Optical Coherence Microscopy Combined with Optical Tweezers for Cellular Mechanics Research

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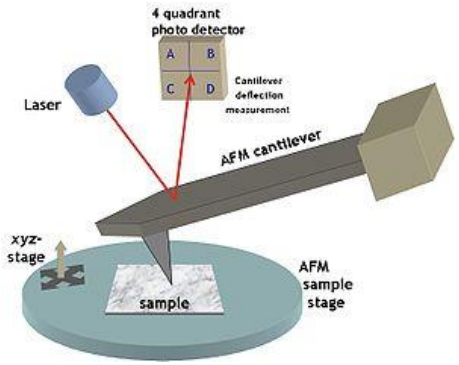
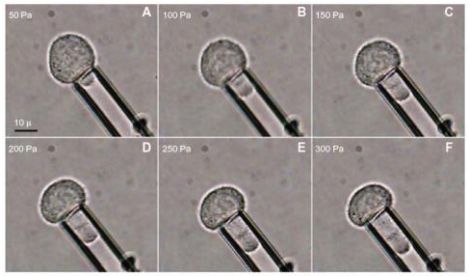
Methods of Studying Cellular Mechanics

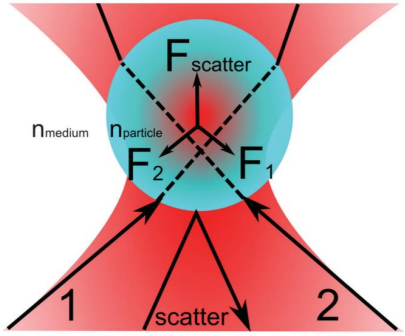
Atomic Force Microscopy



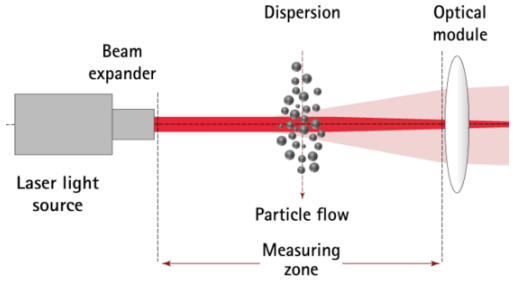
Micropipette Retraction Method



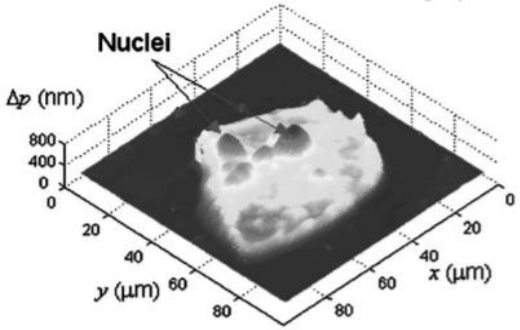
Optical Tweezers



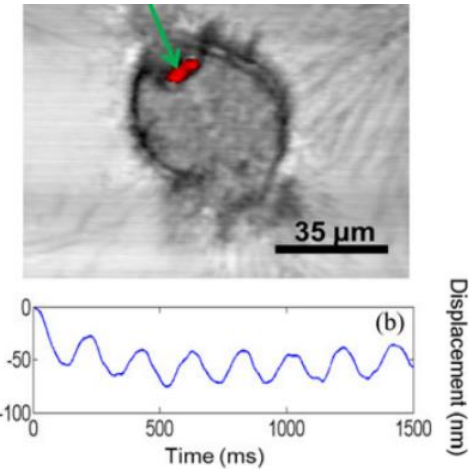
Dynamic Light Scattering Elastometry



Optical Coherence Microscopy



Magnetic Field Cytometry[1]

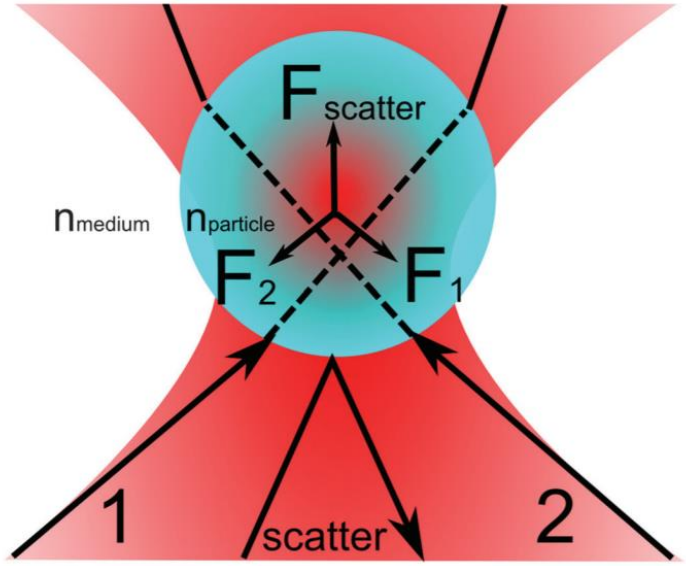


Aim: to develop a method that can non-invasively create mechanical excitation in a single living cell and detect its response in 3D space

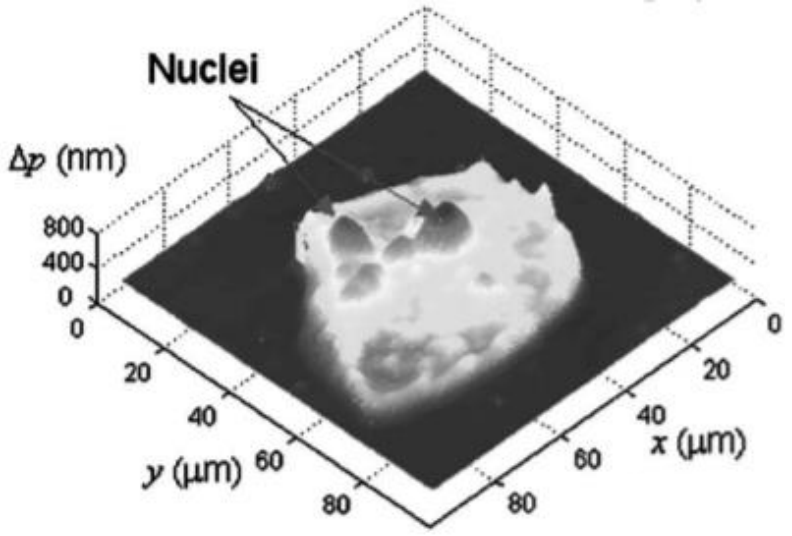
[1]Vasilica Crecea, Benedikt W. Graf, Member, IEEE, Taewoo Kim, Gabriel Popescu, and Stephen A. Boppart, Fellow, IEEE, IEEE J. Sel. Top. Quantum Electron. **20**, No. 2 (2014)

