



Forschung Austria, Alpbach, 22.8.2007

# Magnetic Nanoparticles for Biomedical Applications: An Example of Knowledge Transfer

Nadezhda Kataeva\*, Hubert Brückl

Austrian Research Centers, Division Nano-System-Technologies, Vienna

\*N. S. Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Moscow

[www.nanosystemtechnology.com](http://www.nanosystemtechnology.com)



Nanotechnology

Biotechnology

# Where do you come from ?



Austria 16  
international 11 (in ARC in total: 92 out of 524 in 2006)

1  
Russia

1  
Canada



1  
Albania

1  
Hungary

1  
Greece

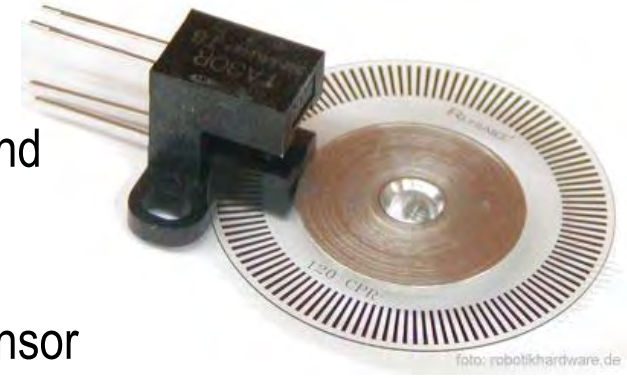


Vienna



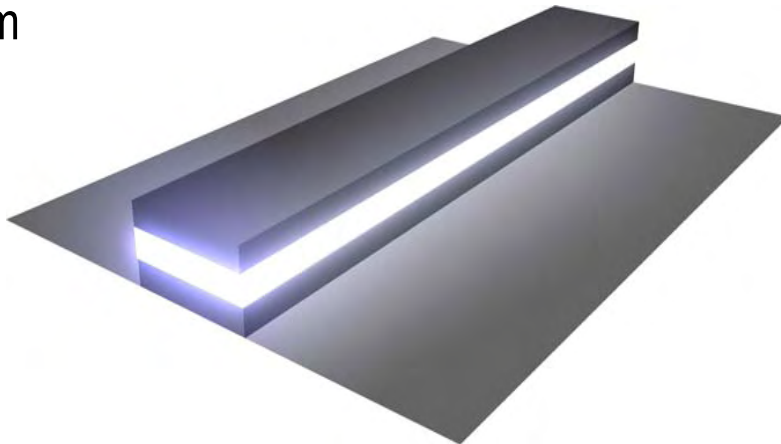
## *NanoSensors*

- magnetoresistive sensors and memories: GMR, TMR
- self-organized nanowires
- bio-inspired acceleration sensor
- gas sensors (CO, CO<sub>2</sub>)
- IR bolometer



