PATLiSci –
Probe Array Technology for Life Sciences

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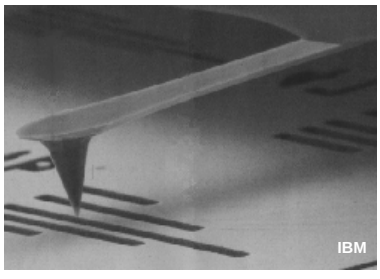
PATLiSci

csem centre suisse d'électronique et de microtechnique

PATLiSci – Probe Array Technology for Life Science Applications

Probe Technology for Cancer Research and Detection



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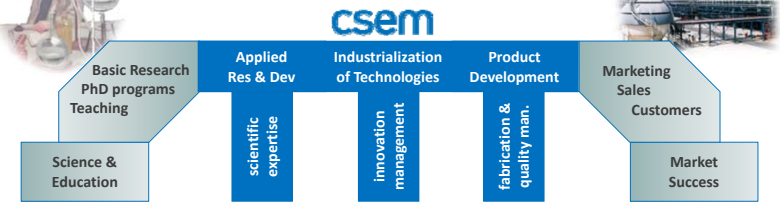
CSEM profile

Bridge from Science to Innovation



CSEM is a non for profit organization, with the mission to

develop and transfer of microtechnologies to the industrial sector,

in order to reinforce its competitive advantage

PATLiSci – Probe Array Technology for Life Science Applications

Project Partners

E. Meyer
Ch. Gerber
Uni Basel
Cantilever sensors

H. Heinzelmann
CSEM (Coord)
Probe array technologies

H.P. Herzig
EPFL-IMT
Optics

N. de Rooij, P. Vettiger, J. Brugger
EPFL-IMT, *MEMS design & fab*

H. Vogel
EPFL
Membrane prot. immobilisation

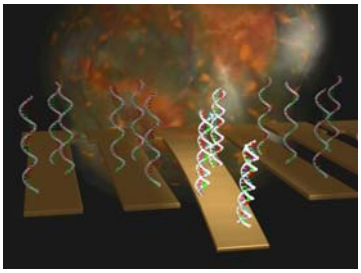
P. Romero
LICR U Lausanne
Head & neck carcinoma

D. Rimoldi
LICR U Lausanne
Melanoma

P. Renaud
EPFL-IMT
Fluidics

A. Mariotti
CePO, CHUV
Melonoma progression

Nanomechanical Sensing



detection <u>in liquids</u> :

- *BRAF mutation* in DNA samples
- capture of *melanoma cells*

detection <u>in the gas phase</u> :

- *volatile organic compounds* for early diagnosis

Cantilever is a Nanomechanical Sensor

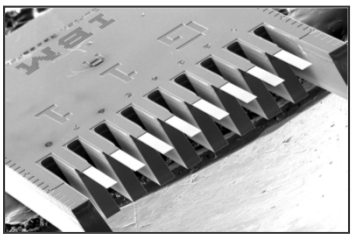
specific adsorption/docking of molecules creates mechanical stress → bending

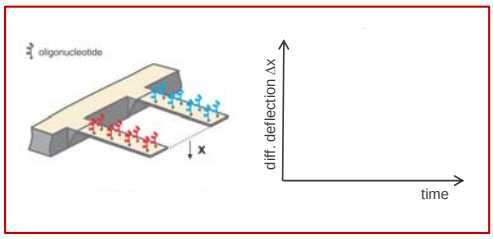
B-Raf oncogene in 50-60% of all melanoma tumors

melanoma naevus (National Cancer Inst.)

