Master projects

If you are interest in any of these projects contact associate professor Magnus Lilledahl at magnus.lilledahl@ntnu.no or in my office at D4-191

1 Clinical applications of nonlinear optical microscopy

Our groups main interest is in using advanced biophysical measurement techniques to provide novel insight into biological system and pathological conditions to improve the treatment of medical conditions. Our work covers advanced microscopy and spectroscopy, image analysis, statistical analysis and biomechanics with the aim of combining data from diverse disciplines to improve our understanding of biological systems. We also try to work as closely as possible to the clincal application to guide our efforts.

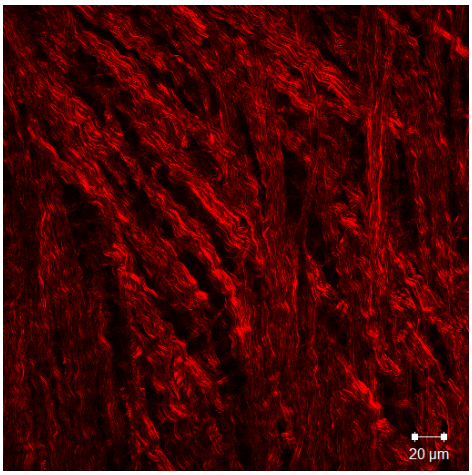

Figure 1: Collagen fibers in cartilage

Currently we are heavily involved in a technique called nonlinear optical microscopy which can generate three dimensional (3D) images of biological structures without any labeling. A major effort is to try to extract as much information as possible from this data to understand as much as possible about the biological system that we are interested in. We especially focus on a technique called second harmonic generation (SHG) which can be used to detect ordered biological molecules like collagen, myosin and cholesterol crystals.

Currently we are involved mainly in a clincially relevantl systems: cartilage and related diseases, tissue engineering, cardiovascular disease and breast cancer.

There are many possibilities for a project or a master thesis. Some ideas are outlined below but the actual project can be tailored to the students individual interests. We are open for ideas! Focus can be adjusted between biology, programming, experimental work, data analysis, modelling and theory.

Our group currently consists of 2 PhD students, 1 post doctoral fellow and 1 master student.

There are more projects here than we have capacity for so projects will given first come-first serve.

2 Projects

Any of these projects can be taken both as a project (fordypningsprosjekt), a master project or both (unless otherwise noted). There is varying detail in the description which indicates varying degree of freedom in designing the project.

2.1 Scattering properties of SHG

It is well known that the scattering pattern of SHG depends on the size and orientation of the scatterers. However, a quantitative model for this has not been developed. We are currently interested in developing more quantitative measurements based on this principle as well as looking into what type of clinical data which can be extracted from these measurements. We will probably need coroborative data, either from electron microscopy or superresolution techniques.

This project will involve:
`sample preparation, microscopy, theoretical studies, data analysis, electron microsopy and superresolution microscopy`

2.2 Superresolution imaging of collagen fibrils

Once (when I grew up) it was believed that Abbes diffraction limit really was the limit and that it was not possible to see things which were smaller than approximately half the wavelength in an optical microscope. Then came superresolution techniques which changed everything. Regular SHG is limited by the diffraction limit, but by staining the collage fibrils it should be possible to achieve better understanding of the biological structure.

This project will involve:
`sample preparation, immunhistochemistry, superresolution imaging and image analysis.`

2.3 Relating biomechanical and structural parameters

The mechanical properties of many types of tissues are primarily linked to the distribution of long chained collagen molecules which provide structural integrity to the tissue.

These molecules aggregate into microfibrils which again combine into mature fibres. The size, direction, and density of these structures are determines much of the biomechanical properties of tissue. Collagen fibers can be imaged with SHG. SHG microscopy makes it possible to generate three dimensional images of the collagen structure of fresh tissue without fixation or staining. This is a tremendous advantage for future potential for in-vivo imaging

We are developing a custom made setup for simultaneous SHG microscopy of collagen fibres and measuring the mechanical strain and stress applied to the tissue. This will allow us to study the microstructural properties that underlie the macroscopic mechanical properties. A better understanding of this relationship shows promise in a wide array of clinical applications.

This project will involve:
`Systems integration, data collection, analysis and interpretation, building aparatus, programming, automatization`.