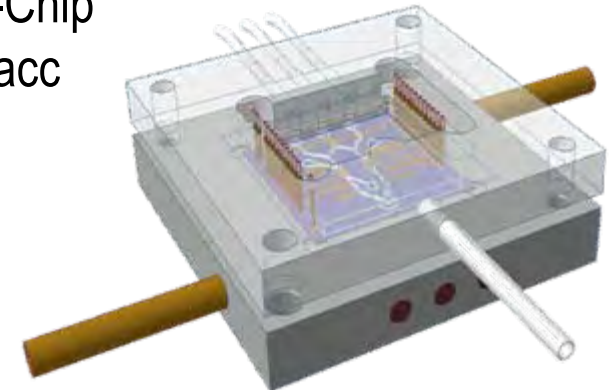
## *Integrated photonic devices*

- sensors
- telecom



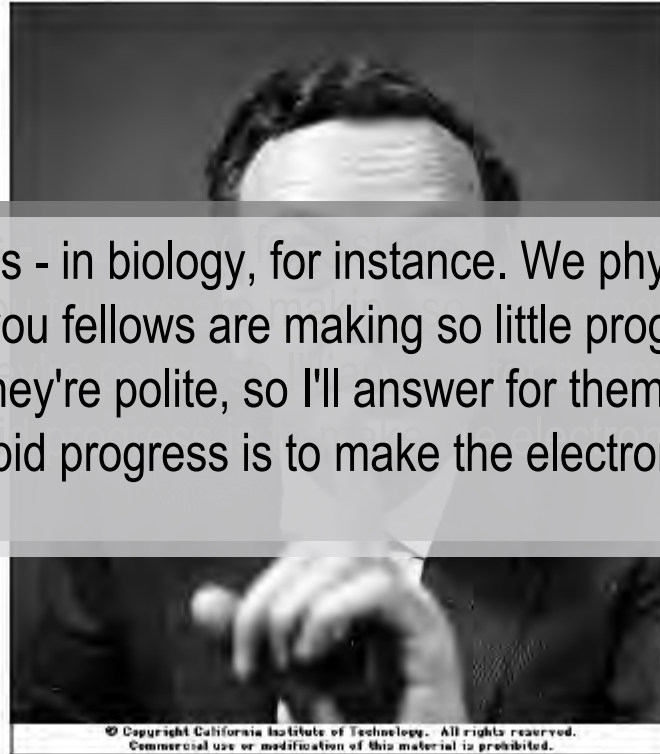
## *On-chip diagnostics*

- MagLab-on-a-Chip
- Cell-Chip
- Hybacc





1959: „There is plenty of room at the bottom“

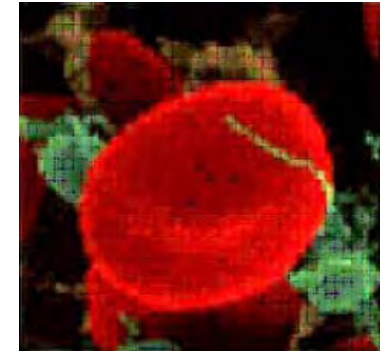
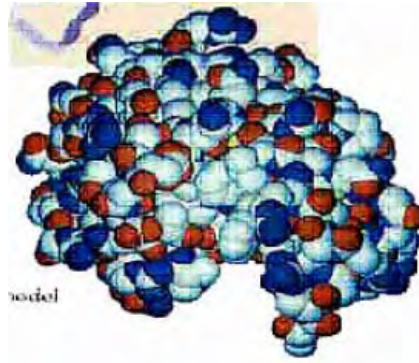
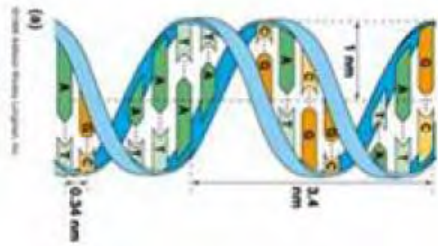


We have friends in other fields - in biology, for instance. We physicists often look at them and say, "You know the reason you fellows are making so little progress?" They could answer us - but they're polite, so I'll answer for them: "What *you* should do in order for *us* to make more rapid progress is to make the electron microscope 100 times better."

- "Kleinheit" ermöglicht neue Funktionalitäten
- Eroberung des Nanokosmos für technische Anwendungen



o  
r  
g  
a  
n  
i  
c



DNA base

DNA turn

Protein

Virus

Bacteria

Cells

0.1nm

1nm

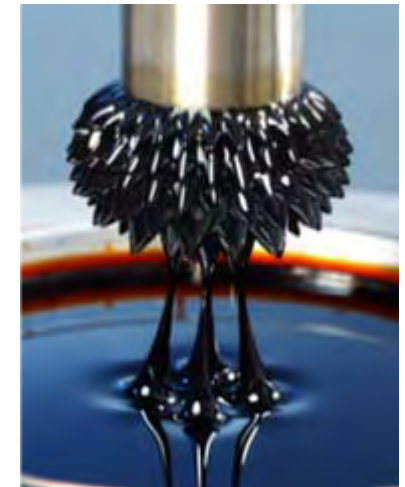
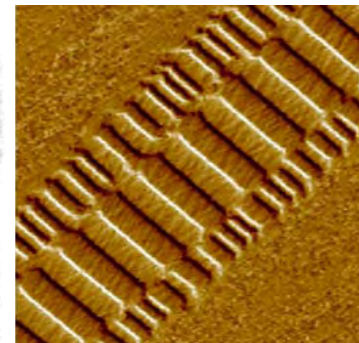
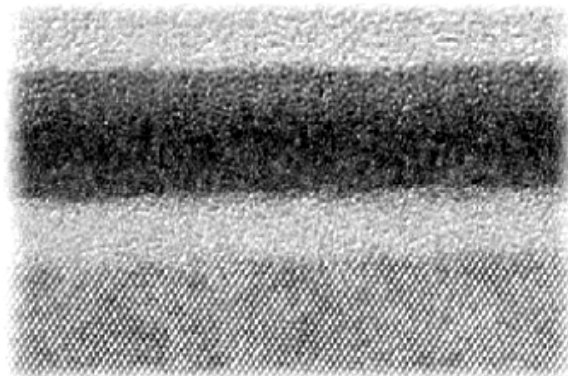
10nm

