Professor johan.botker@sund.ku.dk <a href="#">Researcher Profile</a></p> <p><b>Research focus:</b> Computational simulations, image analysis, manufacturing and processing of pharmaceuticals, solid state characterisation, multivariate data analysis.</p>	 <p><b>Jukka Rantanen</b> Professor jukka.rantanen@sund.ku.dk <a href="#">Researcher Profile</a></p> <p><b>Research focus:</b> Process analytical technologies, pharmaceutical materials science, bulk powder analysis, spectroscopy, computational pharmaceuticals</p>
 <p><b>Mingshi Yang</b> Associate Professor mingshi.yang@sund.ku.dk <a href="#">Researcher Profile</a></p> <p><b>Research focus:</b> Pharmaceutical article engineering, pulmonary drug delivery, and tissue engineering.</p>	 <p><b>Anders Østergaard Madsen</b> Associate Professor a.madsen@sund.ku.dk <a href="#">Researcher Profile</a></p> <p><b>Research focus:</b> Crystallography, pharmaceutical materials science, synchrotron-based techniques, computational pharmaceuticals.</p>

### Examples of projects

<p><b>Hot melt processing of biopharmaceuticals</b></p>	
	<p>In this project, the amorphous environment created by various polymers in a hot melt process will be studied to see whether it is sufficient to prevent the degradation caused by heat, and therefore would enable protein formulations to be produced by hot melt processing. This will be investigated by monitoring structural changes in both the solid and the liquid state. Several process and formulation variables form a good basis for the application of Design of experiments (DoE).</p>
<p><b>Supervisors:</b> Lene Jørgensen and Johan Peter Bøtker</p>	

<p><b>Processing and physical stability of proteins</b></p>	
	<p>Maintaining the physical stability of proteins is crucial in both formulation and manufacturing, since the biological activity may otherwise be reduced. We will expose a protein to various types of stresses, formulation components, processing and use advanced techniques to characterize the changes that we observed. In this project, you will gain knowledge of basic protein formulation, effect from various types processing and excipients and you will get experience with techniques to study protein stability and structure.</p>
<p><b>Supervisor:</b> Lene Jørgensen</p>	



**Master project in industry or abroad**

You could also do your project in the pharmaceutical industry, Medico industry or at a University abroad (e.g. University of Otago, School of Pharmacy, Dunedin, New Zealand). This requires planning, so short notice project are often not possible. You need to plan 6 months-1 year ahead. You will be asked to supply a copy of your grades, as you will need to work independently. The projects topics in industry are typically defined in detail 2-3 months before the actual start of the project.

**Supervisor:** Lene Jørgensen

**Information-rich pharmaceutical products**

Data-enriched edible pharmaceuticals (DEEP) enable encapsulation of both the drug and the sensitive information in a single dosage unit. This can pave the way against counterfeiting of medicine. The goal of the project is to explore the further possibilities of efficient and secure data storage within edible drug-containing dosage unit, and fully characterize the obtained dosage forms by employing the up to date analytical tools and the standard pharmacopeia methods.

**Supervisors:** Natalja Genina and External from the Department of Computer Sciences or PhD student Ilari Ahola.

**Feasibility of printed medicine**

Currently, there is only one commercially available 3D printed medicine, and one is on the way. If the needs of the patients are identified, the situation can be different in the near future with more printed drugs coming to the market to provide more exact pharmaceutical treatment in society. The aim of the project is to explore the patients' attitude towards the idea of getting personalized digital drug product by conducting interviews and showing the possibilities of 3D printing.

**Supervisors:** Natalja Genina and Sofia K. Sporrøng

**Development of personalized medicine by 2D and 3D printing**

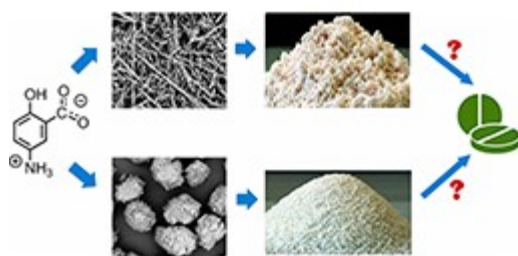
Delivering an accurate dose of active pharmaceutical ingredients (API) and tailoring their release profile are the key factors to produce efficient pharmacotherapy, including the fixed dose combination drug products. With current dosage forms, tunable dosing and tailoring multidrug products' properties are difficult and perilous. The evident flexibility of the printing technology allows commercial on-demand fabrication of individualized dosage forms. The overall goal is to produce novel solid dosage forms with easily adjustable doses and release profiles.

**Supervisors:** Natalja Genina and Johan Bøtker

**Image analysis of pharmaceuticals**

In this project, image analysis of e.g. the tablet coating quality is investigated using MATLAB programming. The project will revolve around creating MATLAB scripts for segmenting objects in images and constructing and operating analytical scripts as well as artificial neural networks for classification purposes. This project will thus focus on optimizing both the process of obtaining the images and the programming needed to analyse the images.

**Supervisor:** Johan Peter Bøtker

**Optimization of bulk properties of pharmaceuticals**

Particle properties determine the successful manufacturing of solid dosage forms. Shape and size distributions are critical parameters affecting flow ability of materials. However, it is a huge scientific challenge to translate these particle characteristics into optimal final formulation. There are several new innovative approaches to investigate powder rheology together with solid form analysis, making a huge impact in commercial scale process and product optimization. This project will investigate powder rheology as a part

of solid dosage form development, as well as implementation of process analytical technologies (PAT) in an industrial setting. The projects topics in industry are typically finalized in detail 2-3 months before the actual start of the project. This project can also be performed as an industrial project at AstraZeneca, LEO Pharma, Lundbeck or Novo Nordisk.

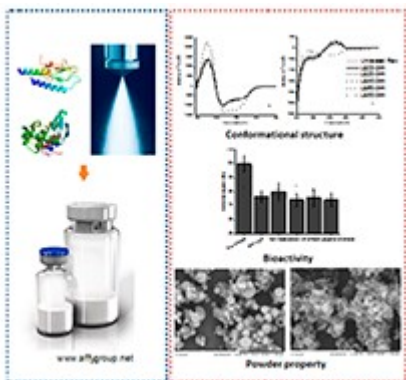
**Internal supervisors:** Jukka Rantanen

**External supervisors:** AstraZeneca, LEO Pharma, Lundbeck or Novo Nordisk

**Pulmonary drug delivery**

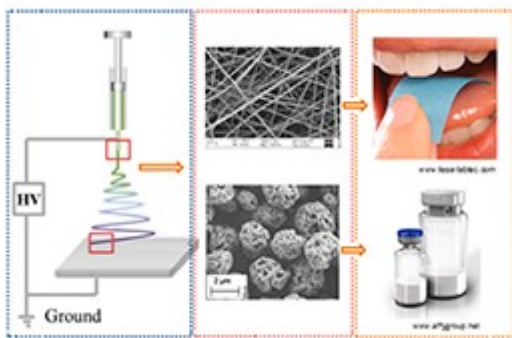
Lung diseases including chronic obstructive pulmonary disease (COPD), respiratory infections and lung cancer are leading cause of death world-wide. Inhaled drugs can directly reach the sites of the diseases, lower side effect, and improve pharmacological effect. The aim of this project is to utilize particle engineering technology to improve the efficacy of inhaled products by improve lung deposition, modulating dissolution rates and absorption of inhaled drugs. This project can be carried out at University of Sydney or Shenyang Pharmaceutical University, China.

**Supervisor:** Mingshi Yang

**Spray-dried protein formulations**

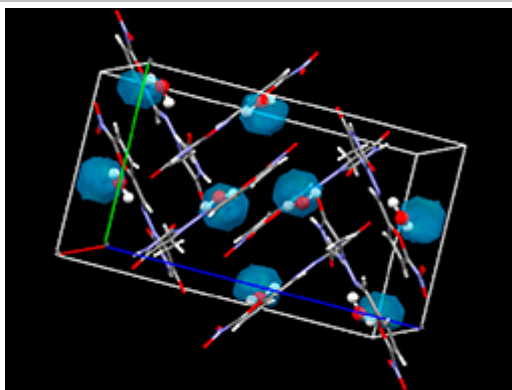
The spray-drying process may be less expensive, but more efficient to process proteins or peptides as compared to other drying techniques. This technique has additional potentials in not only stabilization of the proteins but also engineering the protein formulations into dry particles for various pharmaceutical applications, e.g. inhalable, injectables, and oral administration. This project is intended to investigate the influence of formulation and process variables in the spray-drying process on particle characteristics and physicochemical stability of the protein formulations. This project can be carried out at Novo Nordisk.

**Supervisor:** Mingshi Yang

**Electrospraying/Electrospinning in pharmaceutical application**

Electrospraying/Electrospinning are emerging technologies in the pharmaceutical field to fabricate micro/nano-structured materials for drug delivery and tissue engineering. This project aims to explore the application of this technology and investigate to promote this technology in the pharmaceutical field for producing orodispersible films, wound dressing, and injectable depot microparticles.

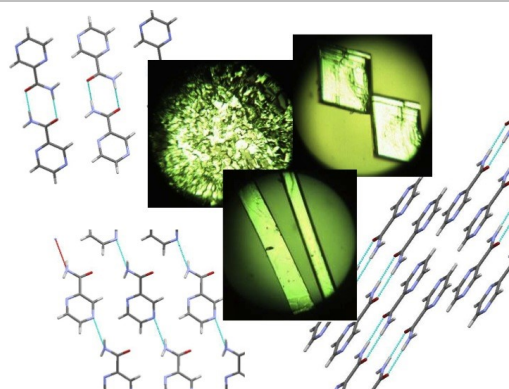
**Supervisor:** Mingshi Yang

**Anhydrate-hydrate systems in pharmaceutical products**

During production and storage of solid state dosage forms the role of hydrate formation cannot be underestimated. The transformation between hydrates and anhydrides occurs as a function of temperature and humidity, and severely affects the properties of the crystals.

The aim of this project is to understand how the water activity level and the temperature can influence the ratio of the anhydrate and hydrate forms of different model compounds, and how the properties of the bulk material changes as a consequence of these transformations.

**Supervisors:** Anders Ø. Madsen, Jukka Rantanen

**Crystal growth and dissolution – simulation, observation and analysis**

Crystalline drugs and excipients are the main components of solid state dosage forms. Their growth and dissolution behaviour are crucial for both tablet production and oral drug delivery. In this project, we observe the growth and dissolution of crystals in different conditions using visual microscopy in combination with X-ray diffraction techniques and correlate these observations with computer simulations. Depending on your skills and interests, the project can be laboratory based or involve Monte Carlo simulations of crystal growth, python programming to develop machine-learning approaches to automate analysis of microscopy images and videos.

**Supervisor:** Anders Ø. Madsen

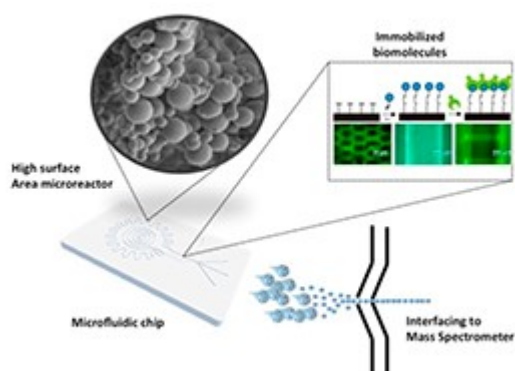
**Application procedure and dates**

If you are interested in writing your thesis with the Manufacturing and Materials group, please write an email to one of the supervisors with more information about you. There is no deadline.

## Microscale Analytical Systems





[www.pharmacy.ku.dk/research/microscale-analytical-systems/](http://www.pharmacy.ku.dk/research/microscale-analytical-systems/)

Our research group develops analytical chemical tools for tackling many challenges in pharmaceutical and medical research, especially in situations where sample size is limited, where the molecules of interest are only present in small concentrations, or where a large number of samples needs to be processed in a short time frame. To enable this cutting-edge analysis we develop and apply technologies such as micro-nano engineering, microfluidics, and polymer science for next generation high-throughput workflows, e.g., in protein characterization, peptide analysis, drug transport studies, and drug delivery.



Main focal areas of the group are modern separation techniques (e.g. LC, CE) coupled to mass spectrometry, advanced sample preparation methods (e.g.,  $\mu$ SPE,  $\mu$ EME), traditional spectroscopic techniques (e.g., NMR, IR, Raman) and a range of microfluidics-driven techniques (e.g., droplets, micro-nano particle fabrication); furthermore, we apply *ex vivo* models and develop microphysiological *in vitro* models (i.e., organ-on-a-chip) that are all intended to understand drug-target interactions, investigate drug metabolism, and getting insight into disease progression and therapeutic efficacies.

