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PATLiSci RTD 2010

FNSNF

Personalized medical Diagnostics based on Nanomechanics

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Introduction

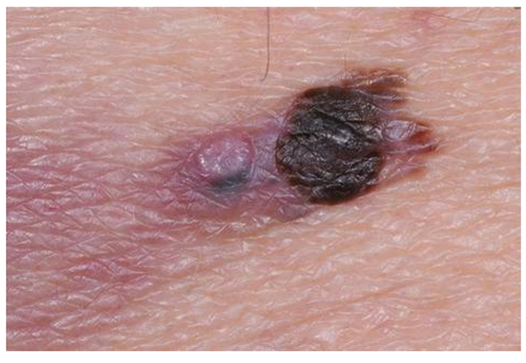


Fig. 1. Picture of a melanoma nevus

Metastatic melanoma represents one of the most difficult tumors to treat. Fortunately, the cure rate of early melanoma results in a much better prognosis and, therefore, an accurate early diagnosis of precursor lesions and of primary tumors is of crucial importance. We apply nanomechanical sensors to detect melanoma specific mutations.

We are focusing on the BRAF gene which is involved in cell growth and is mutated in melanoma cells. This mutation is found in 50 to 60% of all melanomas and recently a drug was released on the market that targets the mutated protein. By identifying this particular mutation the drug can be prescribed specifically to patients that carry the mutation.

Nanomechanical Microcantilever Biosensors

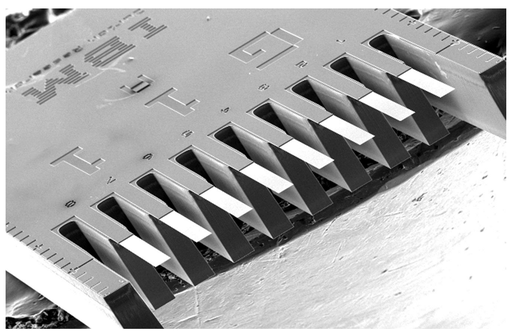
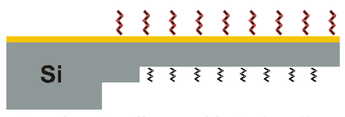


Fig. 2. Microfabricated array of eight silicon cantilevers, each coated with a sensitive layer for molecular recognition. **The molecular recognition will create a surface stress which in turn results in the bending of the cantilevers.** Such devices represent ultrasensitive sensors for the detection of biochemical reactions in liquid environments.

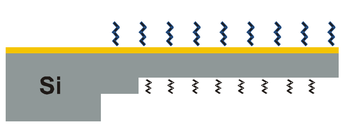
-Passivation layer (PEG Silane)

-Au/Ti layer for thiol binding

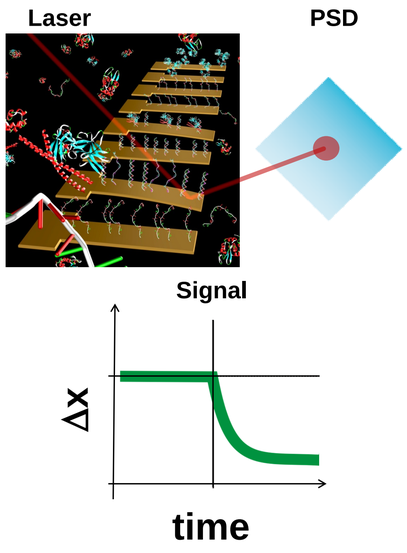
- Self Assembly layer of Thiol-oligonucleotides



