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FNSNF

Parallel Cantilever Sensing and Force Spectroscopy for Cancer Characterization

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Squeeze information out of your cells!

This is the catchy slogan that might describe our project best.

We will develop a **measurement module** for a scanning force microscope to perform **parallel force spectroscopy** for **identification of cancer cells** by their **elastic properties** and chemical **recognition of related biomarkers** by nanomechanical sensing.

The main advantage will be to provide **rapid diagnostic tools** for cancer identification by paralleled mechanical cantilever sensors **for investigation of the elastic properties of biopsy samples** through statistical evaluation of a large number of **force vs. distance curves**, as **cancer cells differ from healthy cells in elasticity**. The cantilever array approach reduces diagnosis times from 3 hours to minutes, allowing faster decision on the appropriate therapy. Rapid biomarker tests based on cantilever sensors complement information on the status of the tumor.

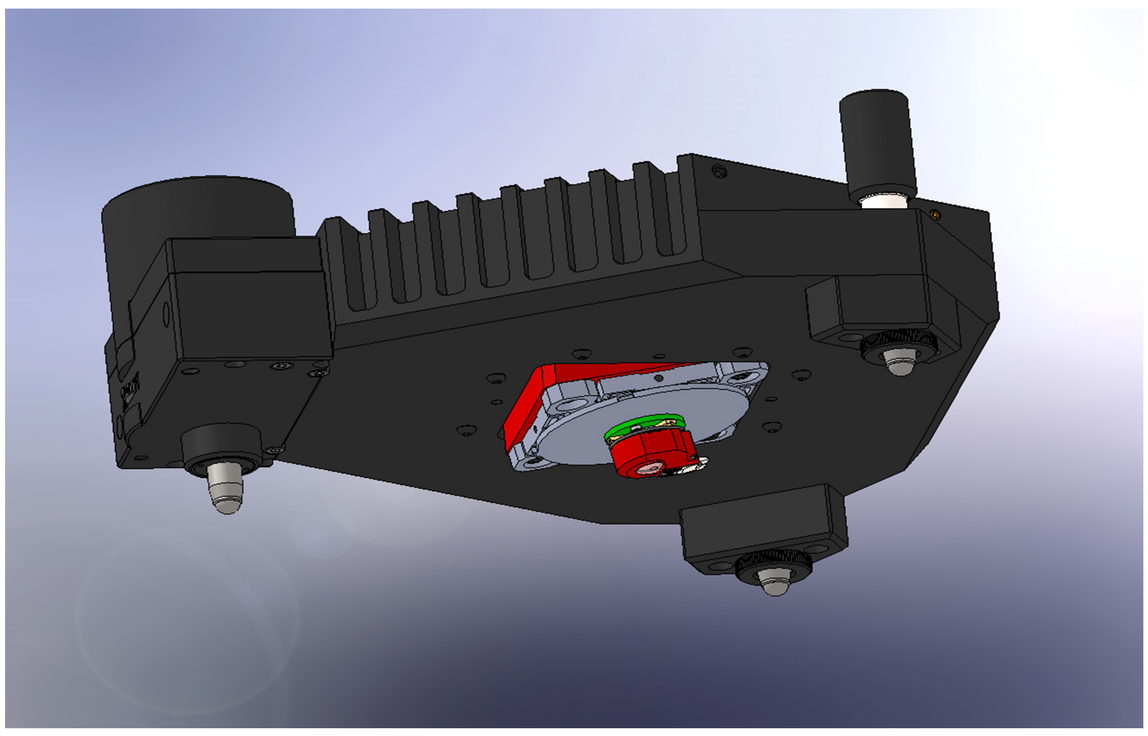
The instrumental setup will be based on a modified **NanoSurf FlexAFM** scanning force microscopy head equipped with a **cantilever array** instead of a single cantilever.

Two case studies will be performed in collaboration with end users from hospitals: 1) Diagnosis of **breast cancer**, 2) Diagnosis of **melanoma** (skin cancer).

Modified FlexAFM scan head

In collaboration with NANOSURF the project partners will develop a measurement setup based on modified commercial FlexAFM scanner. To allow use of 8 cantilevers instead of only one cantilever, the Z-actuator and optical unit of the FlexAFM head has to be tilted by 10° in order to increase the free optical aperture.