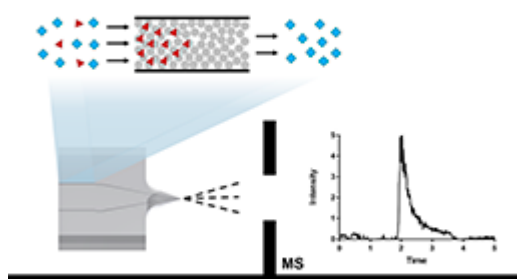
### Potential thesis supervisor

 <p><b>Jörg P. Kutter</b> Professor jorg.kutter@sund.ku.dk <a href="#">Researcher profile</a></p> <p><b>Research focus:</b> Microfluidic devices for bioanalytical challenges in pharmaceutical and related life sciences.</p>	 <p><b>Claus Cornett</b> Associate Professor claus.cornett@sund.ku.dk <a href="#">Researcher profile</a></p> <p><b>Research focus:</b> Quantitative analysis of pharmaceutical compounds from plants; human metabolism and drug validation.</p>
 <p><b>Nickolaj J. Petersen</b> Associate Professor nickolaj.petersen@sund.ku.dk <a href="#">Researcher profile</a></p> <p><b>Research focus:</b> Miniaturized analytical techniques, in particular separation methods coupled to mass spectrometry, for pharmaceutical analysis</p>	 <p><b>Stig Pedersen-Bjergaard</b> Professor stig.pedersen-bjergaard@farmasi.uio.no <a href="#">Researcher profile</a></p>



## Examples of projects

### Lab-on-a-Chip for next-generation sample separation and analysis



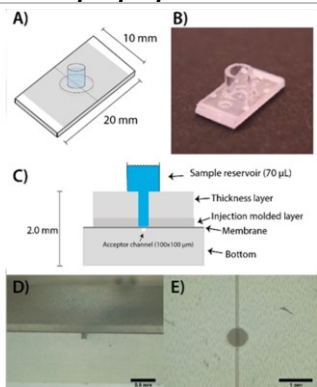
The analysis of complex protein mixtures is of tremendous importance for pharmaceutical drug discovery. To identify potential drug targets, complex mixtures such as blood, cell cytoplasm or secretome have to be screened.

High-throughput screenings involve large numbers of samples and compounds, which are, however, only available in small amounts. Therefore, the sample preparation has to be miniaturized, integrated and automated. Ideal platforms to meet these requirements are microfluidic devices, which allow the precise control of chemical reactions and the integration of other functional elements (so-called

lab-on-a-chip). For instance, microchip liquid chromatography provides high separation efficiency, resolution, and sensitivity. During such a project, a microscale device capable of chromatographic separation will be further developed to enable direct coupling to highly sensitive analytical methods, such as mass spectrometry (MS).

**Supervisors:** Jörg P. Kutter, Nickolaj J. Petersen; No of students: 1-2

### Advanced sample preparation methods on microfluidic chips



Analysis from complicated matrices (i.e., cell cultures) requires advanced sample preparation tools. This is particularly challenging when small sample volumes are involved. Here, we develop techniques such as electro-membrane extraction to, e.g., monitor drug transport through cell-based models of natural barriers (so-called organ-on-a-chip systems).

**Supervisors:** Jörg P. Kutter, Nickolaj J. Petersen, Stig Pedersen-Bjergaard; No of students: 1-2

### Quality assurance and development of Plant medicine



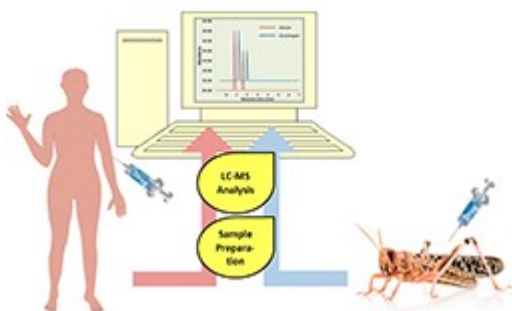
Focus will be on characterizing plant based raw materials. Earlier and ongoing projects have been centered around Cannabis and Quinine, a current project (funded by DANIDA) is studying *Synadenium glaucescens* from Tanzania, and profiling industrial hemp, primarily via terpene profiles.

BYOP (Bring Your Own Plant...), if You have a special interest in a plant medicine, and access to plant material, let's negotiate.

Analytical methods used: HPLC-UV, HPLC-MS, GC-MS and NMR.

**Supervisors:** Nickolaj Petersen and Claus Cornett; No of students: 1-2



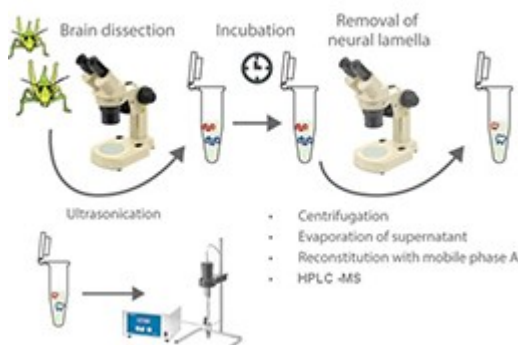
**Streamlining the grasshopper in vitro model**

Finding human drug metabolizing enzymes in other species, such as insects, can reduce the number of animal experiments in pre-clinical trials in drug discovery and development. Within this project, you will work with the grasshopper *Schistocerca gregaria*, to find relevant drug metabolizing enzymes in the grasshopper's "blood" – the hemolymph. You will learn, how to inject drug compounds into the grasshopper and how to collect samples, and how to set up and run enzyme assays, and how to prepare these samples for instrumental analysis with LC-MS or UV detection. Finally, you will be able to evaluate drug metabolism in the grasshopper's hemolymph and

conclude on the relevance of your findings for the grasshopper model in early drug discovery and development.

Analytical methods used: HPLC-UV, HPLC-MS, GC-MS and NMR.

**Supervisors:** Nickolaj Petersen and Claus Cornett; No of students: 1-2

**Grasshopper model for drug permeation and metabolism studies in brain**

Small animal models are a tool in early drug discovery to predict drug uptake and metabolism. Recently, the grasshopper *Schistocerca gregaria* has been introduced as a model to investigate drug uptake and metabolism in the grasshopper brain. In order to optimize throughput we will investigate the feasibility of using frozen grasshopper brains, as the excision of the brains is time consuming, so the possibility of using previously frozen brains would enable well-plate methods or microanalytical methods.

Analytical methods used: HPLC-UV, HPLC-MS

**Supervisors:** Nickolaj Petersen and Claus Cornett; No of students: 1-2

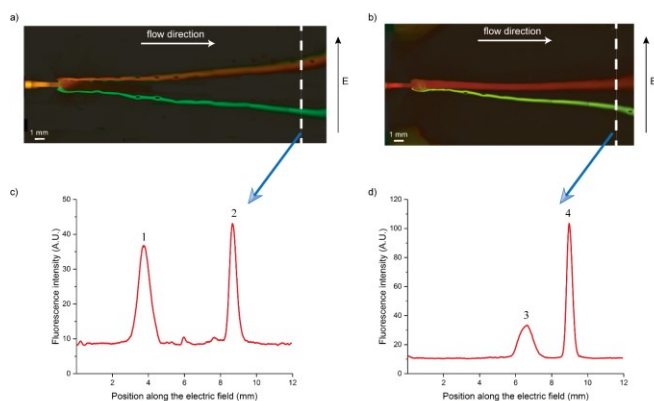
**Capillary electrophoresis coupled to MS**

Capillary electrophoresis (CE) provides great potential for a wide range of molecular formats, from small peptides to proteins, DNA and nucleotides. With CE-MS analysis, information about the degradation pathways, post-translational modifications and process-related impurities could be acquired which would otherwise be difficult to obtain with LC-MS.

Samples from Novo Nordisk that have been stress tested for stability will be investigated to compare advantages and limitations compared to traditional LC-MS.

Analytical methods used: CE-MS, HPLC-MS

**Supervisors:** Nickolaj Petersen; No of students: 1

**Tailor-made projects in collaboration with industrial partners**

Please approach us to inquire about possibilities to define projects together with industrial partners!

This could both be together with researchers from a larger (pharmaceutical or medical) company or with highly engaged scientists from start-up companies.

As the interests and timelines for many companies are very dynamic, a clear project goal will only be defined together with the company when we have identified a suitable student.

Analytical methods used: separations, sample prep, microfluidics, assay development, sensors, ...

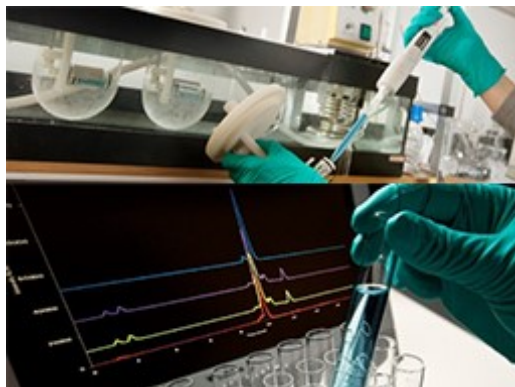
**Supervisors:** Jörg P. Kutter and colleagues; **No of students:** 1-2

**Application procedure and dates**

If you are interested in writing your thesis with Microscale Analytical Systems, please write an email to one of the supervisors with more information about you. There is no deadline.

## Pharmaceutical Physical and Analytical Chemistry

[www.pharmacy.ku.dk/research/pharmaceutical-physical-analytical-chemistry/](http://www.pharmacy.ku.dk/research/pharmaceutical-physical-analytical-chemistry/)



The main purpose of the Pharmaceutical Physical and Analytical Chemistry (PPAC) Group is to develop novel approaches for physical chemical characterization of drugs and delivery systems. The work paves the way for design of effective novel medicines and a better understanding of the fate of drug substances and delivery systems through application of quantitative analytical methods.

The PPAC group applies physical chemical approaches in combination with advanced analytical techniques (ICP-MS, SAXS, UV-Imaging and Taylor dispersion analysis) to advance understanding of fundamental processes in drug design, development and characterization. Common to the activities is a focus on the interplay between basic physical

chemical properties of drug substances and excipients, kinetics and transport processes in relation to both drug delivery and analytical methods.

**Keywords:** analytical chemistry, cubosomes/hexosomes, drug delivery, excipients, injectables, *in vitro* release, LC-ICP-MS, metallo-drugs, nanoparticles, preformulation, SAXS, Taylor dispersion analysis.

### Potential thesis supervisor



**Jesper Østergaard**

Professor

[jesper.ostergaard@sund.ku.dk](mailto:jesper.ostergaard@sund.ku.dk)

[Researcher Profile](#)

**Research focus:** Physical chemical characterization of drug substances and delivery systems.

Development of methods for physical chemical characterization, transport studies, *in vitro* release and dissolution testing (e.g., UV imaging, capillary electrophoresis (CE), Taylor dispersion analysis (TDA)). Molecular interactions. Study of non-covalent interactions of drugs substances and development of affinity methods based on affinity CE and TDA. Development of parenteral depot formulation principles (intra-articular and subcutaneous administration). Kinetics. In relation to drug transport processes as well as chemical kinetics and stability testing. Design of prodrugs.



**Stefan Stürup**

Associate Professor

[stefan.sturup@sund.ku.dk](mailto:stefan.sturup@sund.ku.dk)

[Researcher Profile](#)

**Research focus:** Our general research interest is to develop and apply advanced analytical techniques for exploration of novel drug delivery systems and gain knowledge of the uptake, distribution, and metabolism of inorganic and bioinorganic molecules and drugs in biological systems. To pursue this interest we apply LC-ICPMS, CE, and LCMS.



### Anan Yaghmur

Associate Professor

anan.yaghmur@sund.ku.dk

[Researcher Profile](#)

**Research focus:** 1) Design of soft drug nanocarriers based on cubosomes, hexosomes, and other related nanodispersions. 2) In situ formation of parenteral dosage forms with tunable liquid crystalline nanostructures. 3) Cancer cubosomal and hexosomal nanomedicines. It is also of my interest to design theranostic cubosomal and hexosomal nanomedicines. Development of methods for physical chemical characterization, transport studies, *in vitro* release and dissolution testing (e.g., UV imaging, capillary electrophoresis (CE), Taylor dispersion analysis (TDA)). Molecular interactions. Study of non-covalent interactions of drugs substances and development of affinity methods based on affinity CE and TDA. Development of parenteral depot formulation principles (intra-articular and subcutaneous administration). Kinetics. In relation to drug transport processes as well as chemical kinetics and stability testing. Design of prodrugs.



### Susan Weng Larsen

Associate Professor

susan.larsen@sund.ku.dk

[Researcher Profile](#)

**Research focus:** Investigation and application of physicochemical approaches to improve understanding of processes in drug delivery including parenteral depot design, profiling of drugs and analytical approaches for *in vitro* release testing. Research projects are related to i) development of parenteral sustained release drug delivery systems including in situ suspension-forming injectables, in situ formed liquid crystalline nanostructures and prodrug approaches and ii) development and utility of *in vitro* release methods to predict *in vivo* performance of depot formulations for the subcutaneous and intra-articular route of administration.



### Huiling Mu

Associate Professor

huiling.mu@sund.ku.dk

[Researcher Profile](#)

**Research focus:** Our research aims at exploring the application potentials of functional excipients based on a better understanding of excipient effects on drug release and absorption, as well as interactions between excipients and drug molecules. We use both lipids and polymeric excipients, and are especially interested in lipid excipients due to their versatility and stability, as well as the potential in controlling drug release. The main research activities include designing and characterizing drug carriers such as microparticles, films and foams, optimizing formulations for specific applications, and developing *in vitro* models to evaluate formulations with sustained drug release properties.



### Bente Gammelgaard

Professor

bente.gammelgaard@sund.ku.dk

[Researcher Profile](#)

**Research focus:** Analytical chemistry. Our general research interest is to develop and apply advanced analytical techniques for exploration of novel drug delivery systems and gain knowledge of the uptake, distribution, and metabolism of metal-based drugs, trace elements, peptides and proteins, and nanoparticles in biological systems. Selenium metabolism is a special interest. To pursue this interest we apply LC-ICPMS, CE- ICPMS, and LCMS.