100nm

1 $\mu$ m

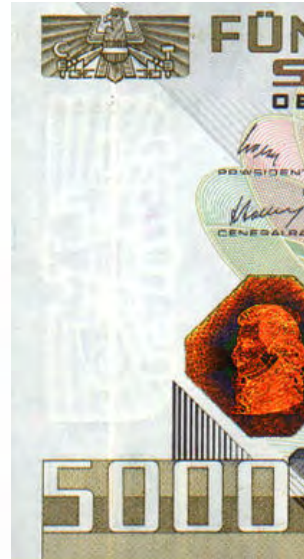
10 $\mu$ m

i  
n  
o  
r  
g  
a  
n  
i  
c





- lubricant (shock absorber, ..)
- magnetic ink (security feature on banknotes, ..)





Notebook, PC, etc



Mobile Phone



Palm Top

- magnetic recording (particulate media, annual turnover: 50 Milliarden US\$)
- magnetic computing by interacting magnetic particles (logic)
- cleaning of wastewater
- magnetic glue (AC heating for hardening)
- polymer shape memory initiated by AC heating with magnetic nanoparticles
- magnetic aerogel (embedded NdFeB particles in light, transparent material)



## Magnetic beads are already applied in

- ❖ cell separation
- ❖ purification
- ❖ magnetofection

Magnetic particles label cancer cells by specific binding. The targeted cell can be separated by a magnet (one out of  $10^9$ ).



## Magnetic beads and nanoparticles are intended to find application in

- ❖ biochip sensors
  - DNA/RNA analysis (R&D, med. industry, clinics)
  - disease-causing agents (infection)
  - environmental pesticide (agriculture, water control, ..)
  - recognition of BC weapons (military)
- ❖ contrast enhancement in imaging by MRI, TEM, SQUID, ...
- ❖ cancer treatment (hyperthermia, selection of malign cells)
- ❖ drug delivery by gradient fields (e.g. to inner ear, blood-brain barrier, ..)
- ❖ on-chip manipulation
  - ❖ reaction acceleration: hybridization of DNA in biochips
  - ❖ basic research: measurement of bond forces
- ❖ ...
- ❖ single molecule detection and manipulation