Method Used

Optical Tweezers:
submicron precision object manipulating[1,2]



Optical Coherence Microscopy (OCM):
detecting displacements with 10 nm accuracy, building three-dimensional images of objects[3,4]

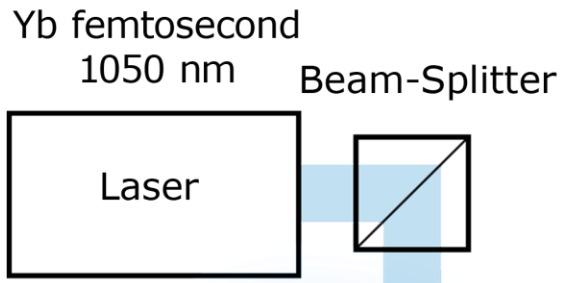


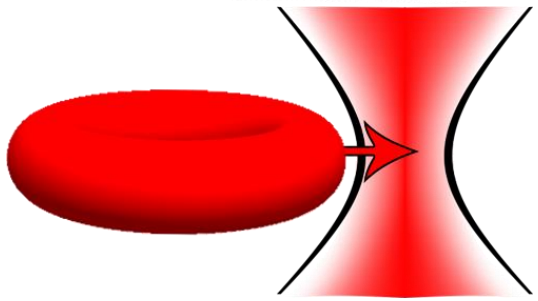
Combination Advantage:

The ability to create non-invasive excitation on the cell surface with tweezers, while simultaneously detecting membrane displacement using phase OCM and studying the three-dimensional structure of the cell. Using cell response on external excitation it is possible to obtain more information about mechanical properties of cells.

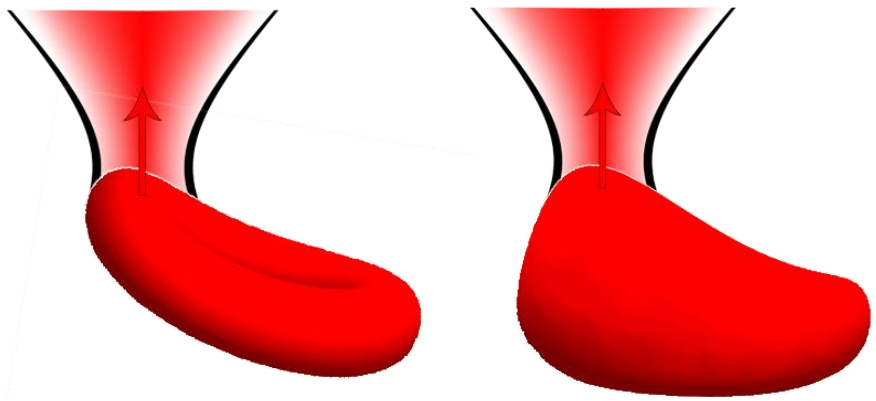
[1] Keir C. Neuman and Steven M. Block, Review of Scientific Instruments **75**, No. 9, p. 2787 (2004)
[2] Rauch, P., & Jähnke, T. Microscopy Today, **22**(4), p. 24-31 (2014)
[3] A. F. Fercher et al, Rep. Prog. Phys. **66**, p. 239 (2003)
[4] Chulmin Joo et al, Opt. Lett. **30**, p. 2131-2133 (2005)