## Examples of projects

### ***Characterization of nanoparticulate drug delivery systems***

This project focuses on the development of new methods to characterize nanoparticulate drug delivery systems, e.g., liposomes, cubosomes, nanocrystals. New methods based on capillary electrophoresis, Taylor dispersion analysis and UV imaging will be developed. It is important that the methods require limited amount of sample as nanoparticulate drug delivery systems are usually only produced in small quantities. The methods will allow us to address critical parameters such as incorporation efficiency, release, non-covalent interactions, aggregation and adsorption.

**Supervisors:** Jesper Østergaard, Henrik Jensen and Bente Gammelgaard

### ***Novel in vitro drug release models for predicting in vivo performance of injectables***

The aim of the project is to develop novel *in vitro* release testing methods suited for predicting the *in vivo* fate of injectables. Such methods are of importance in the development of future drugs for subcutaneous, intramuscular or intra-articular injection. We intend to combine a understanding of the transport processes occurring at the injection site with efficient characterizing techniques for unravelling release mechanisms and predicting the biological fate. The ultimate validation will be establishment of an IVIVC.

**Supervisors:** Jesper Østergaard and Susan Weng Larsen

### ***Compound screening in early drug development using real-time surface dissolution imaging***

Surface dissolution imaging provides new opportunities for visualization and study of drug dissolution mechanisms. The aim of the project is to identify and establish best practices in UV imaging-based dissolution testing. The work will involve development of new methods for selected test compounds.

**Supervisors:** Jesper Østergaard (project may involve an internship at external partner)

### ***Characterization of monoclonal antibodies (mAbs) by Flow Induced Dispersion Analysis***

Characterization of therapeutic mAbs with respect to structure, aggregation and antigen binding using FIDA. Investigation of sensitivity to stress conditions (temperature and chemical denaturation).

**Supervisor:** Jesper Østergaard

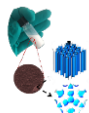
### ***Thesis projects on pharmaceutical analysis with pharma industry or hospital pharmacy***

Characterization of therapeutic mAbs. Raman spectroscopy. Drug stability.

Ask for current possibilities.

**Supervisor:** Jesper Østergaard

### ***Cancer cubosomal and hexosomal nanomedicines***

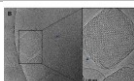


Formation, characterization, and uses of cubosomal and hexosomal nanomedicines for delivery of anticancer drugs.

**Supervisor:** Anan Yaghmur



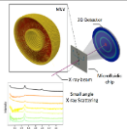
**Multifunctional cubosomal and hexosomal nanomedicines**



Formation, characterization, and uses of cubosomal and hexosomal nanomedicines for multifunctional drug delivery applications.

**Supervisor:** Anan Yaghmur

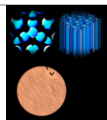
**Continuous production of monodispersed cubosomes & hexosomes**



Combining SAXS to a microfluidic device for the structural characterization of monodispersed drug nanocarriers.

**Supervisors:** Anan Yaghmur (co-supervisor NN)

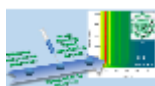
**Cubosomes & hexosomes as versatile nanocarriers for biofilm lung infection treatment**



Development of nanomedicines for treatment of biofilm lung infections. The project involves biophysical characterization studies with relevant biological evaluations.

**Supervisors:** Anan Yaghmur, PhD student H. Jan, and co-supervisor NN

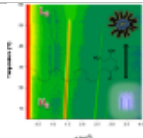
**Design of sustained release injectable liquid crystalline formulations**



In situ formation of liquid crystalline depots with sustained drug release properties. Combination of biophysical investigations with drug release studies.

**Supervisors:** Anan Yaghmur & Susan Weng Larsen

**BRAIN-PENetrating cubosomal and hexosomal NANOCarriers for glioma-targeting delivery**



This project focuses on the formulation of nanocarriers for drug delivery to cancerous brain tumors.

**Supervisor:** Anan Yaghmur

**Local and sustained co-delivery of drugs to improve outcomes following joint replacement**

To improve pain management and prevent infections related to joint replacement surgery, there is a need for efficient drug delivery systems (DDSs) that can maintain and sustain an optimal therapeutic level of multiple drugs at the surgical site. The current project focuses on rational design of parenteral *in situ* forming DDS based on lyotropic non-lamellar liquid crystalline phases for co-delivery of drugs. The drug substances are incorporated in lipids, which self-assemble upon contact with the tissue fluid to form well-ordered inverted type nanostructures (bi-continuous cubic and hexagonal phases). The aims of the project are to i) study incorporation of model drugs with different physicochemical properties in these systems and ii) investigate drug release characteristics from *in situ* formed liquid crystalline phases. Various *in vitro* release methods as well as the presence of biologically relevant fluid will be used to characterize events influencing the sustained release properties.

**Supervisors:** Susan Weng Larsen, Anan Yaghmur and Jesper Østergaard

### A novel prodrug principle to achieve localized and sustained NSAID action after joint injection



Orally administered NSAIDs are intensively used in the treatment of osteoarthritis for pain management and reduction of inflammation. However, oral NSAIDs may evoke severe side effects even after short term use which constitutes impediments to their use. Following direct injection into the injured joint, a high therapeutic NSAID concentration can be accomplished while minimizing systemic adverse effects. As NSAIDs disappear rapidly from the synovial space (half-lives of 0.5-6 h), depot strategies are needed. In the current project, a prodrug-based *in situ* suspension-forming system intended for localized and sustained NSAID action upon intra-

articular injection will be investigated. The project relates to characterization of synthesized NSAID prodrugs and will include: (i) solubility in aqueous buffers and in synovial fluid, (ii) pH dependent stability, (iii) sensitivity to enzymatic cleavage (plasma and synovial fluid), (iv) affinity to proteins and (v) rate of NSAID release from prodrugs using an *in vitro* release model simulating the joint environment.

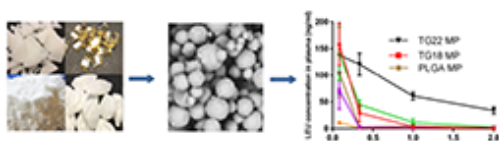
**Supervisors:** Susan Weng Larsen and Jesper Østergaard

### Design of *in vitro* drug release models for predicting *in vivo* performance of depot injectables

Development of *in vitro* release models for quality control as well as formulation design purposes is a critical activity in the characterization of parenteral depot formulations. Ideally, an *in vitro-in vivo* correlation should be established, however, it requires that the drug release mechanism is the same *in vitro* and *in vivo*. The project focuses on characterizing drug release from sustained release formulations for subcutaneous and/or intra-articular administration. The aim of the project is to develop *in vitro* release models to achieve in depth understanding of how formulation designs as well as physiological parameters influence drug release mechanism and rate and drug transport the blood capillaries.

**Supervisors:** Susan Weng Larsen and Jesper Østergaard

### Functional excipients and drug delivery



Excipients play an essential role in drug delivery. Lipid-based formulations can increase the bioavailability of lipophilic drugs by improving drug dissolution and permeation. Both solid lipid particles and polymeric particles are good carriers for sustained drug delivery, but the mechanism of drug release from those particles are different. Hybrid polymer-lipid particles provide better effect in sustained delivery of drugs due to synergistic effect of polymer and lipids. The project aims at evaluating effect of excipients and particle preparation methods on drug release kinetics in order to design efficient drug carriers for specific applications via different administration route.

**Supervisor:** Huiling Mu

***In vitro models to evaluate formulations for sustained drug delivery***

Understanding the release kinetics of drugs from particles is a fundamental prerequisite for efficient design of drug carriers for drug delivery. However, there is no suitable method available to assess formulations with sustained drug release properties *in vitro*. The project aims at establishing bio-relevant *in vitro* models addressing *in vivo* conditions including pH, temperature, and matrix composition.

**Supervisor:** Huiling Mu

***Bioadhesive formulations for local mucosal drug delivery***

Solid lipid formulations can be used for sustained drug delivery. Incorporation of functional excipients in the formulations may create extra application potentials and be used to improve local therapeutic effect by adhesion to the mucosal surfaces (e.g. mouth, eye). The project aims at investigating the potential of combining bioadhesive excipients in formulations and validating the bioadhesive *in vitro*. Nanoparticles, prepared by hot melting and probe sonication method, will be incorporated into thin films or hydrogels, drug encapsulation efficiency and drug release, as well as bioadhesion properties will be evaluated.

**Supervisor:** Huiling Mu

***Stability of drugs exposed to extreme cold***

The Sirius dog sled patrol carries a range of drugs for dogs and humans on their annual expeditions. These drugs are exposed to temperatures down to  $-40^{\circ}\text{C}$ . The aim of the project is to examine the stability of a selection of these drugs by analytical methods.

**Supervisor:** Bente Gammelgaard and external supervisor

***Projects at Department of Forensic Medicine (External projects) – Two students per project is preferred***

Suggestions for projects – the final project can be discussed based on skills and interest:



- ✓ Application of automated pipetting robots in analysis of biological samples from forensic investigations – e.g. qualitative or quantitative analysis of new psychoactive substances (NPD) or pharmaceuticals
- ✓ Analysis of drugs and drugs of abuse in alternative matrix, such as hair, nails etc.

✓ Use of informatics and statistical methods for optimization and quality control in forensic chemistry

**Supervisor:** Bente Gammelgaard + external supervisor

***Projects at the National Research Center for the of Working Environment (External projects)***

- ✓ Method development of 2D-LC-MS-MS method for metabolites of organophosphate esters in urine
- ✓ Dermal uptake of PCBs using an ex vivo skin model and GC-MS-MS analysis (collaboration w. SDU)
- ✓ Method validation and analysis of pesticides on silicone wristbands from farmers in Uganda using GC-MS-MS

**Supervisor:** Bente Gammelgaard + external supervisor

***Determination of trace element impurities in drug products (External project)***

This project entails development and validation of new ICP-OES based analytical methods to comply with Pharmacopeia requirements for elemental impurities. The project is a collaboration with Lundbeck Pharma A/S.

**Supervisors:** Stefan Stürup

***UHPLC-ESI-MS/MS for quantification of isotope labeled metabolites***

Development and validation of a UHPLC-ESI-MS/MS method for quantifying of isotope labelled glucose metabolites such as citrate, succinate, glutamate and glutamine. The final method will be applied for determination of isotopologues in cell samples.

**Supervisors:** Stefan Stürup, Laura McNair (ILF), Blanca Garcia (ILF)

***Stability assessment of protein based drugs***

In this project, the FIDA methodology is utilized for stability assessment of protein based drugs. While protein based drugs have proven efficient for the treatment of a range of serious diseases, a number of challenges remains in developing and formulating these drug compounds. Notably, they are known to be structurally labile and efficient methods for assessing stability are currently suboptimal. In this project we take advantage of the fact that structural changes can be monitored as size changes, change in optical properties and altered function (binding ability).

**Supervisors:** Jesper Østergaard

**Application procedure and dates**

If you are interested in writing your thesis with Pharmaceutical Physical and Analytical Chemistry, please write an email to one of the supervisors with more information about you. There is no deadline.

## Physiological Pharmaceutics

[www.pharmacy.ku.dk/research/physiological-pharmaceutics/](http://www.pharmacy.ku.dk/research/physiological-pharmaceutics/)



In the Physiological Pharmaceutics group (PhysioPharm) we work with oral and mucosal drug delivery. We develop novel drug delivery systems (DDS) to improve drug bioavailability and/or to ensure the maximal therapeutic effect with fewest possible side-effects. We work with both poorly soluble drugs and peptides, and focus on lipid-based DDS and customized release. We develop DDS for special populations (e.g. children; the elderly and patients with hypochloridia or inflammatory bowel disease). We use *in vitro* models of the mouth, eye and the gastro-intestinal (GI) tract that we are continuously improving in order to make them as physiologically relevant, and predictive for bioadhesion, dissolution, release and permeation, as possible. In addition, we also use and develop *in silico* models to further understand the absorption and metabolism of the drug.

**Note 1:** As a general rule, a co-supervisor will be allocated to each master student, often a PhD student from the PhysioPharm Group, or a person from the industry or from other institutions.

**Note 2:** All of us have close contact to the industry and other universities – so come talk with us if you desire a master project in the industry – or abroad.

### Potential thesis supervisors



**Jette Jacobsen**

Associate Professor

[jette.jacobsen@sund.ku.dk](mailto:jette.jacobsen@sund.ku.dk)

[Researcher profile](#)

**Research focus:** Mucosal drug delivery, oromucosal (buccal, sublingual), ocular, bioadhesion, ex vivo permeation, liquid-semi solid- solid formulations, xerostomia.



**Daniel Bar-Shalom**

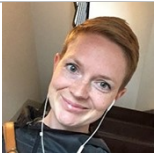

Associate Professor

[daniel.barshalom@sund.ku.dk](mailto:daniel.barshalom@sund.ku.dk)


[Researcher profile](#)

**Research focus:** Pediatric and geriatric formulations. Functional excipients. Implementing learnings from food science and material science into pharmaceutical science.