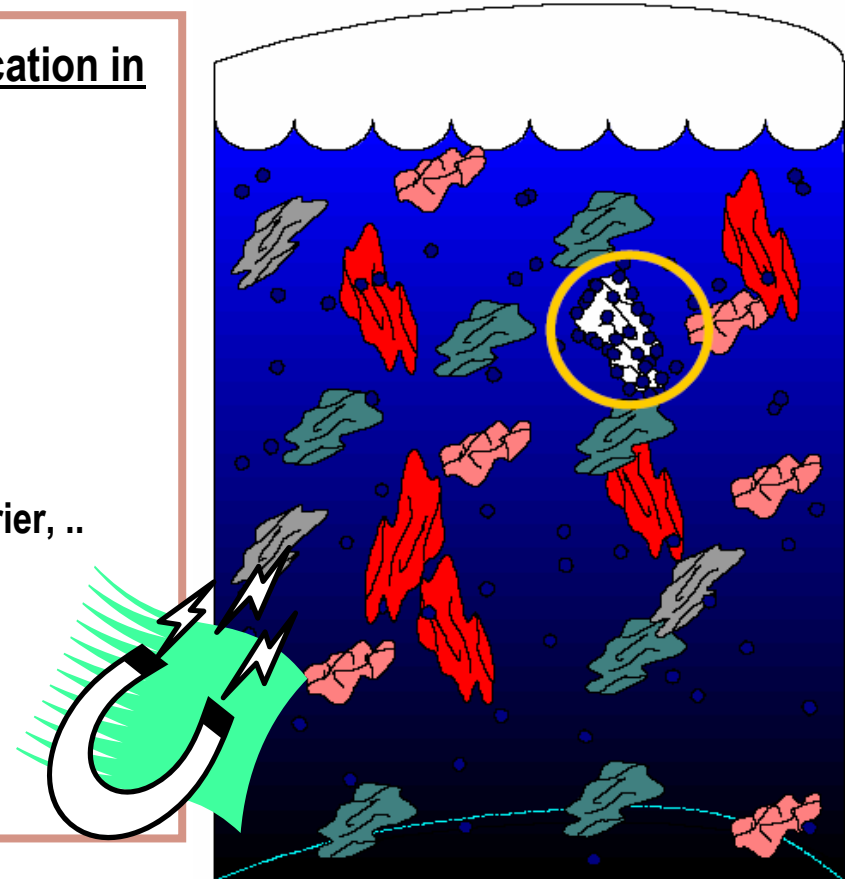


image from NVE Inc.



ESF-EMBO Symposium

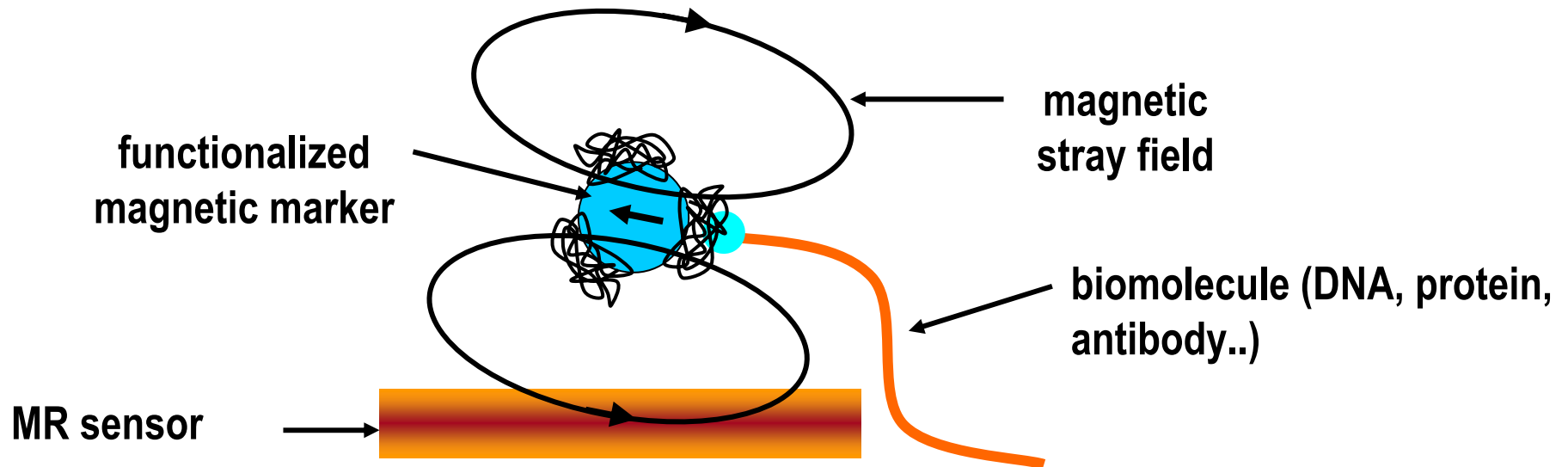
# Biomagnetism and Magnetic Biosystems Based on Molecular Recognition Processes

Hotel Eden Roc, Sant Feliu de Guixols (Costa Brava) • Spain  
22-27 September 2007

**Vancouver, Canada May 21-24, 2008**  
**7<sup>th</sup> International Conference**

## Scientific and Clinical Applications of Magnetic Carriers

A meeting devoted to the preparation, analysis, use and application of magnetic microspheres and nanoparticles in basic and clinical research.