2.4 Correlative microscopy

Optical microscopy can provide detailed functional information while electron microscopy provides superior resolution. By combining these techniques enhanced information can be acquired. This is called correlative microscopy. The challenge is to develop techniques to overlay the two images, and the appropriate preparation techniques. Several electron microscopy techniques are potential candidates: TEM, STEM, SEM and FIB-SEM (utilizing FIB-SEM will require a project/master combination).

This project will involve:
`Sample preparation, optical and electron microcopy, data analysis, programming`

2.5 Correlating MRI and microscopy data

Even though optical microsopy can provide images with amazingly detailed information, they are not so simple to employ in a clinical setting. Then, more common clinical imaging techniques like MRI and CT are necessary. Thus, what we want is to try to correlate MRI imaging data with microscopy data to be able to extract as much information as possbile from the MRI data. We especially want to look into an MRI technique called diffusion tensor imaging and especially look at information whic can be aqcuired from cartilage tissue samples.

This project will involve:
`Optical microscopy, MRI imaging, image analysis, modelling`

2.6 Fluorescence lifetime imaging

We recently acquired a fluorescence lifetime microscope at our department. By utilizing lifetime information together with imaging it is possible to gather additional information about the sample. It has been shown that FAD and NADH are the primary fluorophores in cells and that these changes lifetime depending on their state. In this project we want to establish this technique for use in future projects in tissue engineering.

This project will involve:
`Cell culturing, optical microscopy, data analysis`

2.7 Diffusion in cartilage samples

Articular cartilage (the tissue which covers the end of the bones in joints), does not have any blood supply so the cells in the cartilage need to get oxygen and nutrients through diffusion. This diffusion will vary depending on the cartilage tissue structure. It is very important for how the cartilage react to damage, and its ability to heal itself. Diffusion of molecules in tissue can be studied by fluorescence recovery after photobleaching (FRAP) and fluorescence correlation spectroscopy (FCS). In this project we want to determine spatially dependent diffusion parameters accross the tissue for use in modelling of how the tissue will react to traumatic injuries

This project will involve:
`Sample preparation, FRAP, FCS, programming, modelling`

2.8 Polarization resolved SHG

We recently installed polarization resolved SHG on our microscope system and want investigate what feature we can derive from these techniques. Creative ideas welcome!

This project will involve:
`microscopy, data analysis, theory`

2.9 Image analysis

To analyze our 3D SHG images we have employed several different image analysis techniques, especially Fourier transforms. The network of collagen fibers is quite complicated so we want to look into using more localized frequency techniques like wavelets for analyzing the data

This project will involve:
`Mathematics, programming, image analysis, microscopy`

2.10 Big data in breast cancer

We are in the process of collecting SHG images of biopsies of breast cancer patients from over 900 patients. For this patients we also have a lot of clinical and biochemical information. The question is how the pattern of the extracellular matrix corresponds to the aggresiveness of the cancer.

This project will involve:
`Image analysis, data mining and programming`

2.11 Tissue engineering

SHG is ideal for imaging collagen in-vivo. Can we culture cells and track the formation of collagen in real time? Can we extract living chondrocytes (cartilage cells) from cartilage and grow them in the lab and visualize their bahvior in real time?

This project will involve:
`sample preparation, cell culturing, microscopy`

2.12 Nonlinear microscopy in food production

Meat and fish is basically muscle and connective tissue - both which can be measured with SHG! Thus there is a potential for usage as a food quality control technique. Also Coherent anti-Stokes Raman scattering (another nonlinear optical technique) can be used to measure the lipids and you basically have all the ingredients of animal foods. Did you ever wonder what constitutes the ultimate steak at the microscopic level? Then this could be the project for you!

This project will involve:
`Microscopy, gourmet cooking skills`

2.13 Collagen crosslinking

Collgen fibrils can be optically crosslinked by use of photosensitizers. Can we *draw* optically scaffolds for tissue engineering?

This project will involve:
`Microscopy, photochemistry, programming`

2.14 SHG of uric acid crystals

sssh...don't tell anyone. Uric acid crystals has a strong SHG signal. This has not been published and needs to ba analyzed! Did anyone say "Nobel price"?

This project will involve:
`recieving the nobel prize`