	<p><b>Ragna Berthelsen</b> Assistant Professor ragna.berthelsen@sund.ku.dk <a href="#">Researcher profile</a></p>		<p><b>Anette Müllertz</b> Professor anette.mullertz@sund.ku.dk <a href="#">Researcher profile</a></p>
<p><b>Research focus:</b> Human gastro-intestinal physiology. Design and development of predictive <i>in vitro</i> models, simulating the gastro-intestinal tract. Use of <i>in vitro</i> models to evaluate oral drug performance, and formulation design, as well as to study and to understand mechanisms of drug solubilization and absorption. Special focus on drug delivery to the pediatric population.</p>		<p><b>Research focus:</b> Development of predictive <i>in vitro</i> models, based on human or rat gastro-intestinal physiology. Lipid-based drug delivery systems. Small-scale methods to evaluate solubility, dissolution and supersaturation propensity of drugs. Application and development of <i>in silico</i> PBPK models to evaluate release effect on pharmacokinetics.</p>	

### Examples of projects

<b><i>In vitro in vivo correlation of oromucosal lubrication and bioadhesiveness</i></b>	
	<p>- of selected polymers with different physico-chemical properties (charge, molecular size, chemical structure, HLB) aiming at a platform for screening of oromucosal bioadhesiveness. Today, human <i>in vivo</i> studies of oromucosal bioadhesion are sparse. Examples of qualitative and quantitative <i>in vitro</i> bioadhesion methods to be validated in this project: Zeta potential, tissue-based tensile strength, rheology, tissue-based retention model, turbidity, contact angle. Initially, an application to authorities for study of human <i>in vivo</i> oromucosal bioadhesiveness must be written.</p>
<p><b>Supervisor:</b> Jette Jacobsen</p>	

<b><i>Safety and enhancement of oromucosal drug permeability</i></b>
<p>These projects aim at evaluating excipients (e.g. absorption enhancers, bioadhesive polymer, co-solvents, buffering pH, surface active preservatives, flavours ect.) to gain a mechanistic knowledge of <i>in vitro</i> mucosal permeability of drugs with different physico-chemical properties by employing physiological relevant transport studies with cell cultures or <i>ex vivo</i> animal mucosa in side-by-side diffusion cells (e.g. sublingual or buccal mucosa). Potential formulations are liquids (e.g. original product and generics), drugs printed on bioadhesive films (for individualized personal medicine) or solids. The projects may be planned in collaboration with pharmaceutical industrial partner and Chr. Janfelt to perform high-resolution MALDI mass spectrometry imaging of drugs and excipients.</p>
<p><b>Supervisors:</b> Jette Jacobsen, Miriam Kolko (ILF), Susan Weng Larsen, Natalja Genina, Christian Janfelt</p>

**Bioadhesive formulations for alleviation of xerostomia**

Xerostomia (dry mouth) can be a very disabling state of health. Xerostomia can be due to e.g. use of medicine or illness (Sjögrens syndrome, radiation therapy in cancer). We hypothesize that each, salivary proteins and lipids, contribute to maintain functions of saliva in bulk and at the mucosal surface. The projects will focus on formulation of a physiological relevant composition for daily care and as a drug delivery system. The work may comprise preparation and characterization of semisolid or liquid bioadhesive formulations with and without drugs, development of *in vitro* cell culture based methods for oromucosal spreadability/wettability (i.e. measurement of single-sided contact angle and surface tension) or friction of formulations, characterization of bioadhesiveness (retention time and force), and mucosal hydration rate. The projects are in collaboration with an external clinical specialist in oromucosal medicine and pathology.

**Supervisors:** Jette Jacobsen, Hailing Mu and Daniel Bar-Shalom

**Development of “instant pudding” vehicles**

There are different scenarios requiring different solutions: (a) Individual, single dose commercial products to be produced by the industry, (b) Vehicles to be added to magisterial compounded products at the hospital or community pharmacy and (c) Vehicles for mass treatment in the developing world where a whole village is treated at once (for example, with anti-parasitic combinations) etc.

The projects are usually carried out in collaboration with interested parties (pharmaceutical and food industry, raw materials suppliers, analytical instrumentation producers and academic partners. Many of those abroad)

**Supervisors:** Daniel Bar-Shalom, Ragna Berthelsen

**Paediatric/Geriatric drug delivery**

Children and the elderly are special population groups from the oral drug delivery perspective. Their swallowing (in)abilities are different from those of the “average population” (those able to swallow tablets and capsules). The elderly and chronically sick children tend to take multiple drugs, thereby complicating the treatment.

Our approach is to individually microencapsulate the drugs to eliminate the (bad) taste problem, to prevent unfortunate interactions between the drugs when in combination and to provide controlled release, if possible. The microencapsulates are mixed with dry, “instant pudding” formulations, and just before administration water is added, resulting in a pleasant, easy to swallow pudding/applesauce mass.

**Supervisor:** Daniel Bar-Shalom, Ragna Berthelsen

**Development of the dispensing systems for Microencapsulate/Pudding products**

It is not sufficient to have the components of the product, a dispensing strategy and device are needed too. Project in this part involve collaboration with design experts.

**Supervisor:** Daniel Bar-Shalom, Ragna Berthelsen

**Development of microencapsulated particles for children and elderly**

Different applications require different solutions. The drugs used at the hospital are a very heterogeneous group, those given in anti-parasitic treatments are notoriously water insoluble, in single doses and long-term stability is expected.

**Supervisor:** Daniel Bar-Shalom

**Oral controlled release of high dose, highly soluble drugs**

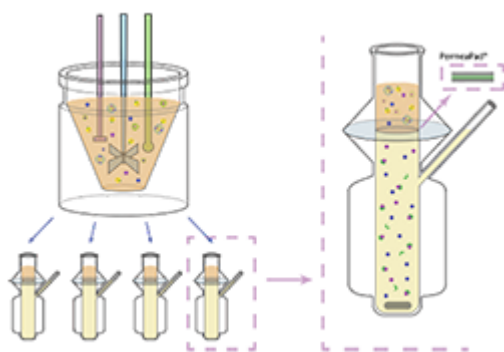
The problem of insoluble drugs is much researched all over the world, including people in our own department. The opposite problem has been largely ignored, but it is there and represents an interesting “niche”.

**Supervisor:** Daniel Bar-Shalom

**Probiotics as therapeutic agents**

Our GastroIntestinal Tract, GIT is the home of a rich population of microorganisms, in fact, there are more microorganisms there than cells in the entire human body. The focus has been on the delivery of selected microorganisms to the lower GIT and on “fecal transplantation” (transferring feces from a healthy patient to another suffering from certain diseases. Getting the bacteria - alive! - to the target is a tricky problem, far from satisfactorily solved. Other areas, nose, mouth (which might or might not be considered a part of the GIT), vagina and skin are other areas where “flora manipulation” is being explored.

**Supervisor:** Daniel Bar-Shalom, Anette Müllertz

**Development a combined gastrointestinal digestion and permeation *in vitro* model.**

In order to achieve a systemic response following oral administration, a given drug needs to dissolve (or be solubilized) in the gastrointestinal (GI) fluids and permeate the intestinal mucosa to reach the systemic circulation. As many poorly water soluble drugs are affected by the co-administration of food, or formulated in a lipid based drug delivery system to ensure GI drug solubilization, the GI digestion processes will affect the drug absorption. Therefore, two key parameters to evaluate in order to predict the *in vivo* performance of orally administered poorly water soluble drugs are the drug solubilization during GI digestion and the permeation across

the intestinal mucosa. As these two processes affect each other, a predictive *in vitro* model needs to mimic both processes simultaneously. The purpose of the present master's thesis project is to develop and evaluate a combined GI digestion and permeation *in vitro* model.

**Supervisors:** Ragna Berthelsen, Mette Klitgaard (phd student) and Anette Müllertz

**Lipid based drug delivery systems for the pediatric population**

As the pediatric population differs from the adult population in many aspects, the design of drug delivery systems (DDS) for the pediatric patient requires careful considerations. In oral administration, the physiological conditions of the gastro-intestinal tract is so complex that the rate and extent of drug absorption are influenced by many factors, especially when the drug solubility is low, it often causes incomplete absorption and low bioavailability, seriously affecting the drugs clinical efficacy and the treatment of the disease.

The project may involve: 1) construction of a pediatric lipid based DDS, and 2) *In vitro* evaluation of the designed DDS, studying drug

solubilization capacity and mechanism, stability and drug release profiles using *in vitro* pediatric digestion model, and 3) studies of the permeation of poorly soluble drugs following administration of the designed DDS.

The study will be conducted in collaboration with hospital-pharmacists from Rigshospitalet.

**Supervisors:** Ragna Berthelsen

**Is intestinal mucus an important factor in solubilization and absorption of poorly soluble drugs?**

Efficient oral therapy is dependent on a good and reproducible drug absorption. However, many active drug candidates suffer from poor water solubility, which makes it difficult to formulate them into delivery systems with high and reproducible bioavailability. One important factor influencing this, is the poor understanding of the actual conditions in the gastrointestinal tract, and the factors that are limiting for the drug absorption. Therefore, the tools that are used in the development process are in many cases not predictive for the *in vivo* situation. One example is the media that are used for predicting the drug dissolution in the intestine, which often underestimates the *in vivo* dissolution. We hypothesize that the intestinal mucus layer has a larger solubilization capacity than the intestinal fluids and is therefore a major player in the absorption mechanism for poorly water soluble drugs. Thus, the mucus layer need to be included in *in vitro* models simulating drug dissolution and absorption.

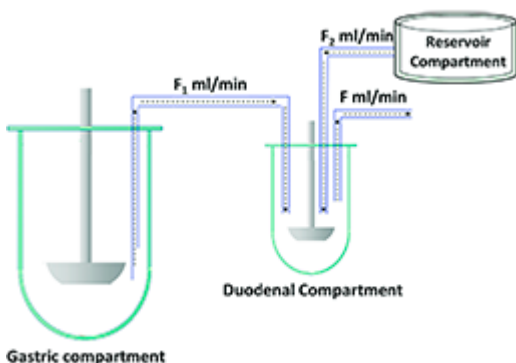
This project aims to elucidate the impact of the intestinal mucus layer in dissolution, solubilization, diffusion and absorption of poorly water soluble drugs. The project will be directly linked with the current PhD project of Mette Klitgaard.

**Supervisors:** Mette Klitgaard (PhD student), Anette Müllertz, Jette Jacobsen, Ragna Berthelsen

**Development of a targeted drug delivery system by use of micro-containers**

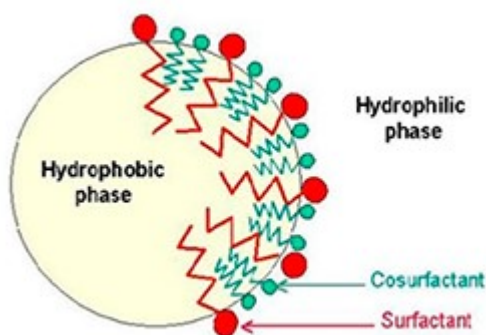
Inflammatory bowel disease (IBD) affects more than 50,000 people in Denmark. Current treatment options are not effective and are often associated with severe side effects due to systemic uptake of the drug. The aim is to develop a DDS that targets only inflamed areas of the gastrointestinal tract in IBD patients. This can be achieved e.g. by functionalizing the surface of the DDS. Newly developed DDS will be tested *in vitro*, and the promising DDS will be investigated *in vivo* in a preclinical IBD rodent model.

**Supervisors:** Anette Müllertz, Thomas Rades & Maja Nørgaard Kristensen (PhD student)

**The effect of gastric transfer rate on supersaturation and precipitation of poorly water soluble weak bases**

A large solubility difference in the low pH stomach and neutral pH small intestine is a challenge for many new drugs. This solubility difference can lead to supersaturation and subsequent precipitation in the small intestine. This can lead to a large variability in pharmacokinetic studies. Supersaturation is an unstable system, where the concentration of a compound exceeds the (thermodynamic) solubility and over time will precipitate. The aim is to establish a novel two-step dissolution model with a gastric and an intestinal compartment to investigate the effect of gastric transfer rate on small intestinal supersaturation and precipitation of formulations of poorly water soluble weak bases.

**Supervisors:** Anette Müllertz & Jakob Plum (Post doc, Leo Pharma)

**Functionalized self-emulsifying DDS (f-SEDDS) for oral delivery of peptides or proteins**

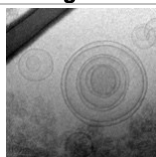
Self-emulsifying drug delivery systems (SEDDS) are solutions of oil, surfactant and co-surfactant spontaneously forming an oil/water emulsion upon mixing with an aqueous medium. SEDDS have shown great potential to improve the bioavailability of peptides by the advantages of mild preparation conditions, protection against enzymatic hydrolysis and build-in permeation enhancement. We will develop functionalized SEDDS (f-SEDDS) with e.g. mucoadhesive properties. F-SEDDS will be characterized by particle size, zeta-potential and *in vitro* digestion. The performance of the developed f-SEDDS will be evaluated by *in vitro* cell culture study and *in vivo* animal models.

**Supervisor:** Anette Müllertz

**Assessing the relation between release profile and pharmacokinetics using PBPK models**

Physiologically based pharmacokinetic (PBPK) modelling is important in the drug development process to understand the relation between drug release, absorption and plasma profile. However, there are still shortcomings in the input (absorption) profiles in the PBPK models, e.g. the entire drug solubility profile in the GI tract is not considered. We want to apply PBPK models to different solubility and dissolution profiles, from selected formulations. We will use the softwares GastroPlus and SimCyp.

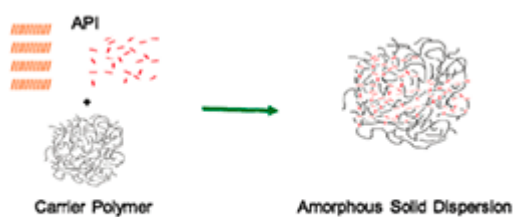
**Supervisors:** Anette Müllertz, Ragna Berthelsen, Jakob Plum (Post doc, Leo Pharma)

**Simulating food effect on poorly soluble drugs**

Many poorly soluble drugs have positive food effect; they have a better bioavailability in the fed state. This is a problem for the reproducibility of the therapeutic effect and it is therefore desired to develop DDS that abolish the food effect. The aim is to develop *in vitro* models, simulating the fed state GI tract, and by use of this to develop formulations without food effect.