-Sensing Cantilever with **Probe oligonucleotide**



-Reference Cantilever with **Unspecific oligonucleotide**



Concentration Dependent Detection of BRAF mutation in DNA

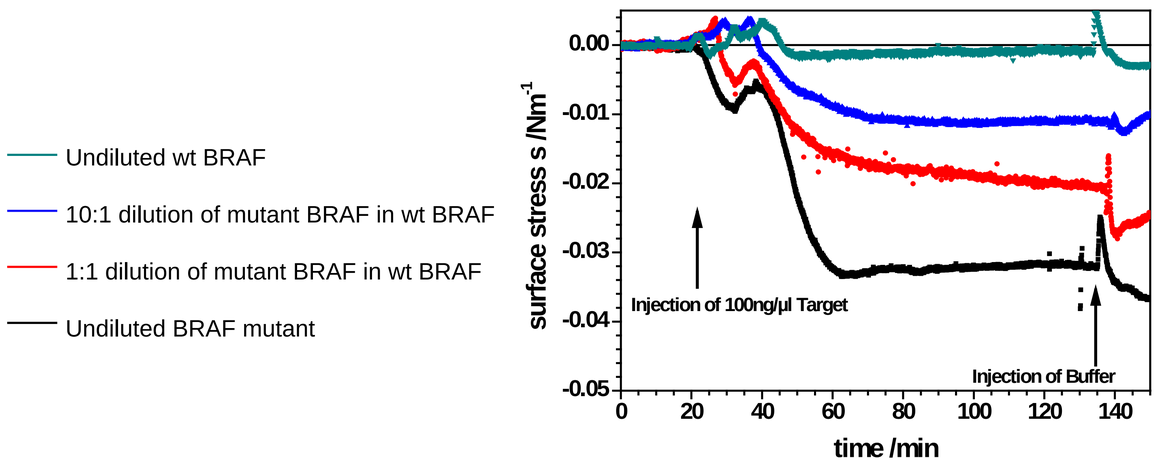
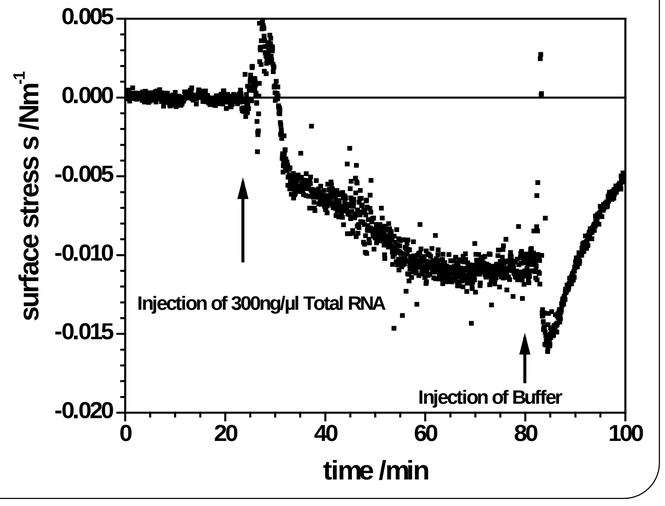


Fig. 3. Here we show sensitivity and specificity with a DNA hybridization experiment to detect the mutated gene. We use a thiol-oligonucleotide for the recognition of the mutated BRaf gene (mutE). Thereafter, DNA prepared from normal cells (wtV) and melanoma cells (mutE) were injected containing varying ratios of wtV to mutE DNA.

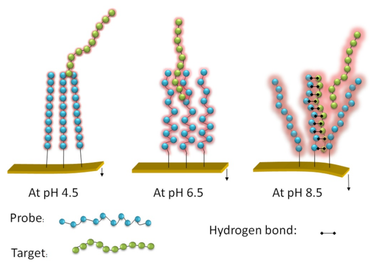
Detection of BRAF mutation in total RNA

Fig. 4. **mRNA** detection of mutated BRAF in a background of total cellular RNA isolated from cell cultures. The BRAF mutation is detected within minutes.

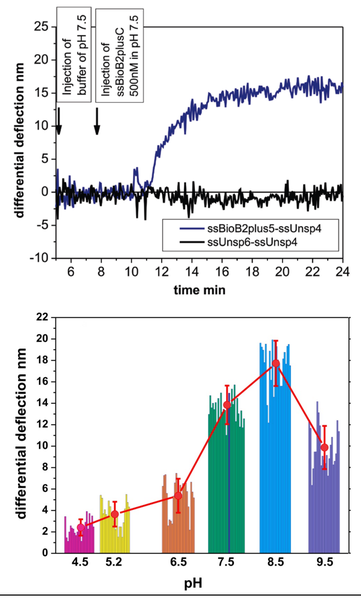


Optimization of DNA Hybridization Efficiency by pH-Driven Nanomechanical Bending

- „ideal“ pH of 8.5 for maximized accessability and DNA hybridization efficiency
- Differential Cantilever bending signal is largest at pH 8.5



J. Zhang et al, Langmuir **28**, 6494−6501 (2012)



Conclusion/Outlook

The use of RNA is another step towards lowering sample preparation steps and time, facilitating the analysis of skin cancer.

Determination of ultimate sensitivity and specificity of BRAF RNA detection and comparison with current technology.

Further reading: **Backmann, N. et al. (2005), PNAS 102(41); Zhang, J.et al. (2006), Nature Nanotechnol. 1(3); Huber, F. et al. (2006), Biosens. Bioelectr. 21(8); Braun, T. et al. (2009), Nature Nanotechnol. 4(3).**