Setup

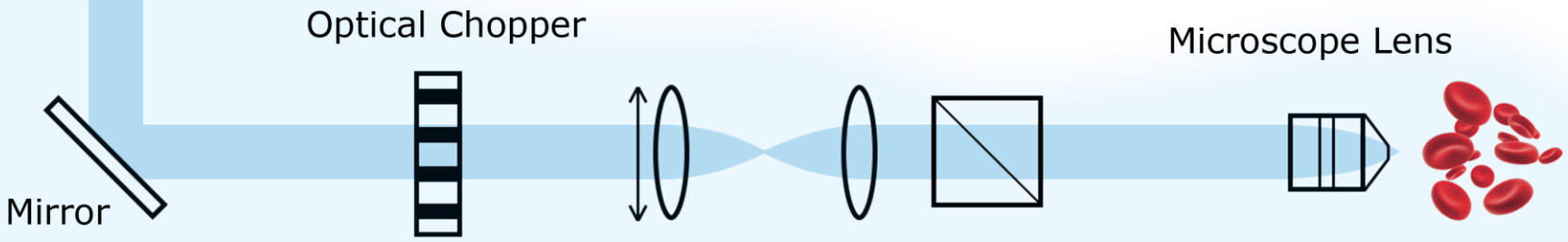




Cell moving

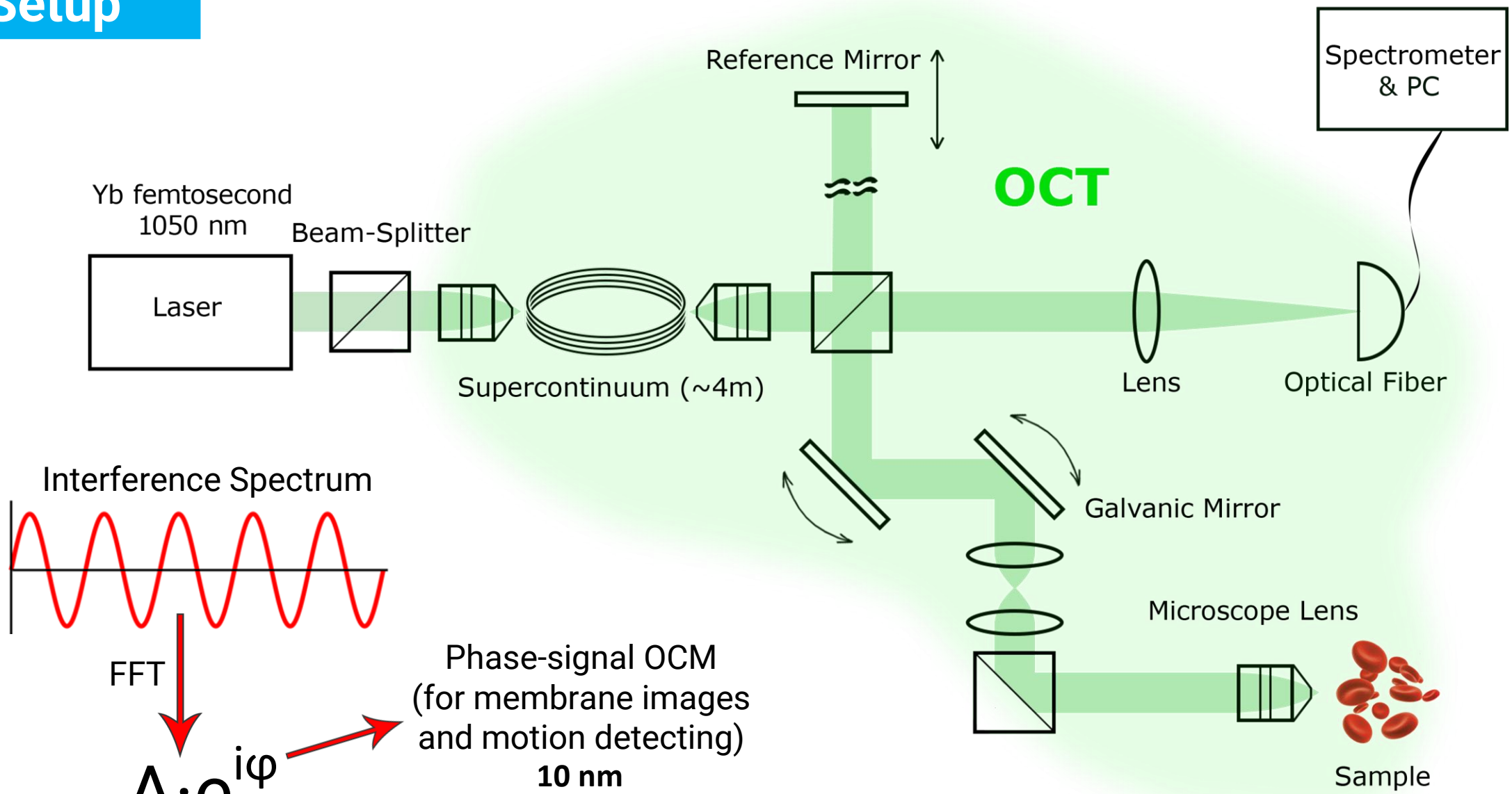


Whole cell / cell membrane excitation



Tweezers

Setup



Interference Spectrum

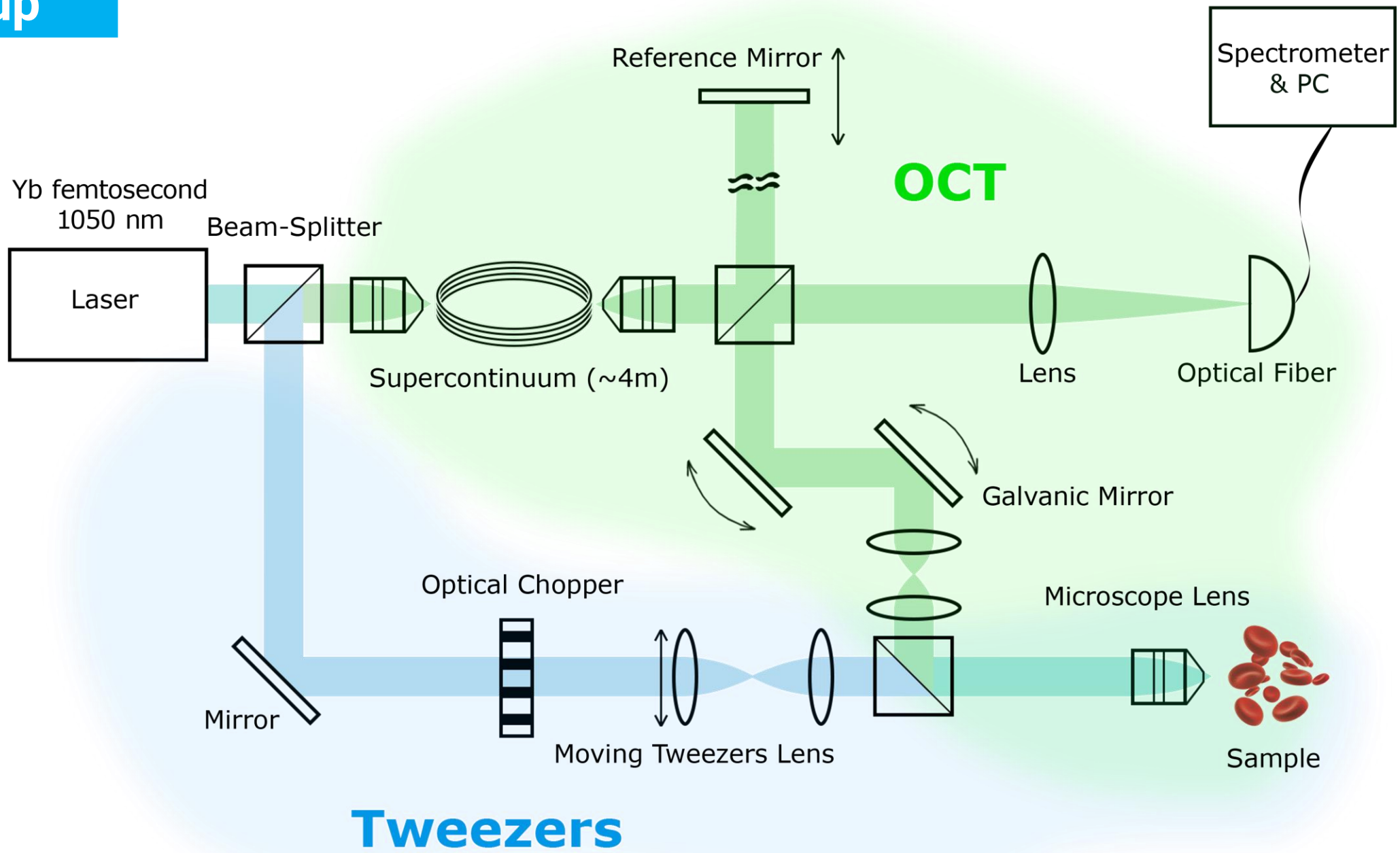
FFT

$A \cdot e^{i\varphi}$

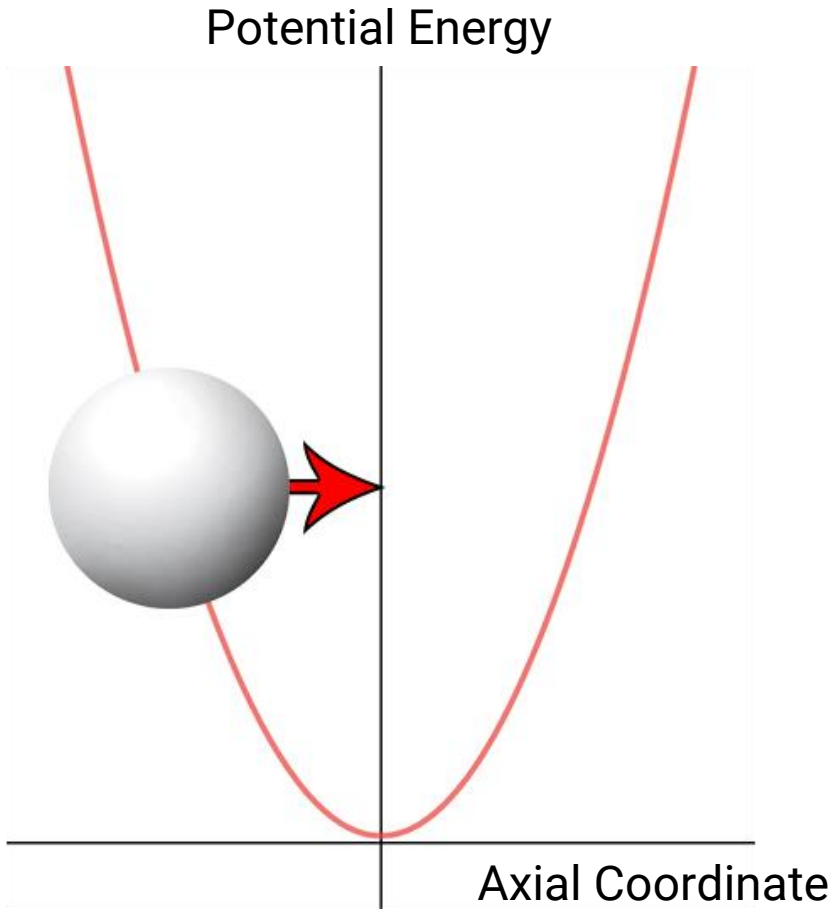
Phase-signal OCM
(for membrane images
and motion detecting)
10 nm

Amplitude-signal OCM
(for reflectance)
1 mkm

Setup


Reference Mirror
Spectrometer & PC
OCT
Yb femtosecond 1050 nm
Beam-Splitter
Laser
Supercontinuum (~4m)
Lens
Optical Fiber
Galvanic Mirror
Optical Chopper
Microscope Lens
Mirror
Moving Tweezers Lens
Sample
Tweezers