**Supervisor:** Anette Müllertz



**Development of a predictive in vitro dissolution-, permeation model for evaluating amorphous solid dispersions**

Many drug molecules suffer from low aqueous solubility, which results in low oral bioavailability. Some of these drug molecules can benefit from the formulation principle of amorphous solid dispersion (ASD), in which the drug is molecularly dispersed in a polymer matrix. Dissolution of ASDs might result in a supersaturated solution of the drug, thereby increasing the absorbable drug amount in the gastrointestinal fluids. The aim of this project is to develop an in vitro model, predicting the in vivo performance of such ASD formulations.

**Supervisors:** Anette Müllertz & Jacob Rune Jørgensen (Postdoc)

**Application procedure and dates**

If you are interested in writing your thesis with Physiological Pharmaceutics, please write an email to one of the supervisors with more information about you. There is no deadline.

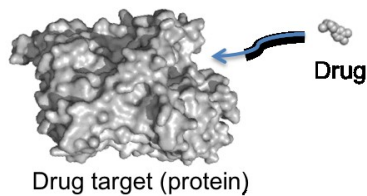
## Protein Analysis Group

[www.pharmacy.ku.dk/research/protein-analysis-group/](http://www.pharmacy.ku.dk/research/protein-analysis-group/)

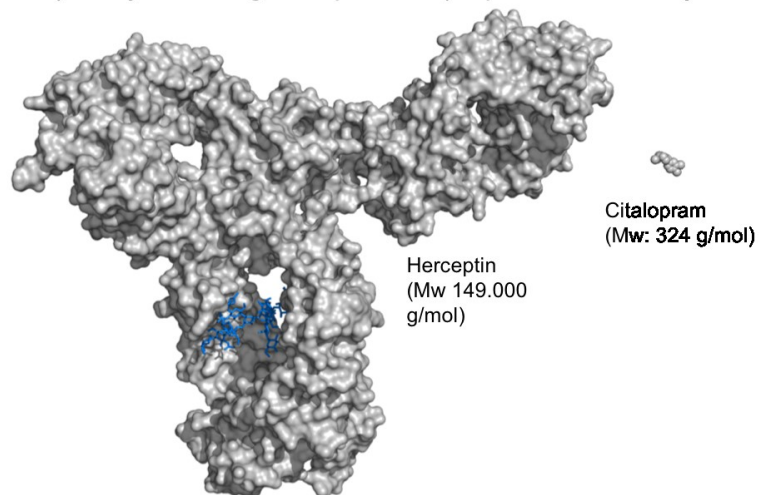


The vast majority of drugs work by binding to and changing the function of proteins in the human body. Furthermore, many new drugs are themselves protein-based (so-called biopharmaceuticals) and these complex drugs account for the most rapidly growing drug in the pharmaceutical industry. Analysis of proteins is therefore at the core of pharmaceutical research.

### 1) Most drugs target proteins!



### 2) Many new drugs are proteins (biopharmaceuticals)!





Through the thesis projects below, you can get hands-on laboratory experience of how to work with proteins and learn state-of-the-art techniques for detailed analysis and characterization of proteins, protein-drug targets and biopharmaceuticals (keywords: protein chemistry, biophysics, liquid chromatography and mass spectrometry).



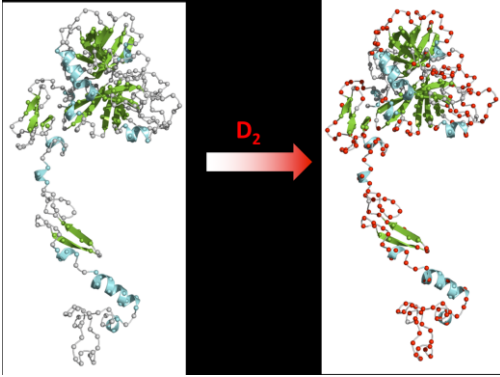
Our research focus on the use of mass spectrometry to provide the critical information concerning quantity, quality, structure and interactions of proteins - which is needed to guide and develop new and improved drugs. In particular, we have world-leading expertise with the HDX-MS technique, an incredibly sensitive method for studying the conformation, dynamics and interactions of proteins. Furthermore, the lab is also equipped with instrumentation to perform cross-linking mass spectrometry (XL-MS) and by this technique we can provide structural constraints which can be used for modelling of proteins and protein complexes.

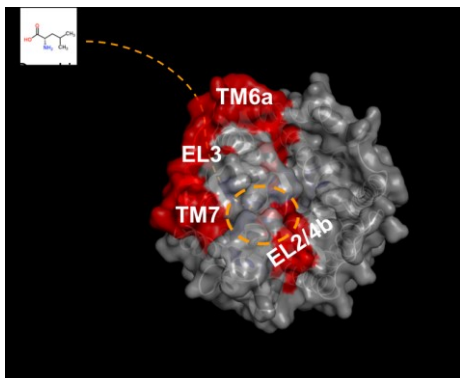
**Examples of publications involving past master thesis projects:** [Møller et al. 2019](#) ; [Svejdal et al. 2019](#) ; [Trabjerg et al. 2017](#) ; [Trabjerg et al. 2015](#) ; [Qiu et al. 2016](#) ; [Jensen et al. 2016](#) ; [Hongjian et al. 2014](#)

### Potential thesis supervisors

	<p><b>Kasper D. Rand</b> Professor kasper.rand@sund.ku.dk <a href="#">Researcher Profile</a></p>		<p><b>Esben Trabjerg</b> Assistant Professor esben.trabjerg@sund.ku.dk <a href="#">Researcher Profile</a></p>
<p><b>Research focus:</b> Protein Analytical Chemistry, HDX-MS (&amp; see above)</p>		<p><b>Research focus:</b> Protein cross-linking mass spectrometry (XL-MS), HDX-MS</p>	

### Examples of projects

<p><b>Analysis of the structure and dynamics of biopharmaceuticals</b></p>	
	<p>Analysis of the primary and higher-order structure of protein-based drugs is critical for both understanding molecular action as well as monitoring and comparing drug product quality. In this suite of projects, you will apply a new powerful analytical technology that uses mass spectrometry to measure the hydrogen/deuterium exchange of proteins in solution (HDX-MS). By HDX-MS, we can obtain detailed information on the structure and dynamics of biopharmaceuticals. You will use this technique to analyze and compare the structural properties of new potential protein drugs in development and thus help to achieve a molecular understanding of their pharmaceutical</p>
<p>properties and function in the human body. Work will be done in close collaboration with researchers at UCPH or industrial collaborators such as Biogen Idec (USA), Roche (Germany) and Novo Nordisk (Denmark), depending on the project. There is typically also the possibility to perform parts of the project at the industrial collaborator.</p>	
<p><b>No. of students: 1-2</b></p>	

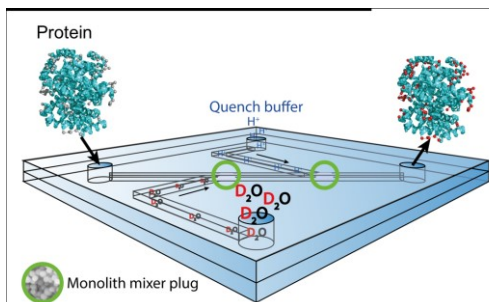
**Understanding the binding of drugs to target proteins of the human body**

HDX-MS is a very sensitive method to study the binding of small molecule ligands or large protein-based drugs to naturally occurring protein receptors in great detail. By performing HDX-MS of the protein receptor in the absence and presence of a single or a panel of potential ligands, we can map the binding site of ligands on the protein receptor and study the structural effects of binding. In this project, you will use HDX-MS to study both the binding of ligands (small molecule or large protein-based) to important new pharmacologically interesting protein receptors. Work will be conducted in collaboration with academic/industry collaborators.

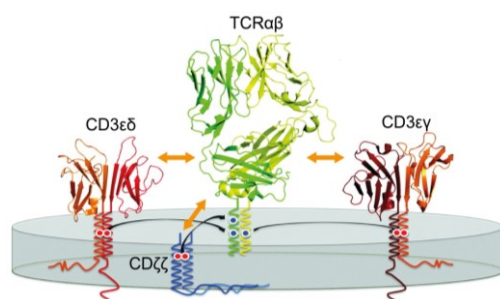
**No. of students: 1-2**

**Coupling microfluidics and mass spectrometry for improved analysis of proteins**

Analysis of protein drugs requires specialized sample treatment and advanced analytical techniques as they are large and complex and often contain modifications (e.g. glycosylations, disulfide bonds). In this suite of projects, we explore the use of microfluidic chips to perform rapid and automated preparation of protein samples (sample concentration, enzymatic reactions, chromatographic separation) for analysis by mass spectrometry. You will learn how to implement protein chemistry and liquid chromatography on a microfluidic device coupled to state-of-the-art protein analysis by mass spectrometry. The project will be done with co-supervision from Jorg Kutter of the Microscale Analytical Systems group and is supported by a large grant to the group from the EU (ERC Consolidator Grant).



**No. of students: 1-2**

**Studying the structure and dynamics of the TCR-CD3 signalling complex**

The T-cell receptor (TCR) signalling complex (TCR-CD3) on the surface of T-cells is essential for the human immune system. The complex allows T-cells to discriminate between healthy and malignant cells via the ability of TCR to bind peptide antigens presented on the surface of target cells by the major histocompatibility complex (MHC). Binding leads to T-cell activation and elimination of the target cell. However, the activation mechanism of the TCR-CD3 complex is not fully understood. In this project you will use HDX-MS and XL-MS to investigate the structure and dynamics of the complex, in a quest to

elucidate the activation mechanism. The project is supported by a grant to the group from the NovoFonden.

**No. of students: 1-2**

**Application procedure and dates**

If you are interested in writing your thesis with the Protein Analysis Group, please write an email to [kasper.rand@sund.ku.dk](mailto:kasper.rand@sund.ku.dk) with more information about you. There is no deadline.

## Social and Clinical Pharmacy Group

[www.pharmacy.ku.dk/research/social-clinical-pharmacy/](http://www.pharmacy.ku.dk/research/social-clinical-pharmacy/)

Social pharmacy seeks to have the broad view of medicines in society and focuses on how medicines are perceived, used, and managed by different stakeholders. Clinical pharmacy seeks to ensure the optimal and rational use of medicines for the benefit of patients and society through collaboration between pharmacists, other health professionals, and the patient. SCP's research ultimately seeks to ensure the benefit of medicines for users, organizations, and society. SCP's research is concerned with the three levels (the user, organization and society) and how they interact to ensure the optimal use of medicines.

### Potential thesis supervisors

<p><b>Anna Birna Almarsdóttir</b> Professor <a href="#">Researcher Profile</a></p>	<p><b>Lourdes Cantarero-Arévalo</b> Associate Professor <a href="#">Researcher Profile</a></p>
<p><b>Lotte Stig Nørgaard</b> Associate Professor <a href="#">Researcher Profile</a></p>	<p><b>Susanne Kaae</b> Professor <a href="#">Researcher Profile</a></p>
<p><b>Charlotte Vermehren</b> Associate Professor <a href="#">Researcher Profile</a></p>	<p><b>Ramune Jacobsen</b> Assistant Professor <a href="#">Researcher Profile</a></p>

In addition to these supervisors, SCP has contact to researchers off campus who are willing and able to supervise, e.g. at hospital pharmacies, Pharmakon, Medicinrådet, regional research centers, etc. Each of these come with ideas that are important to them and can be used as basis for a master project under their supervision, but in close collaboration with the SCP supervisors.

### Project ideas

Master thesis projects may be connected to existing research projects in the SCP Group, but other relevant ideas for master thesis projects within social and clinical pharmacy are also welcome. If you wish to know more about us and what kind of research we do you can have a look at [our website](#) and at our [WHO collaborating center](#). Alternatively, you can use the "[Find a Researcher](#)" option for members of the research group on the website of the University of Copenhagen.

We expect that projects by master students can be within already established areas such as polypharmacy, communication over the counter, medicines use among adolescents, young people and vulnerable population, ethical dilemmas in medicine use among others. We also see new areas emerging that students can work on such as COVID-19 (which ethical and political issues will emerge from the pandemic related to medicines, vaccines and the pharmacists' role).

### The SCP master thesis system

#### The SCP master thesis system

We have a coordinated master thesis student system. We first accept students for the entire group, and we then allocate a supervisor to each student. The contacts regarding master theses are [lou.cantarero@sund.ku.dk](mailto:lou.cantarero@sund.ku.dk) and [anna.birna@sund.ku.dk](mailto:anna.birna@sund.ku.dk). Please do not write to others in the SCP group with questions about thesis projects. The deadline is 15 December, 2021.

On 24 November 2021 at 14:00-16:00, we arrange our own Open House in the SCP group (Building 10, 4.floor). You will be able to discuss with us about possibilities for master theses and our process for selecting students. Note that we do not arrange individual meetings with students. Therefore, if you want to know more, please join us on 24 November 2021. Students selected for master thesis writing in 2023 in our group will be notified in week 51.

#### Sustainable Pharmacy



The 17 United Nations Sustainable Development Goals (SDGs) are a collection of independent but interconnected goals carefully designed to give all of us a better future on our planet. From design, all the way to access and use, pharmaceuticals affect the SDGs directly and indirectly. Sometimes in a positive way (SDG3 'Good health and well-being'), sometimes negatively (environment-related SDGs).

In order to optimize the positive effects and mitigate the negative ones, we need to develop innovative and sustainable ways to develop and deliver pharmaceuticals. Students interested in working on the development of solutions that can contribute to human and planetary sustainability will first identify challenges, and will thereafter receive guidance and support on how to contribute practically to its solutions.

