Clinical applications of multiphoton microscopy

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Introduction: Multiphoton microscopy (MPM)

When very intense light interacts with matter one can have second-order (and higher) optical excitations. These interactions depend quadratically on the electric field and are generally quite weak so one needs very intense light to excite them. The advantage is that if you focus the light strongly, the intensity will only be strong enough at the focus to generate these excitations. One can therefore move the focus around and generate three dimensional images. This technique is used among other things to image biological tissue. We are looking for more clinical applications of this technique and have developed several projects/master theses projects in this area. All the projects can be tailored to the specific interests of the student.

Cartilage

Cartilage is the tissue covering our bones at the joints, a fascinating material which has an increadibly smooth for soft joint motion, and is incredibly strong to be able to support the entire weight of the body. We are working on understanding the mechanical properties of this tissue type. We have several subprojects in this area that can be modified depending on the student's interests.

- Use MPM to image and quantify the 3 Dimensional microstructure of cartilage to understand how the structure achieves it's impressive mechanical properties.
- Collagen is birefringent and much information can be gathered from polarization imaging. A very advanced polarization setup has recently been developed at NTNU and we wish to use this to image cartilage and compare with multiphoton microscopy.
- The resolution of MPM is limited and to image individual collagen fibers we wish to compare this with scanning electron microscopy which has a much higher resolution but lacks the 3D imaging capability.
- We wish to develop instrumentation to simultaneously perform macroscopic mechanical testing while performing microscopic imaging which will greatly improve our understanding of the behaviour of cartilage.

Heart

Heart is a fascinating (and of course important) organ. A complex interplay of electrical signals, muscle contraction and mechanical properties of the heart makes the heart pump the blood the way it should. In this project we wish to use MPM to characterize the distribution of the collagen fibers throughout the heart, to improve the understanding of the mechanical properties of the heart.

Second harmonic generation

Second harmonic generation is a nonlinear optical process where light is converted to light with half the wavelength. This signal is used in MPM to image collagen, myosin and microtubuli. The resolution is limited by the wavelength of the light. However, information about the size of the scattering objects are stored in the relationship between the forward and backscattered light. By comparing these signals it is possible to extract more information about the subresolution structure. We will use this technique on various tissue types to investigate what information can be acquired.

Staining of thick sections

In regular histology tissue is cut in thin sections (about 2-3 micrometers) and stained with various substances to improve the contrast in the images. This sectioning removes much of the 3 dimensional information of the tissue. We wish to investigate the use of stains on thicker sections (100 micrometers) and image these with MPM to investigate how this can reveal structures not visible in regular thin sections.