J. Fritz et al., Science **288**, 316-318 (2000); D. Schmid et al., Eur. J. Nanomedicine **1**, 44-47 (2008)

Principle of nanomechanical biosensing

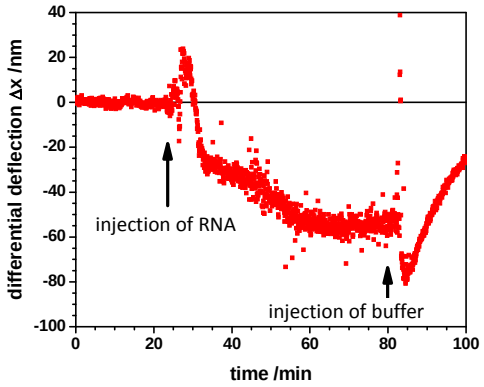




- each cantilever is functionalized for molecular recognition (ex: oligonucleotides)
- Probe cantilevers coated with a specific layer for target capture
- Reference cantilevers coated with a non-specific layer
- Differential measurement reveals net signal and cancels thermal drift

PATLiSci – Nanomechanical Sensing

Detection of single point BRAF mutation in RNA



BRAF mutation in RNA detected within minutes !

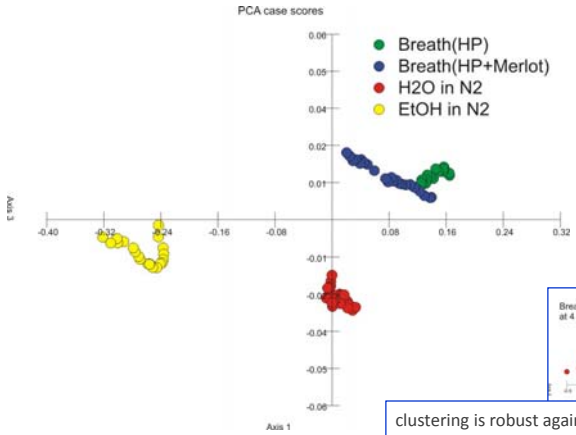
first personalized medical drug:

- 60% of melanoma patients carry the BRAF V600E mutation
- RG7204 shows a significant survival benefit in melanoma.

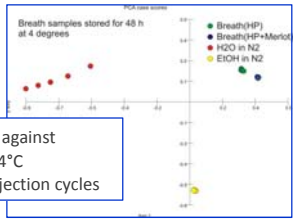
ZELBORAF available in Switzerland since Feb 2012

PATLiSci – Nanomechanical Sensing

Selectivity to breath and VOC samples



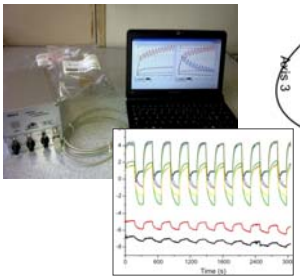
test substance



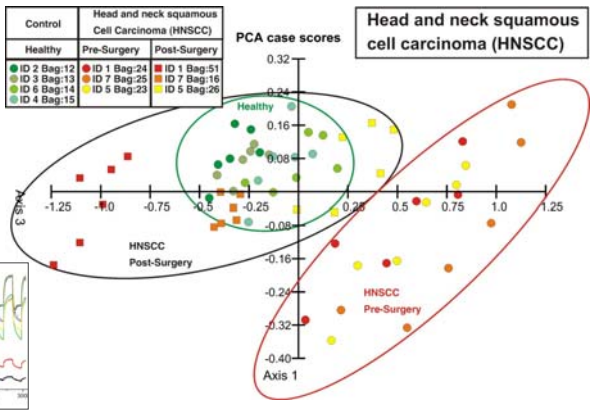
clustering is robust against storage for 48 h at 4°C and variations in injection cycles

Clinical study on head & neck cancer

diseasespictures.com

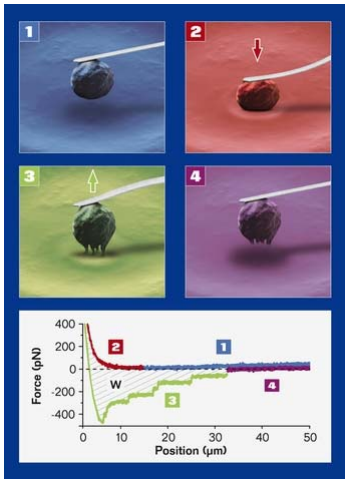


Control	Head and neck squamous Cell Carcinoma (HNSCC)	
Healthy	Pre-Surgery	Post-Surgery
ID 2 Bag:12 ID 3 Bag:13 ID 6 Bag:14 ID 4 Bag:15	ID 1 Bag:24 ID 7 Bag:25 ID 5 Bag:23	ID 1 Bag:51 ID 7 Bag:16 ID 5 Bag:26