Nanosurf will **adapt a series FlexAFM head** for inserting the tilted Z-actuator. We will design and build the add-on bridge part for holding and positioning the VCSEL array in the 1:1 imaging configuration. The control/interfacing/data transfer aspects of the integration demonstrator will be handled by the project partners. The figure shows the design of the modified FlexAFM head.

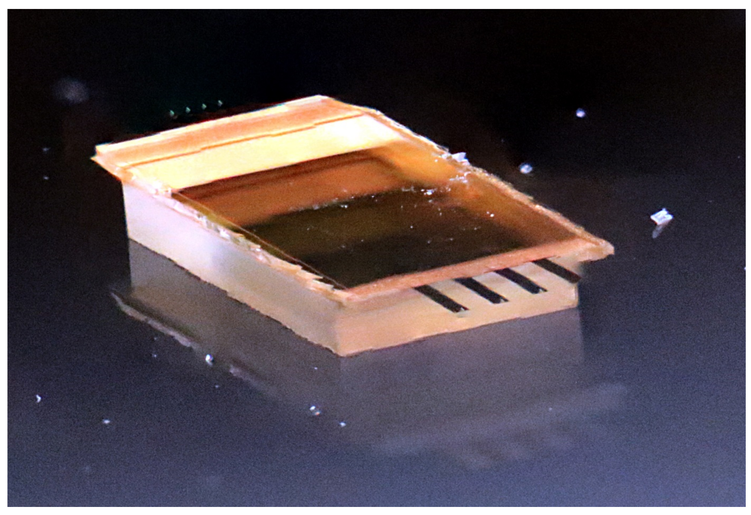


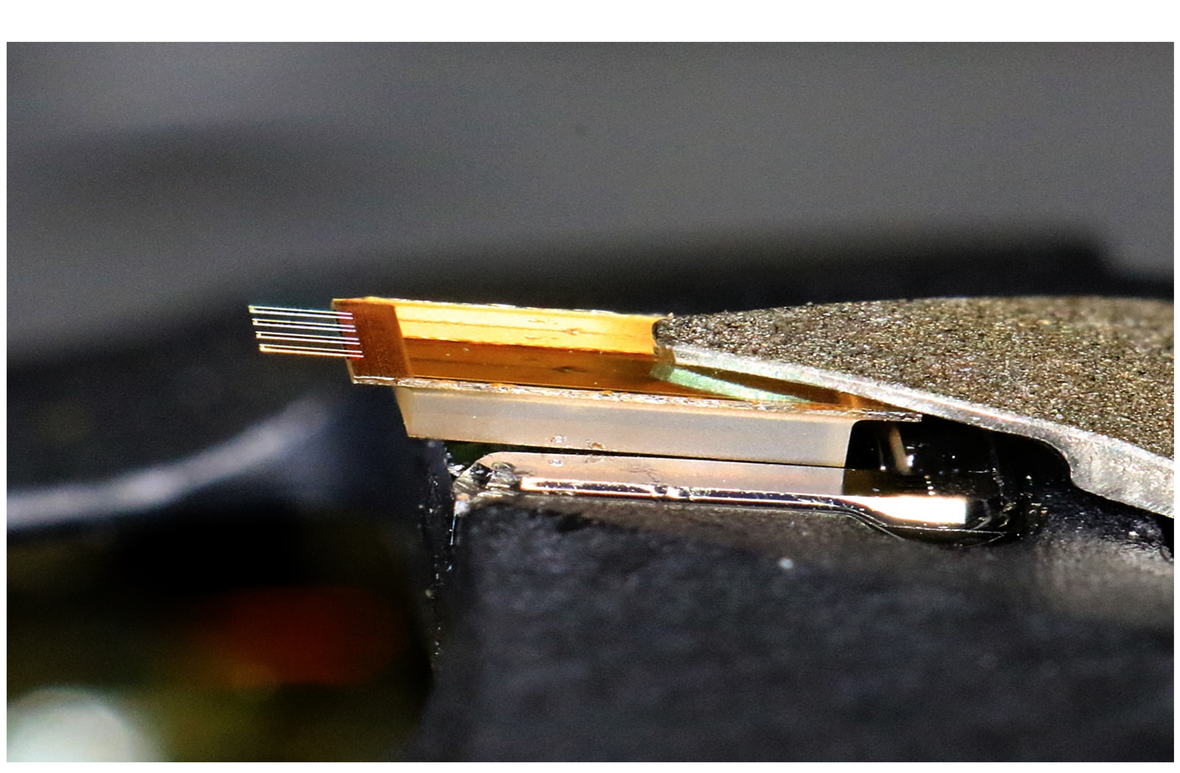
Microfabricated cantilever arrays

Arrays of 4 to 8 cantilevers with tips have been microfabricated for this project for AFM force spectroscopy and cantilever sensing experiments.

Silicon nitride 4-cantilever array with tips

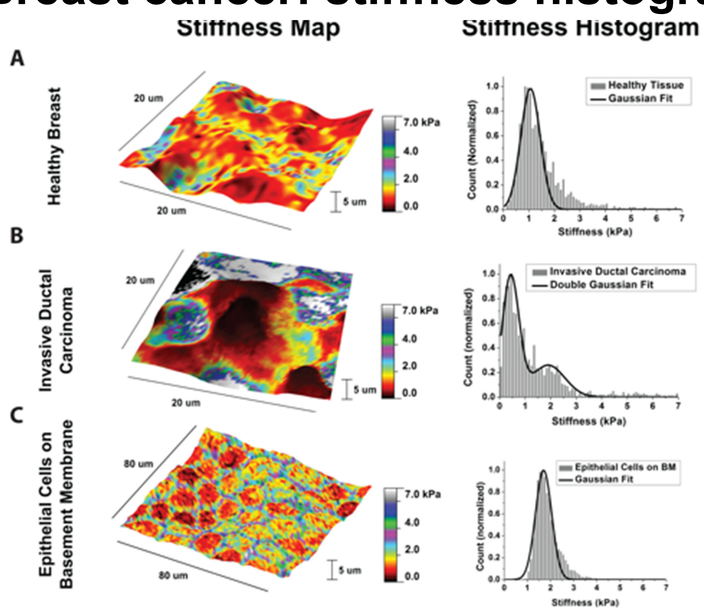
Cantilever length: 500 µm
Cantilever width: 100 µm