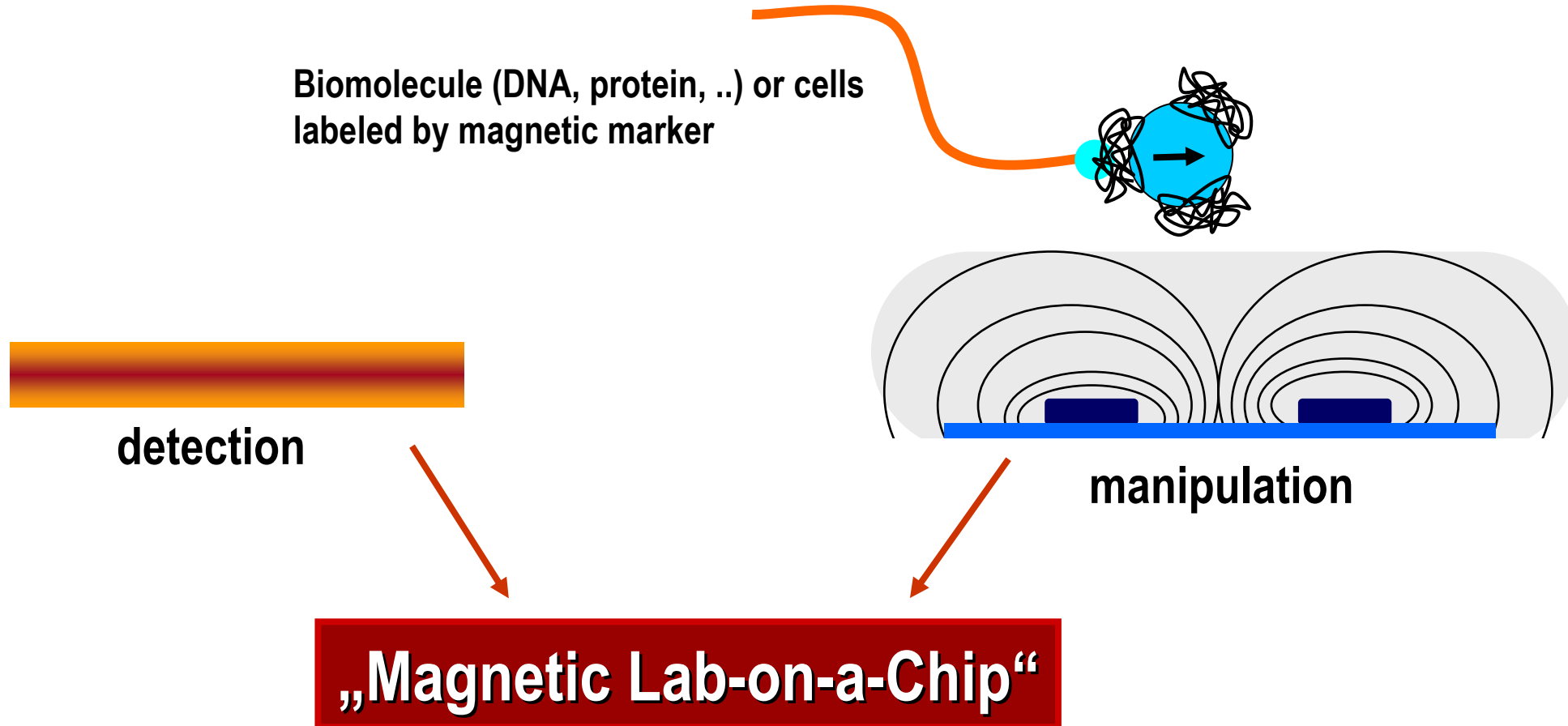


## Advantages

- electronic signals directly available
- small automated detection units
- usable for biochip, disposable test kits, ..