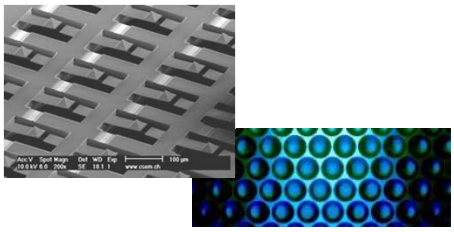
F. Loizeau, H.P. Lang et al., Proc. MEMS (2013).

Force Spectroscopy

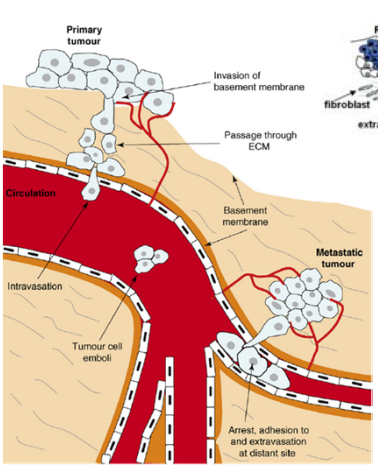


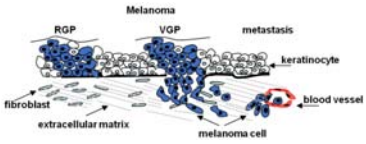
source: JPK

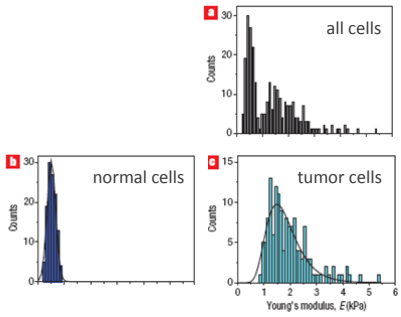
- information about adhesion proteins, cell mechanics, kinetics, …
- statistics! *parallel* force spectroscopy
  - ⇨ novel cantilever deflection readout
  - ⇨ probe array microfabrication
  - ⇨ living melanoma cell array



Motivation: metastatic cancer development



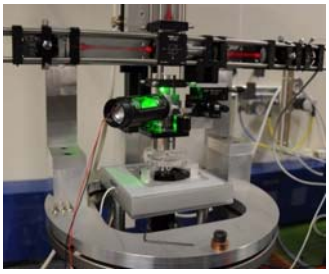


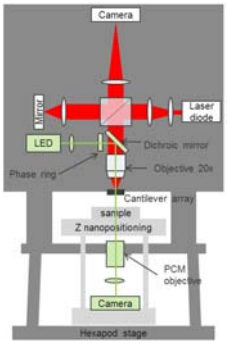


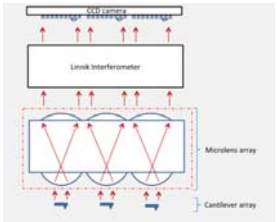
Lee *et al.*, Trends Biotechnol. 2007

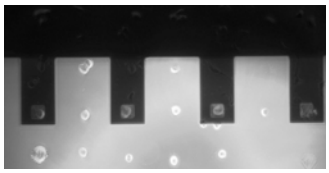
S.E. Cross *et al.*, Nature Nanotech (2007)

