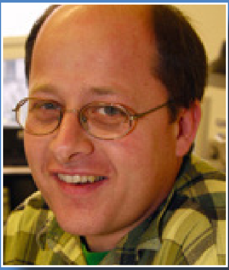
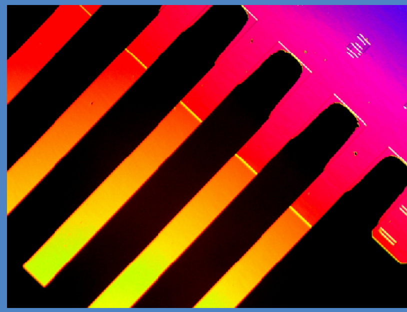


Prof. Ernst Meyer, UniBas

PATLiSci II

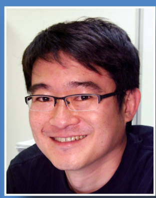
RAPID SENSING OF CANCER



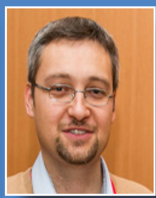
Prof. Katharina Glatz-Krieger, USB

Dr. Harry Heinzelmann, CSEM

Dr. Paul Bernard Henrich, USB

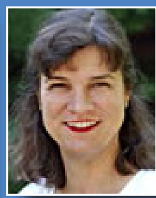


Prof. Roderick Lim, UniBas



Dr. Marko Loparic, UniBas

Prof. Nico de Rooij, EPFL



PD Dr. Rosanna Zanetti-Dällenbach, USB

What it's about…

Developing 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.

Context and project goals

The aim is to develop rapid diagnostic tools for cancer. Highly parallelized mechanical sensors are used to investigate biopsy samples in a fast and reliable way. A large number of force vs. distance curves is acquired on the biopsy sample to get enough statistics for a representative value of the elasticity (Young's modulus) of the cells under investigation. This process is highly automated, which will make the application by the medical doctor easier compared to the optical analysis of histologic specimens. The required time for this type of diagnosis will be reduced from 3 hours to minutes. Therefore, the medical doctor will receive the information promptly and will be able to decide about the therapy. In addition to the elasticity mapping, rapid biomarker tests will be developed to complement the information about the status of the tumor.

Two case studies will be done in collaboration with collaborators from hospitals.

- Diagnosis of breast cancer
- Diagnosis of melanoma cancer.

The reduction of turnaround times is achieved by the simpler specimen preparation (no histologic cuts), the automation of the data acquisition, faster approach cycles, and the parallelization. 1d-arrays of passive probes will be implemented with suitable parallelized deflection sensors. Compared to the current state-of-art, where only one probe is used to acquire 10'000 force vs. distance curves, these arrays will reduce the data acquisition by an order of magnitude. The use of optimized, large bandwidth preamplifiers and smaller cantilevers will further reduce the acquisition time of force vs. distance curves. The data acquisition and processing will deliver quantitative elasticity numbers. Rapid biomarker tests will complement the information about the status of the tumor and help the medical doctor to decide about the future therapy.

How it differentiates from similar projects in the field

In contrast to competitors, the project combines two complementary methods (force spectroscopy mapping for cell stiffness and nanomechanical cantilever sensing for biomarker detection) into a single instrumental platform, which can be handled easily.

Analysis of clinically relevant material such as biopsies instead of cultured cells or chemically synthesized biomolecules. No amplification, labeling and spiking required. Transition from proof-of-principle experiments to a clinically relevant approach.

Quick summary of the project status and key results

The project profits from its predecessor PATLiSci where basic concepts of parallel force spectroscopy and nanomechanical biomarker sensing have been validated.

Here the consortium will fabricate and use optimized cantilever arrays for both parallel force spectroscopy and nanomechanical sensing. First conclusive results on discrimination of breast cancer cells from unaffected cells in tissue using a single cantilever have already been demonstrated. A test setup for cantilever array readout has been assembled to gain experience with parallel cantilever readout for force spectroscopy.

Investigation of RNA in melanoma and wild type cells shows a clear difference in nanomechanical bending response of functionalized cantilevers, in particular the BRAF mutation which is essential for selection of appropriate treatment measures. The BRAF mutation has been successfully detected in biopsy samples. Synthetic oligonucleotide as well as biopsy samples have been investigated successfully to detect the HER2 gene relevant in breast cancer diagnosis.

Success stories

Force spectroscopy measurement and surface properties characterization of 60 native breast tissue biopsies achieved.

For the first time, successful measurements by nanomechanical cantilever sensing on melanoma and breast cancer clinical tissue specimens/biopsies were performed.

Presence in the media

M. Loparic, M. Plodinec, R. Lim and R. Sum. Potentielle medizinische Anwendungen des Atomic Force Microscope. Schweiz Med Forum 13 830 (2013)

Roderick Lim, "Swiss Nanoscience Institute - Die Erforschung der Nanowelt an der Universität Basel"
http://www.youtube.com/watch?v=ixkkfVQ2kmo

Patent

Previously existing patent on force spectroscopy on tissue samples (ARTIDIS): Plodinec, Lim and Loparic. US Patent 8,756,711 B2.

Main publications

Marija Plodinec and Roderick Y.H. Lim, Nanomechanical Characterization of Living Mammary Tissues by Atomic Force Microscopy, Mammary Stem Cells: Methods and Protocols, Springer Humana Press.

François Huber, Hans Peter Lang, Jiayun Zhang, Donata Rimoldi, Christoph Gerber, Nanosensors for Cancer Detection, Swiss Med Wkly. 2015;145:w14092.

"Squeeze out information on your cells!"