**Supervisor:** Lou Cantarero and Holger Grohganz



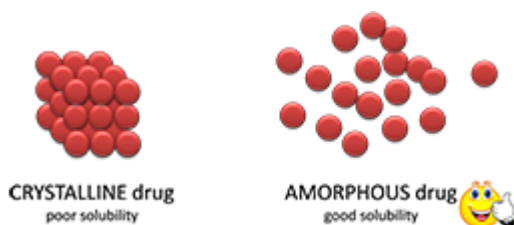
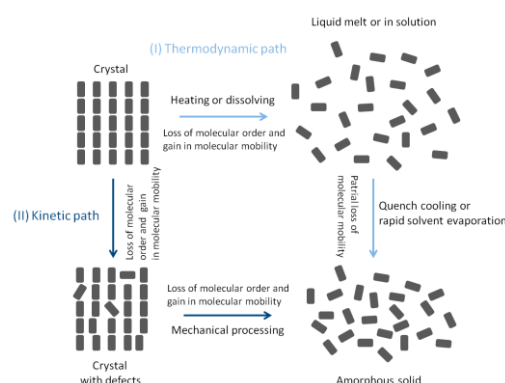
## Solid State Pharmaceutics

[www.pharmacy.ku.dk/research/solid-state-pharmaceutics/](http://www.pharmacy.ku.dk/research/solid-state-pharmaceutics/)

The scientific staff consists currently of the three scientists Korbinian Löbmann, Thomas Rades and Holger Grohganz, and a varying number of PhD students.

We develop drug delivery systems based on high-energy solids. The aims are improved stability of the formulations, and solubility enhancement of poorly water-soluble drugs. We furthermore aim to obtain a deeper understanding of the underlying mechanisms for amorphous stability and have a keen interest in novel formulations approaches and novel excipients. In future, sustainable techniques will play a more important role in pharmaceutical development and it is thus of importance to also focus on this area.

Low solubility is the major challenge for many small-molecule drugs. By stabilizing a poorly water-soluble drug in its amorphous form, its bioavailability can be increased, due to a higher dissolution rate and apparent solubility. Understanding molecular interactions and thereby overcoming the inherent instability of amorphous drugs is one solution to the solubility problem. The amorphous drug can be stabilized with both polymers and small molecules. The amorphous formulation is characterized by a wide range of advanced analytical state-of-the-art methods.



For the production of amorphous formulations of both, small molecules and biomacromolecules, various production techniques, such as ball milling, spray-drying, freeze-drying, microwaves and hot melt processing are applied. Understanding the influence of process and formulation parameters on the solid state of both excipient and drug enables a rational choice of formulation.

### Potential thesis supervisors



#### Holger Grohganz

Associate professor

[holger.grohganz@sund.ku.dk](mailto:holger.grohganz@sund.ku.dk)

[Researcher Profile](#)

**Research focus:** Development of solid dosage forms, including preformulation, formulation, processing and manufacturing together with the relevant solid-state characterization and multivariate analysis. This includes in particular the development co-amorphous systems as well as a deeper understanding of freeze-drying as production technique.



#### Thomas Rades

Professor

[thomas.rades@sund.ku.dk](mailto:thomas.rades@sund.ku.dk)

[Researcher Profile](#)

**Research focus:** Development of solid oral dosage forms, including preformulation, formulation, processing and manufacturing together with the relevant solid-state characterization and quality control. This includes in particular the development of amorphous and co-amorphous systems as well as amorphous solid dispersions.



### Korbinian Löbmann

Associate Professor

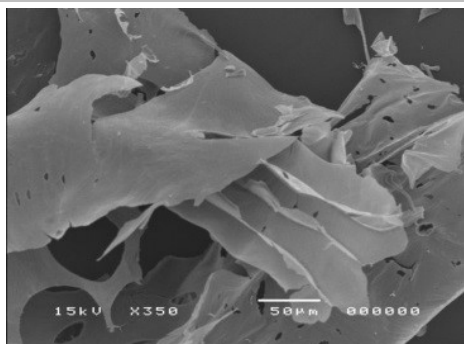
korbinian.loebmann@sund.ku.dk

[Researcher Profile](#)

**Research focus:** Development of solid oral dosage forms, including preformulation, formulation, processing and manufacturing together with the relevant solid state characterization and quality control. This includes in particular the development of new enabling formulation strategies, such as microwave amorphization (in situ amorphization) as well as novel excipients, such as protein based amorphous solid dispersions.

## Examples of projects

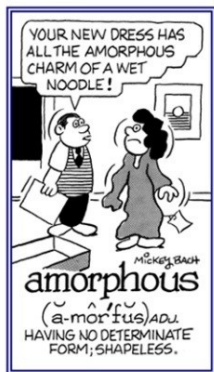
### *Evaluation of preparation methods for co-amorphous formulations*



Low drug solubility is the major challenge for future small molecule drugs. In order to overcome the problematic solubility of BCS class 2 drugs, small excipients are investigated to form co-amorphous formulations. Due to the low solubility, ball milling is used as preferred production process. Due to the low capacity of ball mills, other production procedures, such as freeze-drying, spray-drying and hot-melt processing should be evaluated.

**Supervisors:** Thomas Rades and Holger Grohgan

### *On the role of water in amorphous systems*



Water is generally seen as detrimental for the stability of amorphous drugs and solid dispersions. However, initial in-house work has shown that this may not necessarily be true for all systems especially at low water concentrations. The aim of this Masters project is to determine the water absorption and stability of a range of amorphous systems (pure drugs, amorphous solid dispersions with polymers and co-amorphous systems with amino acids) in the presence of different amounts of water. The student will learn preparative techniques, including ball milling and quench cooling as well as using a wide range of analytical techniques, including X-ray powder diffraction, FTIR spectroscopy, thermal analytical techniques, water determination and dissolution techniques.

**Supervisors:** Thomas Rades and Holger Grohgan

### *Down-stream processing of co-amorphous formulations*



In this project, co-amorphous systems intend to be moved from the powder formulation state towards a more applicable state, i.e. downstream-processing towards a final dosage form, including the investigation of critical processing and formulations parameters of the pharmaceutical performance. A comparison between the amorphous and crystalline forms with regard to downstream processing also needs to be investigated. The effect of various excipients on compactability and compressibility of co-amorphous systems will be connected with the results of pharmaceutical quality testing.

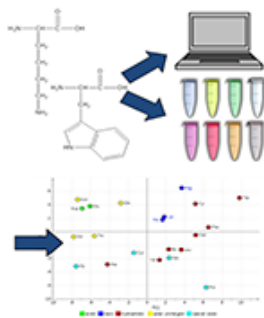
**Supervisors:** Holger Grohgan and Thomas Rades

**Sustainable Pharmacy**

The 17 United Nations Sustainable Development Goals (SDGs) are a collection of independent but interconnected goals carefully designed to give all of us a better future on our planet. From design, all the way to access and use, pharmaceuticals affect the SDGs directly and indirectly. Sometimes in a positive way (SDG3 'Good health and well-being'), sometimes negatively (environment-related SDGs).

In order to optimize the positive effects and mitigate the negative ones, we need to develop innovative and sustainable ways to develop and deliver pharmaceuticals. Students interested in working on the development of solutions that can contribute to human and planetary sustainability will first identify challenges, and will thereafter receive guidance and support on how to practically contribute to its solutions.

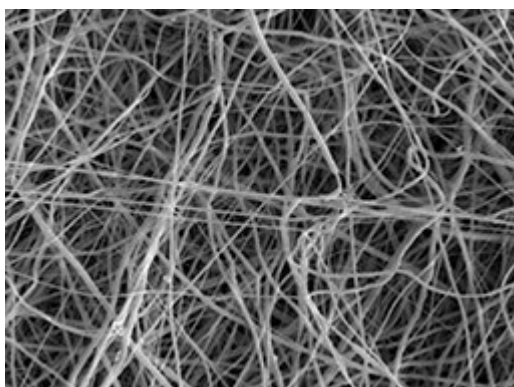
**Supervisor:** Holger Grohganz and Lou Cantarero

**Quality by design (QbD) in the processing of biomacromolecules**

The quality by design (QbD) principle can be expected to influence pharmaceutical processing in the years to come towards the development of more rational processes. Although, freeze-drying and spray-drying are widely used in peptide and protein formulation, the interaction between various excipients and proteins is not fully understood. This project aims to obtain a deeper understanding of the influence of various composition and process parameters on the solid state form of both novel and established the excipients, and the macromolecule. Analytical techniques may include X-Ray powder diffraction, dynamic mechanical analysis, NIR and Raman spectroscopy as well as the application of multivariate data analysis.

and Raman spectroscopy as well as the application of multivariate data analysis.

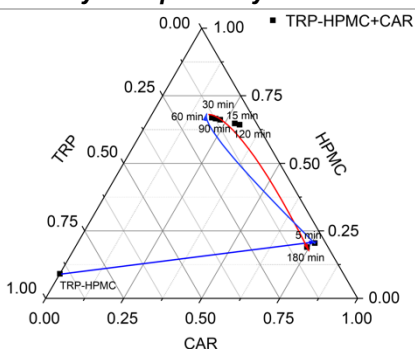
**Supervisor:** Holger Grohganz

**Electrospun amorphous solid dispersions of poorly water-soluble drugs.**

The development of oral dosage forms from poorly water-soluble active pharmaceutical ingredients (APIs) remains a major challenge for the pharmaceutical industry. Preparing amorphous solid dispersions (ASDs) allows increasing the solubility and dissolution rate of an API, hence, increasing its bioavailability. The application of electrical energy during electrospinning can generate ASD nanofibers from drug-loaded solutions and melts. This project focuses on the development of an electrospinning method to produce ASDs. The electrospun fibers will be comprehensively characterized by a range of analytical techniques, including scanning

electron microscopy, X-ray powder diffraction, differential scanning calorimetry and dynamic mechanical analysis. The dissolution rate advantage will also be determined.

**Supervisor:** Thomas Rades and Andrea Heinz

**Ternary amorphous systems**

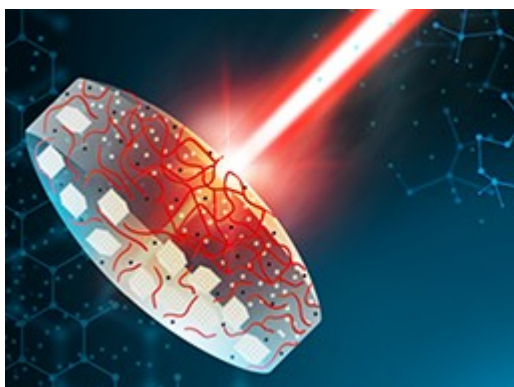
The aim of this Masters project is to determine the properties of ternary amorphous systems (drug, low molecular weight excipient, polymer) in comparison the respective binary systems (drug - polymer or drug - low molecular weight excipient). The student will learn preparative techniques, including ball milling, spray drying and quench cooling as well as using a wide range of analytical techniques, including X-ray powder diffraction, FTIR spectroscopy, thermal analytical techniques, water determination and dissolution techniques.

**Supervisor:** Thomas Rades

**Development of novel Dispersome® formulations**

The novel solubility enhancing Dispersomes® technology is based on the use of whey protein isolate as excipient for amorphous stabilization and solubility enhancement and is the basis of the KU spin-out company ZERION. The projects aim is to further understand the mechanisms behind the amorphous stabilization and solubility enhancement of a given drug when formulated as Dispersomes®. In addition, downstream processes of the Dispersome® formulations into final dosage forms such as tablets or capsules will be investigated. The projects will partly be an industry project and is co-supervised by Zerion scientists.

**Supervisor:** Several projects are available in co-operation with Korbinian Löbmann and scientists @Zerion Pharma ApS

**In situ amorphization using lasers or microwave irradiation**

A major concern of amorphous formulations is their physical instability, which puts the gain in solubility at risk upon long time storage. Using lasers or microwaves, it is possible to transform a crystalline drug into its highly soluble amorphous counterpart within the final dosage form (tablet). The aim of the project is to develop new drug delivery systems that can be "activated" using lasers or microwaves and to understand in depth the mechanism behind the *in situ* amorphization process using microwave irradiation.

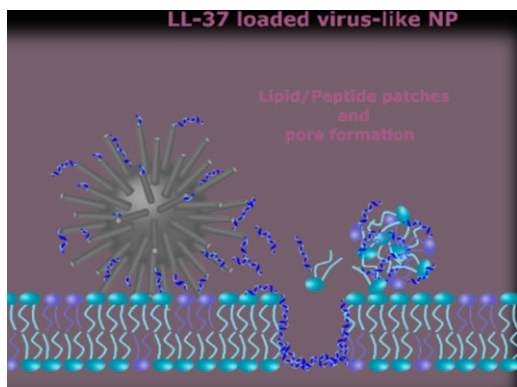
**Supervisor:** Korbinian Löbmann

**Application procedure and dates**

If you are interested in writing your thesis with Solid State Pharmaceutics, please write an email to one of the supervisors with more information about you. There is no deadline.

## Surface and Colloid Chemistry Group

[www.pharmacy.ku.dk/research/surface-colloid-chemistry/](http://www.pharmacy.ku.dk/research/surface-colloid-chemistry/)



The goals of the Surface and Colloid Chemistry Group are to advance the knowledge regarding the membrane interactions of antimicrobial peptides and different nanomaterials, particularly inorganic nanoparticles with potent antimicrobial activities or used as carriers for antimicrobial and anti-inflammatory agents. Both state-of-the-art techniques and innovative approaches are used in the group to evaluate the interactions between these agents and membrane components of cells and bacteria, including for instance fluorescence spectroscopy, DLS, QCM-D, FTIR-ATR, neutron and X-ray scattering.