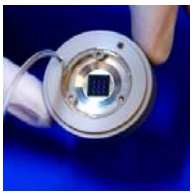
Setup and readout







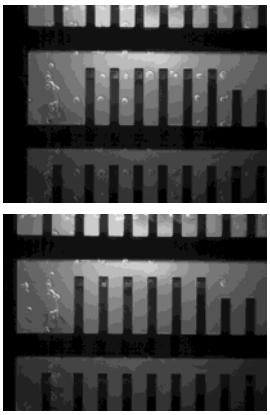


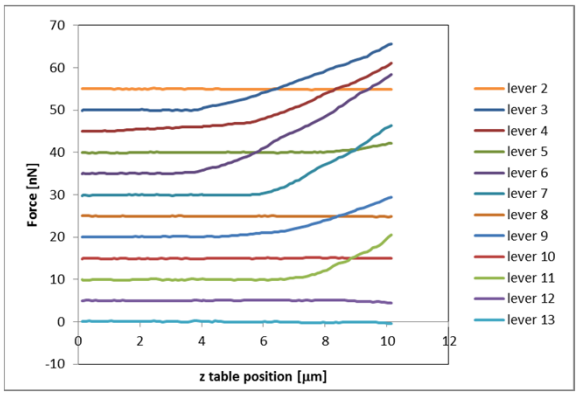


PATLiSci – Force Spectroscopy

Parallel force spectroscopy on living cells

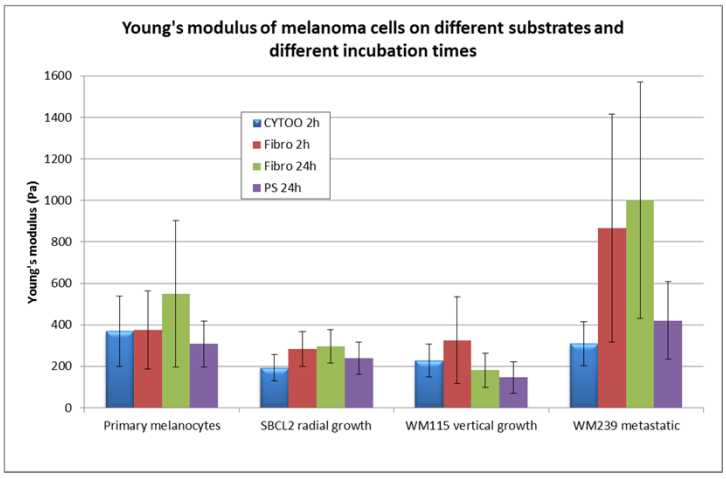
- Proof of Principle parallel force spectroscopy force on WM239 melanoma cells





PATLiSci – Force Spectroscopy

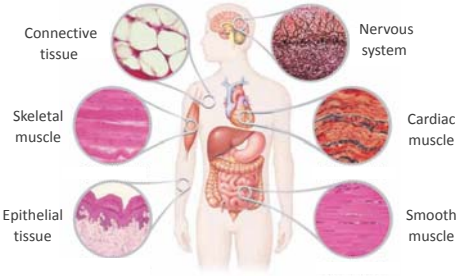
Elasticity of Melanoma cells

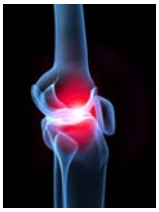


Nanotechnology and Life Sciences

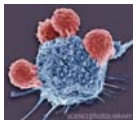
(Elastic) Tissues of the Human body

- Connective loose and dense connective tissues, blood, cartilage, bone
- Epithelial glandular, epithelia (e.g. skin)
- Muscular cardiac, skeletal, smooth
- Nervous central and peripheral nervous systems





- Osteoarthritis
- Atherosclerosis
- Tendinitis
- Cancer
- Pulmonary fibrosis



Nanotechnology and Life Sciences

BioIndenter

csm Instruments KTI/CTI

- a new instrument for indentation of soft biological tissues
- under physiological conditions, with optical control
- validation experiments on cartilage, tendon, cornea, …
- available now!

→ http://www.csem.ch/bioindenter

Summary

- Nanomechanical sensor technology is promising
  - for detection of specific substances (here: biomarkers)
  - for the determination of mechanical properties of very small objects (here: cells)
- PATLiSci II project: further developing sensing technology (diagnostics, therapeutics)
  - mechanical properties on tissue biopsies at high lateral resolution (diagnostics)
- Bioindenter (currently commercialized)
  - tool for investigating tissue rather than cells (diagnostics, …)
- more technologies @CSEM: tissue models for toxicology tests, tissue reactors, etc

Nanotechnology and Life Sciences

BioIndenter

csm Instruments KTI/CTI

Thank you for your attention.