Microbead Motion



Microbead trapping
in harmonic potential of trap

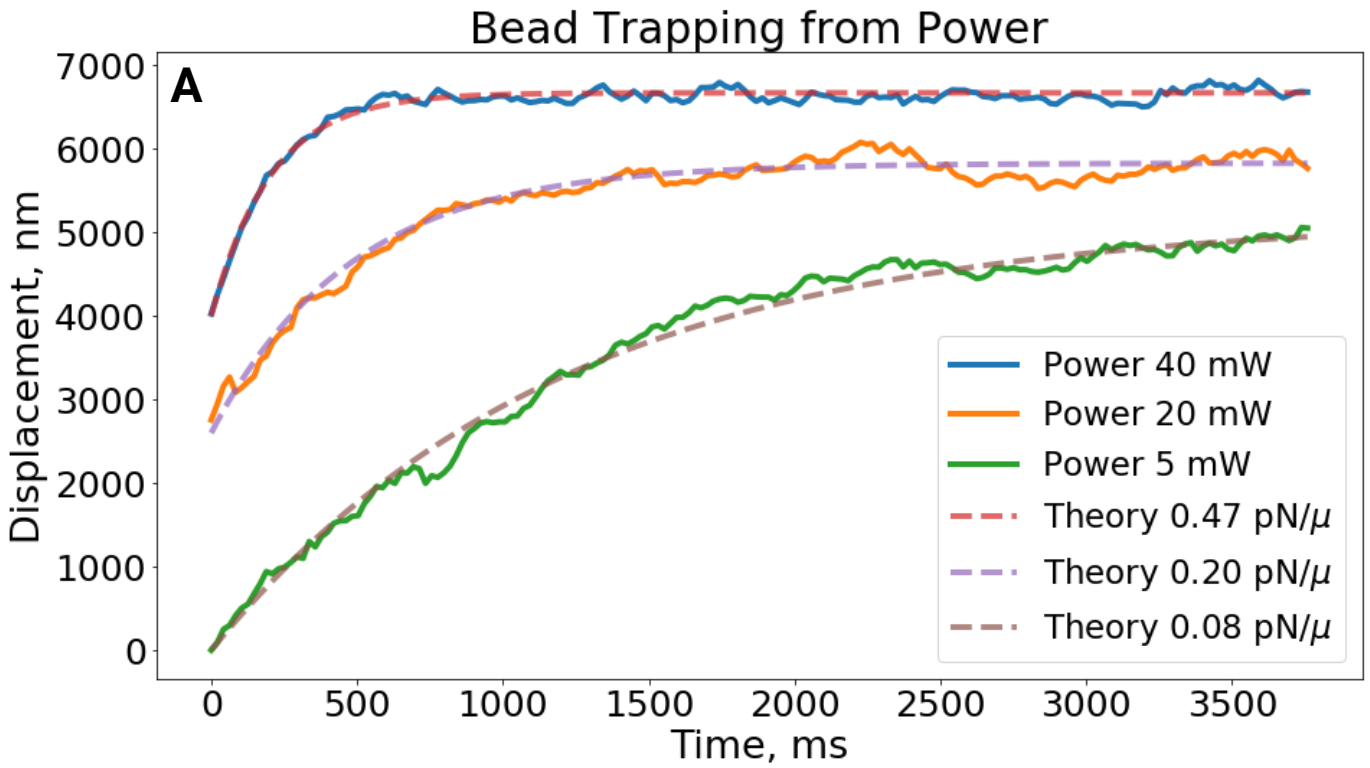
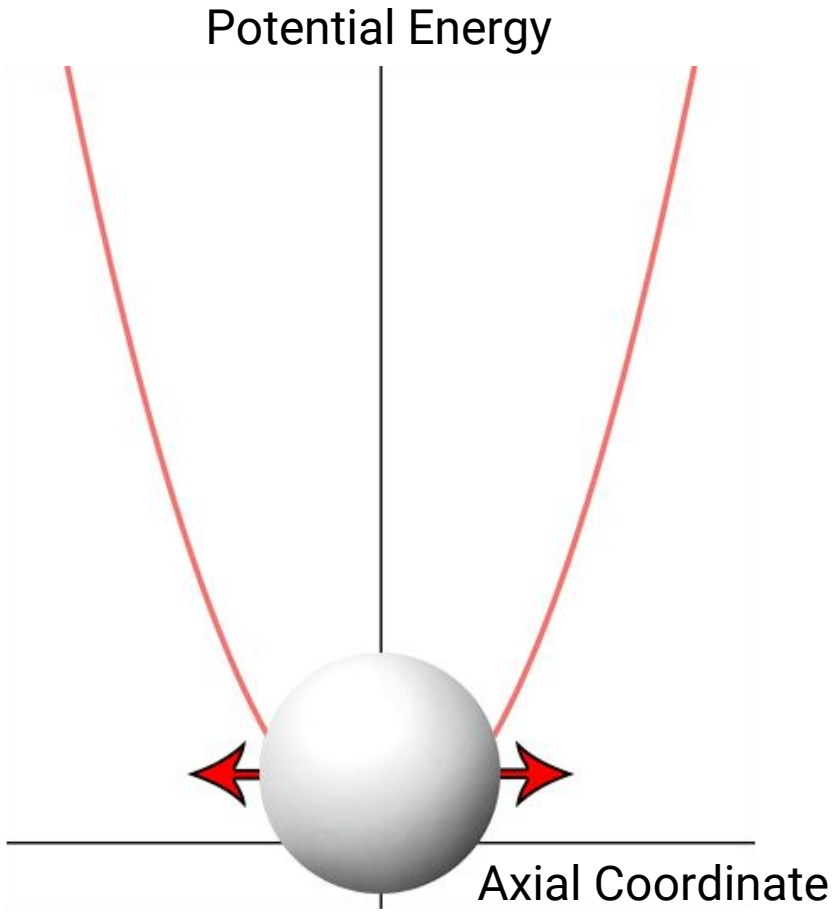


Figure A shows the trajectory of the bead during trapping for different trap powers (obtained with phase-sensitive OCM). The trajectory of the bead in harmonic potential at the indicated trap stiffness is shown as theoretical.