The overarching aim is to take fundamental research about physicochemical properties and mechanisms to a stage where it can be translated to further therapeutic development.

### Potential thesis supervisors



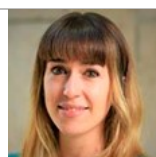
**Martin Malmsten**

Professor

Martin.malmsten@sund.ku.dk

[Researcher Profile](#)

**Research focus:** Microgels, nanoparticles for drug delivery, and host defence peptides for combatting infection and inflammation



**Elisa Parra Ortiz**

Assistant Professor

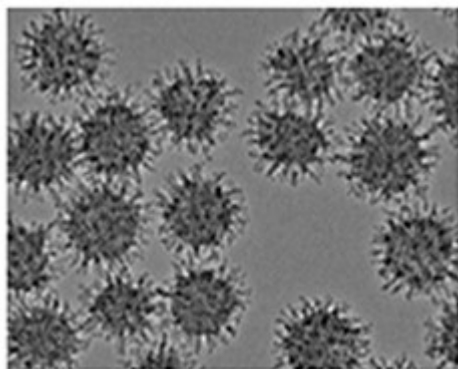
elisa.parra@sund.ku.dk

[Researcher Profile](#)

**Research focus:** Lipid membranes, lipid peroxidation, nanoparticles for drug delivery

### Examples of projects

#### **Membrane interactions of structured silica nanoparticles as antimicrobial agents**



In the wake of increasing bacterial resistance against conventional antibiotics, there is a growing interest in alternative approaches for reaching antimicrobial effects. Among those, nanoparticles are attracting considerable current interest due to the comparatively low cost, good scalability, and broad versatility of such materials, but also due to presently undeveloped bacterial resistance. Here, various nanomaterials offer opportunities for triggered functionalities to combat challenging infections. Although the performance in these diverse applications is governed by a complex interplay between the nanomaterial, the properties of included drugs (if any), and the

biological system, nanoparticle-membrane interactions constitute a key initial step and play a key role for the subsequent biological response. Clarifying key factors controlling membrane binding and destabilization of nanoparticles is therefore key for the successful development of the latter towards therapeutics.

In the present project, membrane interactions will be investigated for mesoporous silica nanoparticles, which offer opportunities in combating challenging infections. For example, both low molecular weight and biomacromolecular drugs can be readily incorporated into such nanoparticles, allowing large drug loads due to their large specific surface area. In addition, silica nanoparticles can be designed to display needle-like surfaces, which may be used to effectively

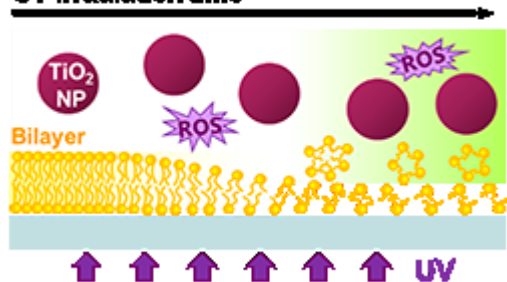


"puncture" bacterial membranes by "needle-like" actions. Within the project, factors determining membrane interactions of "spiky" mesoporous silica nanoparticles will therefore be investigated by previously developed model lipid membranes, in combination with various biophysical techniques, such as QCM-D, FTIR-ATR, and DLS. Results from such biophysical studies, e.g., on effects of membrane composition, structure and charge of the silica nanoparticles, and effects of co-administration of such particles with other potent antimicrobial agents, notably antimicrobial peptides, will be correlated to biological results on antimicrobial effects and cell toxicity for selected systems.

**Supervisor:** Martin Malmsten & Elisa Parra-Ortiz. Number of students: 1

### ***Application of oxidative stress on lipid membranes as a new tool for developing new antimicrobial agents***

#### **UV irradiation time**



Inorganic nanoparticles are very attractive as antimicrobial agents ('nanobiotics'), notably due to the increasing resistance development against conventional antibiotics. Apart from scalability and versatility, such materials offer advantages related to responsiveness of antimicrobial and anti-inflammatory effects and the possibility of controlling them by a range of triggering factors. For instance, oxidative stress is known to be behind the antimicrobial activities of TiO<sub>2</sub> nanoparticles when activated by UV light. However, studies on the mechanisms underlying these activities remain scarce. Based on previous work done by our group on the oxidative destabilization of

lipid membranes, and using different biophysical and surface-chemical techniques such as fluorescence spectroscopy, QCM-D, FTIR-ATR, and DLS, the present project will focus on the effects of TiO<sub>2</sub> nanoparticle-induced oxidation of lipid membranes, lipid degradation, and their consequences for membrane structure and stability. Any potential membrane selectivity that could allow more efficient antimicrobial activities along with reduced side effects will be also explored, for instance the combination with cationic peptide coatings. In a wider perspective, this project will contribute to the mechanistic foundation for the use of photocatalytic nanomaterials as triggerable antimicrobial agents.

**Supervisor:** Martin Malmsten & Elisa Parra-Ortiz. Number of students: 1

### **Application procedure and dates**

If you are interested in writing your thesis with the Surface and Colloid Chemistry Group, please write an email to one of the supervisors with more information about you. There is no deadline.







## Toxicology and Drug Metabolism

[www.pharmacy.ku.dk/research/toxicology-drug-metabolism/](http://www.pharmacy.ku.dk/research/toxicology-drug-metabolism/)



We perform experimental research revealing the occurrence, fate, and toxicological and endocrine effects of xenobiotics, especially pharmaceuticals, with the aim of assessing their risks to humans and biota. We apply various *in vitro*, *ex vivo* and *in vivo* assays and advanced analytical techniques, such as LC-MS and mass spectrometry imaging.

### Potential thesis supervisors

<p><b>Bjarne Styrishave</b> Associate Professor bjarne.styrishave@sund.ku.dk <a href="#">Researcher Profile</a></p>		<p><b>Christian Janfelt</b> Associate Professor christian.janfelt@sund.ku.dk <a href="#">Researcher Profile</a></p>	
<p><b>Andreas Christopher Kretschmann</b> Associate Professor andreas.kretschmann@sund.ku.dk <a href="#">Researcher Profile</a></p>		<p><b>Catharina M. Lerche</b> Clinical Associate Professor Catharina.Margrethe.Lerche@regionh.dk</p>	

## Examples of projects

### Endocrine disrupting pharmaceuticals



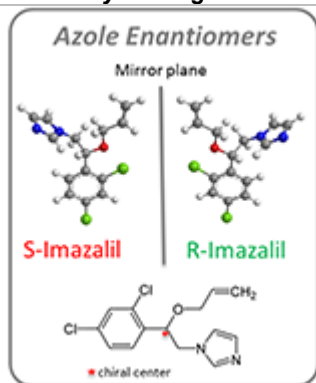
Public awareness concerning endocrine disrupting drugs has increased the last few years, as these are presumed to affect reproductive ability and to increase the occurrence of hormone-dependent cancers. Endocrine disrupting drugs are, however, generally much less potent than physiological hormones, and therefore there is doubt as to whether or not these substances can affect humans.

Recent research indicate that simultaneous exposure to a cocktail of endocrine disrupting drugs, each at a concentration below the effect level, might result in a significant additive or synergistic effect. The

present project wishes to uncover interactions between selected hormone-disturbing substances in various *in vitro* test systems and/or animal experiments with selected endpoints, including hormonal activity, changes in aromatase activity and the impacts of endocrine disrupting drugs on endogenous hormone metabolism.

**Supervisor:** Bjarne Styrishave, No of students: 2-3

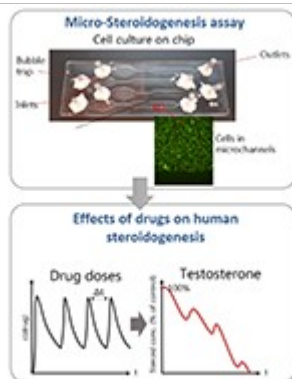
### Endocrine toxicity of drug enantiomers and metabolites



Increasing evidence exists that certain pharmaceuticals disturb the human hormone system and may contribute to endocrine related diseases like infertility, obesity and different types of cancers. It is well known that enantiomers of drugs can differ strongly in their biological activity. Furthermore, drug metabolites formed in the body can be active and possess higher activity than the parent compound. Very little is known about how toxic effects on the hormone system depend on the enantiomeric form and the metabolic products of a drug. The focus of this project are chiral drugs like azole fungicides, which are used for the treatment of severe systemic and superficial

fungal infections. The goal is to elucidate the endocrine toxicity of azole enantiomers and metabolites through pharmacokinetic and –dynamic studies. The practical work includes enzyme and cell based *in vitro* assays as well as *in vivo* experiments. A large part of the project is the development of analytical chemical methods for the identification and quantification of enantiomers and metabolites in different biological matrices with enantioselective HPLC-MS/MS.

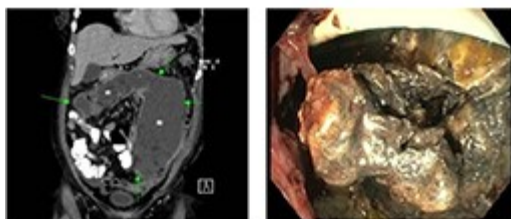
**Supervisors:** Andreas Kretschmann, Bjarne Styrishave, Claus Cornett. No. of students: 1-2

**Development of a microfluidic assay for testing the endocrine disrupting potential of pharmaceuticals**

Currently, the pharmaceutical industry loses more than 80% of their drug candidates during drug development, since existing in vitro and animal tests are too time- and cost-intensive and do not predict adverse effects of drugs in humans with sufficient accuracy. The goal of this project is the development of a microfluidic toxicological in vitro assay, which can assess the toxicity of drugs in a fast, cheap and more human relevant manner. Within this project a miniaturized cell-based in vitro assay will be established on a microchip (endocrine gland on-a-chip) and applied for the testing of adverse effects of drugs on the human steroid hormone system. Work

students will perform includes cell culturing, design/ fabrication of microchips, in vitro toxicity tests as well as analytical chemical measurements.

**Supervisors:** Andreas Kretschmann. No. of students: 1-2

**Pancreatic infections: Local and systemic antibiotics in infected walled-off pancreatic necrosis.**

Severe acute pancreatitis is characterized by organ dysfunction and necrosis of the pancreas. Mortality is high, up to 20%. Infection in the pancreas is a serious complication and is associated with high mortality, up to 20%. After 3-4 weeks the necrosis becomes encapsulated a so-called walled-off necrosis (WON). The primary treatment is systemic antibiotics. However, little is known about the penetration of antibiotics into the necrosis and the ability of

antibiotics to stop the infection. Several factors may influence the activity of the antibiotics, such as the fibrous capsule surrounding the necrosis, the size and the physico-chemical milieu of the necrosis. Using 2D-DESI-imaging and LCMS/MS, this project aims to investigate the distribution of the most commonly used antibiotics in pancreatic necrosis. The purpose is to identify the most effective treatment, thereby decreasing mortality and morbidity in patients suffering from pancreatic necrosis.

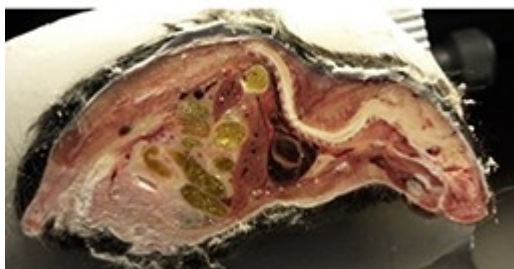
**Supervisors:** Bjarne Styrishave, Christian Janfelt. No. of students: 1-2.

**Danida project: Green Resource Innovations For Livelihood Improvement (GRILI)**

Medicinal plants as green resource products (GRPs) are used as traditional medicine in Tanzania, and are key components for primary health care and livelihoods of more than 50% of the inhabitants. Unfortunately, many herbal products are adulterated with drugs, such as antibiotics, antimalarials and mild analgesics. The present study aims to investigate the adulteration of herbal drugs from Tanzania, by analysing the presence of different drug classes in herbal medicines collected from markets and health providers in Tanzania. Samples will be collected and extracted in Tanzania and transported to Denmark, where the samples will be analysed. The project included approximately 3 months of field work in Tanzania.

**Supervisors:** Bjarne Styrishave. No. of students: 1-2.



**Mass spectrometry imaging of drugs in tissue sections from mice**

Using a new technique with mass spectrometry, Desorption Electrospray Ionization Imaging (DESI-MSI), it is possible to image the distribution of compounds in a sample. In this way, we can follow a drug dosed to a mouse, creating images of the mouse that show the distribution of the drug in the organism, where it is metabolized along with biomarkers of different cell types (e.g. cancer). In this project, a mouse will be dosed with a drug, and subsequently the whole mouse or single organs (brain, liver and kidney) will be cut in thin slices which, are then analysed with DESI-MSI. The aim of the project is to image where the drug goes and in which doses we can see the drug and its metabolites. The project will be planned in

collaboration with pharmacologists or medicinal chemists.