Cantilever pitch: 250 µm
Resonance frequency: 8.2 kHz
Spring constant: 0.1 N/m





Cantilever array in the FlexAFM array holder.

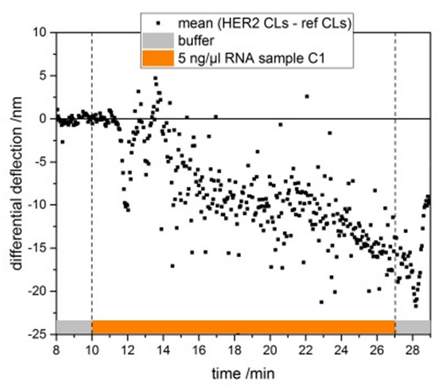
Breast cancer: stiffness histogram and HER2



A. Healthy breast tissue
Single peak in histogram

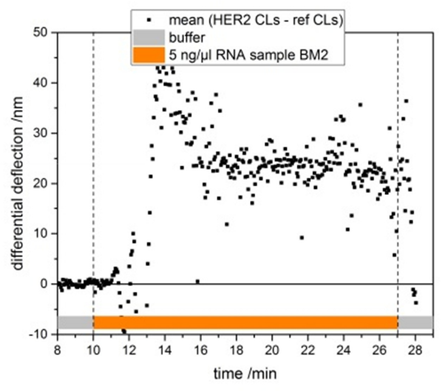
B. Invasive ductal carcinoma
characteristic 2-fold **softer peak due to invasive cancer cells**

C. Healthy MCF10A breast cells
grown on a native basement membrane as a model for the native breast epithelium (similar stiffness)



*total RNA isolated from an invasive ductal carcinoma (**most common form of breast cancer**)*

5ng/µl corresponds to 100 nM



*Total RNA isolated from a fibroadenoma (**benign tumor**)*

No amplification or labeling is required !