Microbead Motion



Microbead Brownian motion in harmonic potential of trap

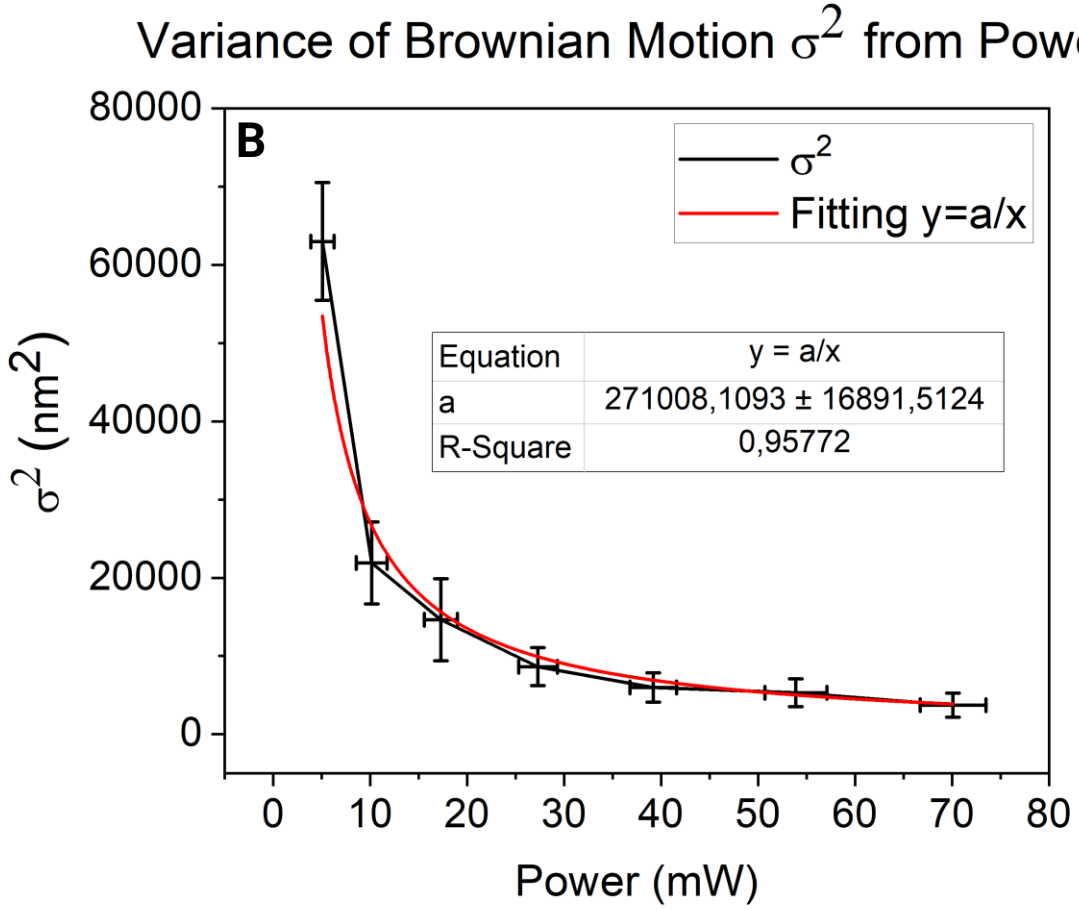
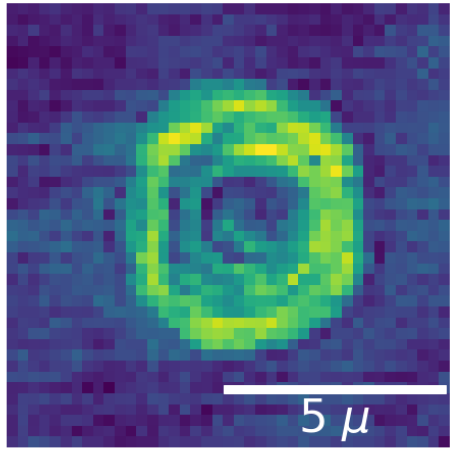
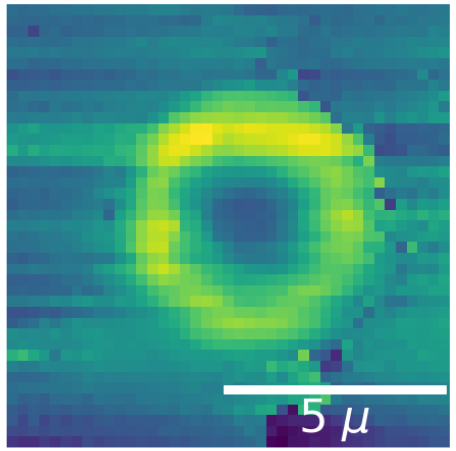


Figure B shows the decrease of z-axis bead Brownian motion variance with increasing trap power (obtained with phase-sensitive OCM).

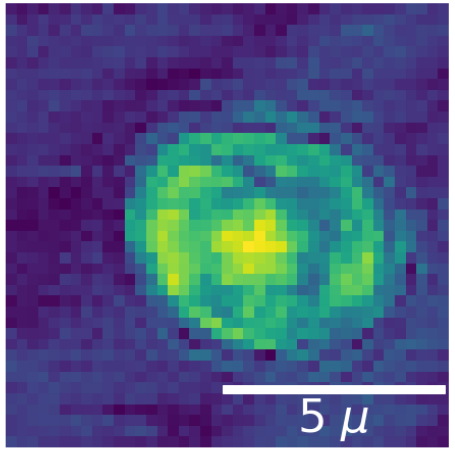
Cell Imaging



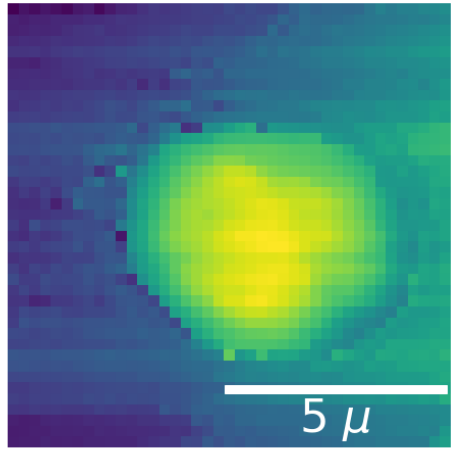
Dyscocyte OCM image
(Amplitude OCM)