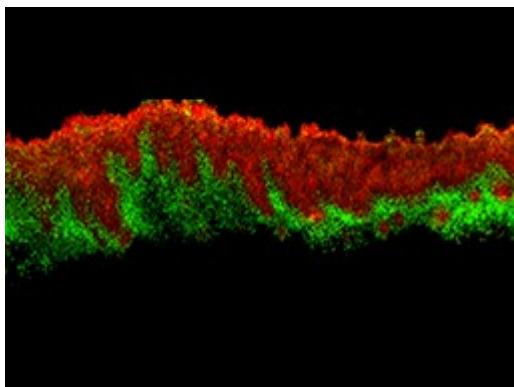
**Supervisors:** Christian Janfelt. No. of students: 1 or 2

**Mass spectrometry imaging of natural compounds in cannabis**

The use of medical cannabis is increasing worldwide, and recently, the Danish government has sanctioned a 4-year pilot programme for the prescription of medical cannabis to Danish patients. More than 500 natural compounds have been isolated from Cannabis Sativa, including the medically important cannabinoids, terpenes and flavonoids. For a deeper understanding of this complex composition, and to ensure products of high and consistent quality, better analytical tools are needed. The aim of this project is to apply mass spectrometry imaging to characterize the distribution of active compounds in Cannabis Sativa leaves, to study the compound

synthesis in the plant during flowering and the impact of environment and growth conditions on compounds of interest in the plant.

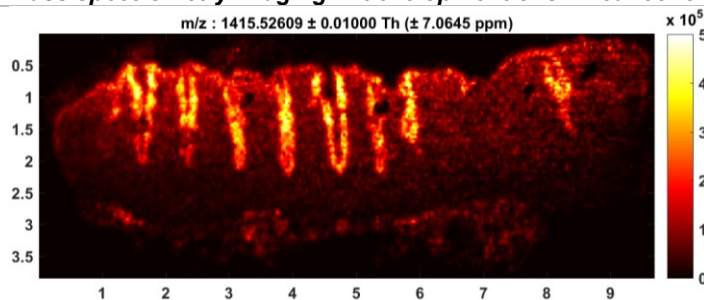
**Supervisors:** Christian Janfelt. No of students: 1

**High-resolution MALDI mass spectrometry imaging for studies in drug delivery**

A new laser-based mass spectrometry imaging setup has been installed, which enables mass spectrometry imaging at the cellular level. The technique, MALDI-MSI, will be used to study the delivery of drugs across biological membranes and barriers in ex-vivo and possibly in-vivo animal experiments. High resolution mass spectrometry images showing the distributions of drugs and other exogenous compounds relative to endogenous compounds such as membrane lipids will provide information about the efficacy and mechanism of new drug formulations. The project will be planned in

collaboration with one of the Drug Delivery groups at the Department

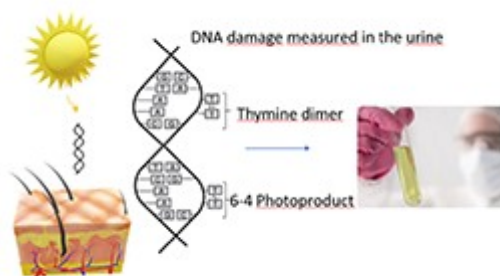
of Pharmacy.  
**Supervisors:** Christian Janfelt. No of students: 1 or 2

**Mass spectrometry imaging in development of skin cancer treatment**

The capabilities of DESI and MALDI MSI to image the distribution of endogenous compounds together with a drug and its metabolites make them ideal in the study of skin penetration of drugs. This project takes place in collaboration with Department of Dermatology, Bispebjerg Hospital, which develops new treatments for skin cancer. One approach is to

ablate channels in the skin in order to be able to perform local, topical chemotherapy of skin cancer. In this project MALDI imaging and LC-MS will be used to optimize the delivery of one or more chemotherapy agents by imaging of tissue sections from difference depths in the treated skin.

**Supervisors:** Christian Janfelt and Catharina Lerche. No of students: 1 or 2

**DNA damage in the urine after UVR-exposure**

Thymine dimer is the major form of DNA damage that happens when ultraviolet radiation penetrates the skin. Nucleotide excision repair (NER) is the main pathway for the repair of thymine dimers. The importance of this process is illustrated by the very high risk of developing skin cancer in individuals with disorders in which NER is defective. NER removes thymine dimers from DNA and subsequently they are excreted in the urine. The aim of this study is to investigate the effect of irradiation dose, exposed skin area, and skin type on the amount of excreted thymine dimers. The study involves irradiation of healthy volunteers, collection of urine samples and LC-MS. The study is part of SCIN-CAG ([read more](#)).

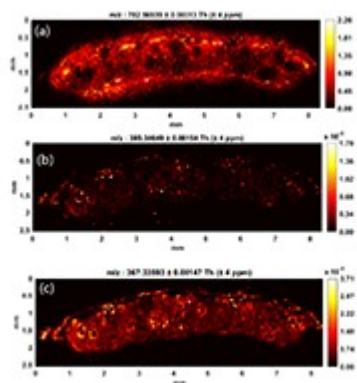
**Supervisors:** Catharina Lerche. No. of students: 1

**Pharmacological photoprotection**

Sun exposure is the primary risk factor for keratinocyte cancer and despite massive prevention efforts, Danish incidences have risen to an estimated 38,500 per year. Pharmacological photoprotection is the concept of using pharmacological compounds before or after exposure to environmental carcinogens e.g. ultraviolet radiation. There is increasing evidence that compounds (e.g. nicotinamide and NSAIDs and less known plant- and marine- derived compounds), may be useful in keratinocyte cancer prophylaxis. The aim is to discover compounds that delay or even reduce photocarcinogenesis. Pharmacological compounds will be tested in

well-established UVR-induced murine models. Laboratory Animal Science certificate is needed for this master project (FELASA A/B/D). The study is part of SCIN-CAG ([read more](#)).

**Supervisors:** Catharina Lerche. No. of students: 1

**Vitamin D-metabolite distribution in the skin analyzed by mass spectrometry imaging**

Vitamin D plays a key role in the maintenance of calcium/phosphate homeostasis and elicits biological effects that are relevant to immune function and metabolism. It is predominantly formed through UVB exposure in the skin by conversion of 7-dehydrocholesterol (7-DHC). Melanin in the skin absorbs UVB irradiation and plays a major role in the protection against skin cancer, higher concentrations of melanin gives a better protection. Vitamin D is formed in all skin types, so the distribution of 7-DHC must be closer to the skin surface than melanin. Mass spectrometry imaging (MSI) enables the ability to gain spatial information of various molecules with spectra being mapped to individual pixels.

The aim of this study is to investigate the vitamin D-metabolite distribution in the skin using high mass resolution instrumentation and relate the findings to melanin in the skin.

**Supervisors:** Catharina Lerche and Christian Janfelt. No. of students: 1

**Application procedure and dates**

If you are interested in writing your thesis in toxicology and drug metabolism, please write an email to one of the supervisors with more information about you. There is no deadline.



## Vaccine Design and Delivery

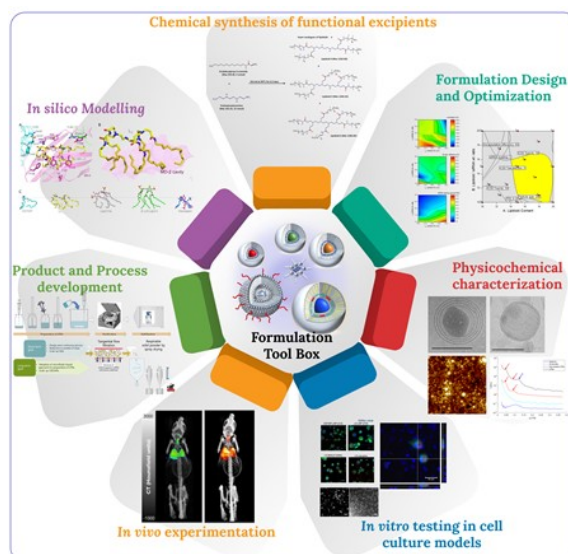
[www.pharmacy.ku.dk/research/vaccine-design-delivery/](http://www.pharmacy.ku.dk/research/vaccine-design-delivery/)



The research focus of the Vaccine Design and Delivery Group is advanced drug delivery. The group uses *in vivo* imaging (e.g., NIR, MRI and SPECT/CT) to guide and optimize the design of new nanoparticle-based delivery systems for vaccines and nucleic acid-based therapeutics to improve therapy. The research in the group is highly interdisciplinary. The team comprises international researchers of various backgrounds, including pharmacists, biologists, biochemists, physicists and biotechnologists.

“Biopharmaceuticals like vaccines and nucleic acid-based therapeutics are challenging from a pharmaceutical perspective, because they are highly complex products, which can only be understood via solid fundamental science. Using systematic knowledge-based quality-by-design approaches, combined with advanced physicochemical and biopharmaceutical assessment, and molecular imaging, we design new delivery systems for biopharmaceuticals to optimize their stability, efficacy and safety” says Professor and Group Leader, Camilla Foged.

The overall research goal is to improve disease prevention and treatment in the fields of infectious and inflammatory diseases, and cancer. The group is addressing drug delivery challenges from bench-to-bedside, via international collaborations, using state-of-the-art technologies. This has fostered innovative solutions and high-impact publications in drug delivery.



### Potential thesis supervisors



#### Camilla Foged

Professor

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[Researcher Profile](#)

One of the primary goals of the Vaccine Design and Delivery Group is to gain new fundamental knowledge that can facilitate the design, optimization and development of novel delivery systems capable of delivering loaded biopharmaceuticals to the intended target site(s). The Vaccine Design and Delivery Group addresses the complex challenges associated with the formulation and targeted delivery of vaccines and nucleic acid-based therapeutics.



#### Aneesh Thakur

Assistant Professor

aneesh.thakur@sund.ku.dk

[Researcher Profile](#)

The immune system plays a vital role in disease protection and therefore drug delivery approaches founded on immunology hold great potential for the development of novel therapeutic and prophylactics against infectious diseases and cancer. Our current research work towards this goal involves three complementary themes: (i) nanoparticle-based formulation strategies to enhance efficacy of subunit and nucleic acid-based vaccines and therapies, (ii) non-invasive vaccine/drug delivery through the mucosa, and (iii) image-guided targeted vaccine/drug delivery, all focused on creating new therapies based on controlled modulation of the immune system. We investigate topics at the interface of immunology, targeted drug delivery, nanotechnology, and imaging to address important health problems that are intractable from a unidisciplinary approach.

#### Abhijeet Lokras

PhD student

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[Researcher Profile](#)

#### You Xu

PhD student

you.xu@sund.ku.dk

[Researcher Profile](#)

### Examples of projects

#### ***Microfluidics-assisted design of next-generation mRNA vaccines - a novel tool for fighting cancers and challenging infectious diseases***

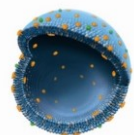


Multifunctional NP

There is an unmet medical need to develop novel vaccines against the so-called "difficult targets" such as AIDS, TB and cancer. One promising strategy is the use of vaccines based on mRNA that encode antigenic proteins from pathogens or tumor cells. Using microfluidics, we will develop multifunctional nanoparticle-based vaccine that both delivers mRNA encoding antigen and induces CTL responses. The efficacy and safety of the mRNA vaccines will be tested in animal models of infection and cancer.

**Supervisors:** Aneesh Thakur and Abhijeet Lokras

**Magnetic resonance imaging-assisted design of a thermostable and self-administrable tuberculosis vaccine for inhalation**

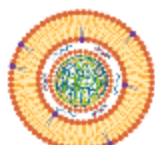


Liposomes

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, which enters the lungs through the respiratory mucosa. The objectives of the project is to develop a dry powder-based vaccine against TB and using MR imaging, to define the specific areas in the lungs, which are optimal for vaccine deposition, efficacy and safety. Using a benchtop aerosol generator, Preciselnhale, we will deliver the dry powder liposome-adjuvanted vaccine formulation in mice lungs and evaluate the safety and pulmonary distribution using mass spectrometry imaging. The immunogenicity and efficacy of the dry powder vaccine will be tested in animal models of Tuberculosis challenge.

**Supervisor:** Aneesh Thakur

**Design and investigation of nanoparticles for targeted delivery of small interfering RNA (siRNA)**

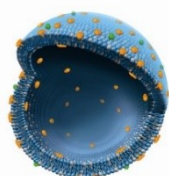


LPNs

Small interfering RNA (siRNA) holds a promising therapeutic potential for treating a variety of diseases *via* gene silencing. However, the physicochemical properties of siRNA often limit its therapeutic efficacy rendering it unfavourable for efficient intracellular delivery. We have developed lipidoid-polymer hybrid nanoparticles (LPNs) and demonstrated safe and efficient intracellular delivery of siRNA. In this project, new generation of lipidoid-based LPNs will be evaluated for their transfection efficiency, safety, and therapeutic effect in animal models of acute inflammation.

**Supervisors:** Aneesh Thakur and You Xu

**Biomimetic surfactant phospholipid liposomes: Elucidating the effect of liposome surface charge and depot effect on pulmonary immunity**



Biomimetic liposomes

The ability to induce airway mucosal immunity is an essential property of future subunit vaccines because several pathogens, *e.g.*, respiratory viruses, enter into the human body *via* the airways. It is well known that protection against these pathogens requires activation of the mucosal immune system, which can only be primed *via* mucosal vaccine administration. However, little is known about how to design safe nanoparticle-based subunit vaccines optimal for the induction of airway mucosal immunity. In this project, the requirement of surface charge and depot effect of liposomes will be evaluated in primary immune cells and animal models by incorporating pulmonary surfactant phospholipids and proteins in the formulations.

**Supervisor:** Aneesh Thakur

**Application procedure and dates**

If you are interested in writing your thesis with the Vaccine Design and Delivery group, please write an email to [camilla.foged@sund.ku.dk](mailto:camilla.foged@sund.ku.dk) with more information about you. Places are given on a first come, first served basis.