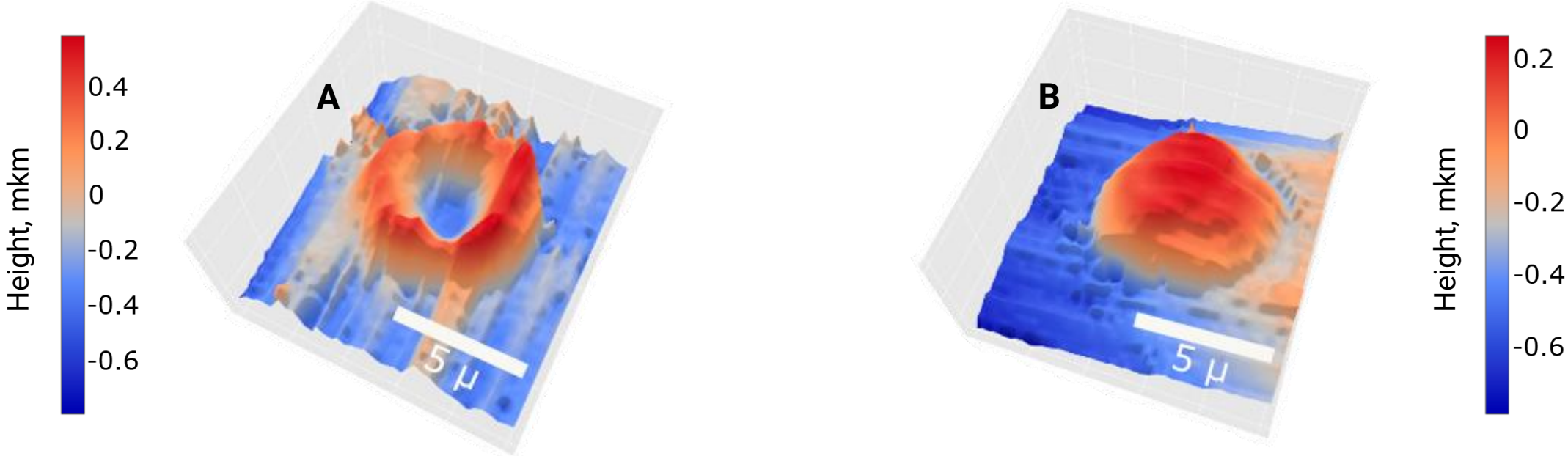
Dyscocyte phase image
(Phase-sensitive OCM)



Spherocyte OCM image
(Amplitude OCM)

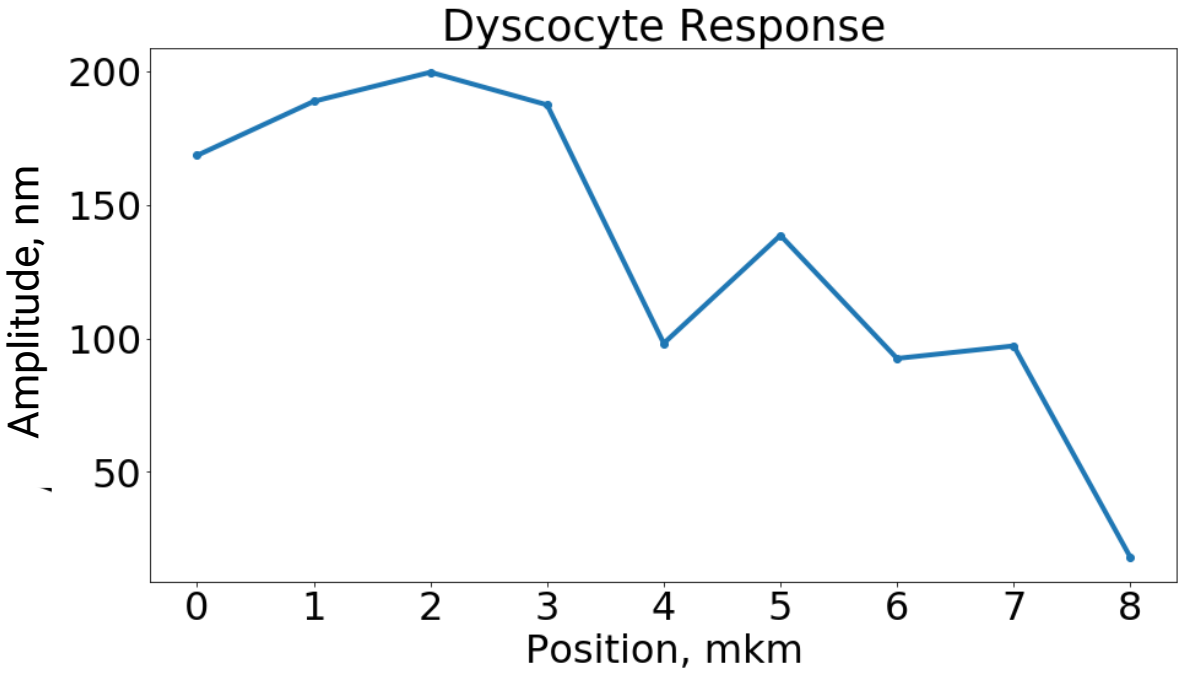


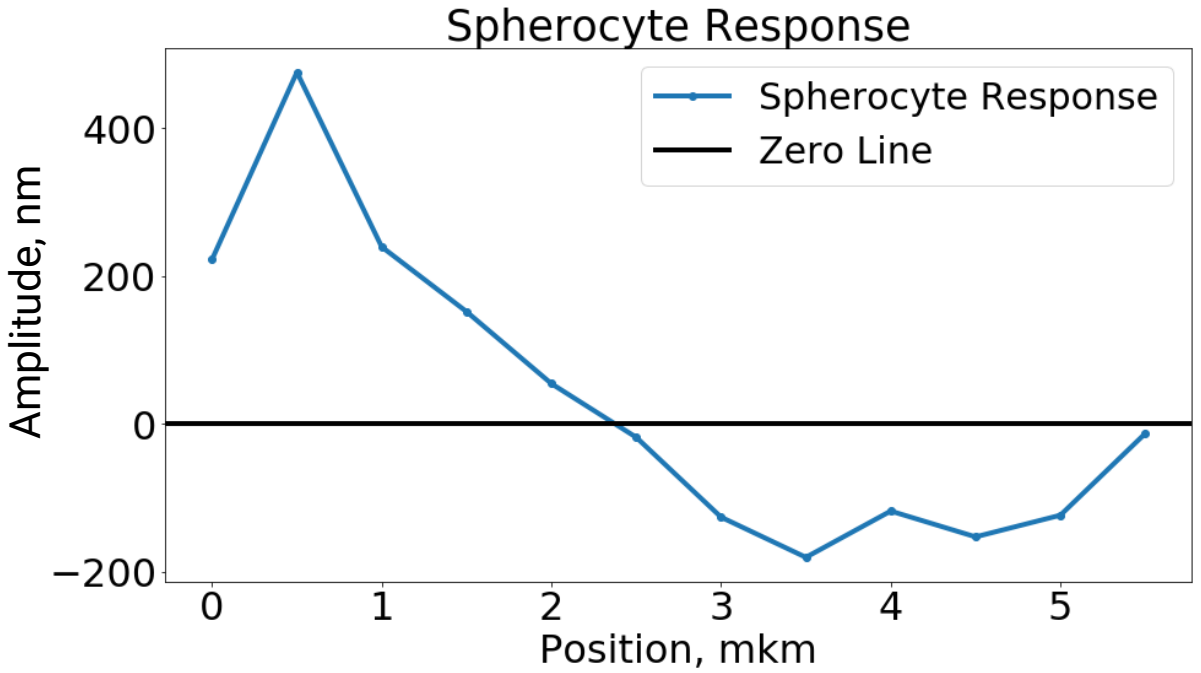
Spherocyte phase image
(Phase-sensitive OCM)

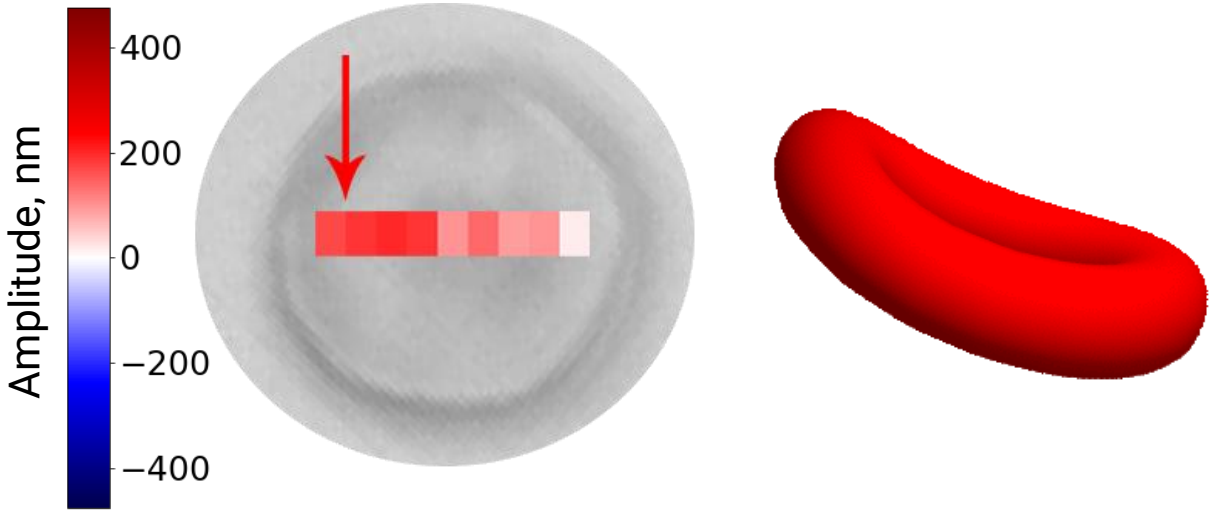


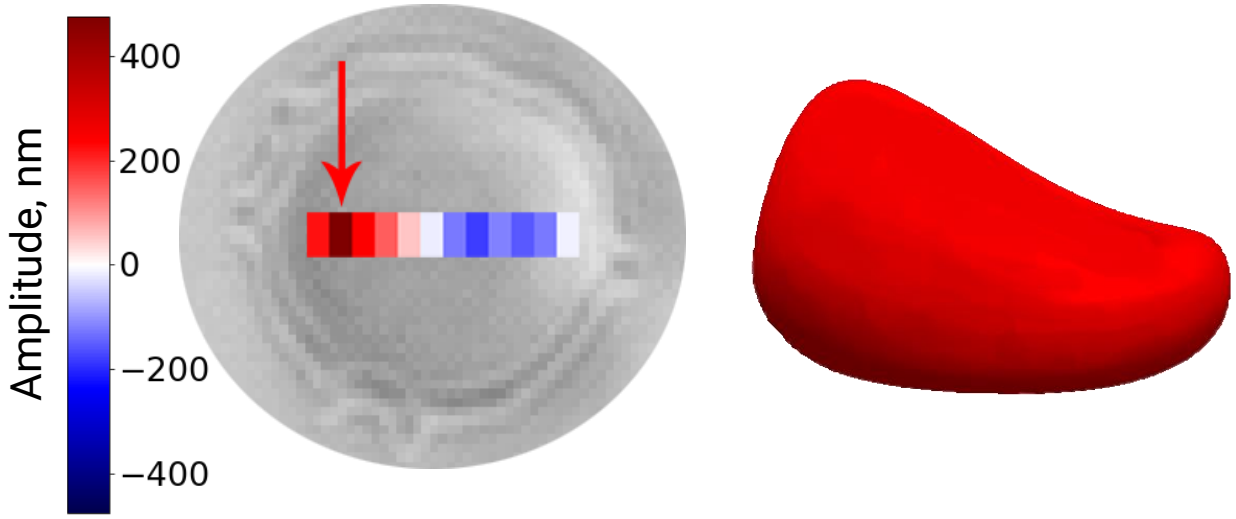
Dyscocyte (**Figure A**) and Spherocyte (**Figure B**) phase images in 3D
(proportions in height are not respected)

OCM + Tweezers









Dyscocyte response and visualization (arrow indicates trap)

Spherocyte response and visualization

Conclusion

1) The developed method allows to non-invasively create mechanical excitation in the cell and to detect its response by recording a 3D phase signal.

2) The developed method made it possible to determine that the **dyscocyte** reacts to an external action by the whole cell oscillations, whereas **spherocyte** reacts to an external action by membrane oscillations only.

Prospects

The developed method in the future can also be used to analyze the movement of not only the membrane, but also the internal structures of the cell, such as the nucleus and organelles.