D. Baselt et al., Biosensors and Bioelectronics 13, 731 (1998)

H. Brückl, M. Panhorst, J. Schotter, P.B. Kamp, A. Becker, „Magnetic particles as markers and carriers of biomolecules“, IEE Proc.-Nanobiotechnol. 152, 41 (2005)



H. Brückl, M. Panhorst, J. Schotter, P.B. Kamp, A. Becker, IEE. Proc.-Nanobiotechnol. 152, 41 (2005)



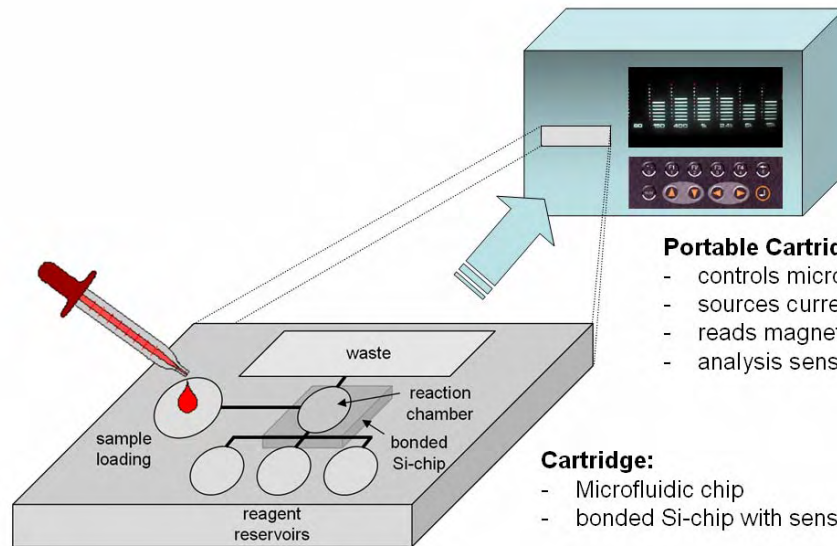
## Aim:

a) magnetic detection in a lab-on-a-chip prototype

b) early recognition of potential sepsis by

- detection of pathogenic bacteria in human blood
- messengers of immune system (cytokines)

c) biomarkers: Interleukin-4, -6, -10, Tumornekrosefaktor- $\alpha$  (TNF- $\alpha$ )

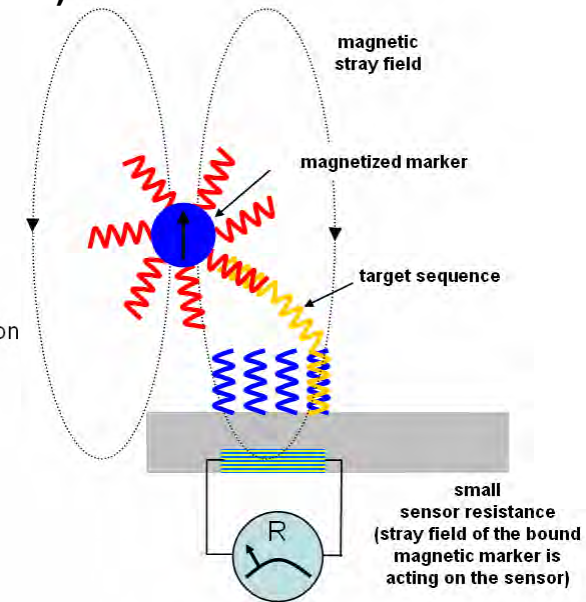


### Portable Cartridge-Reader:

- controls microfluidics
- sources currents for marker manipulation
- reads magnetoresistive sensors
- analysis sensor signals

### Cartridge:

- Microfluidic chip
- bonded Si-chip with sensors



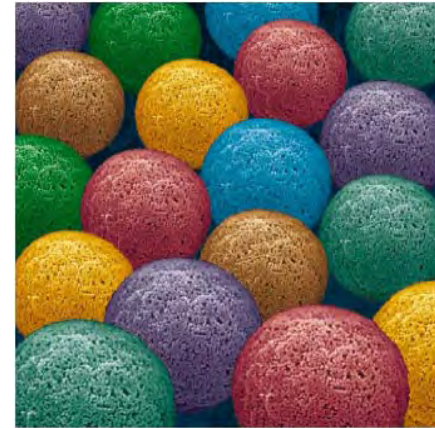
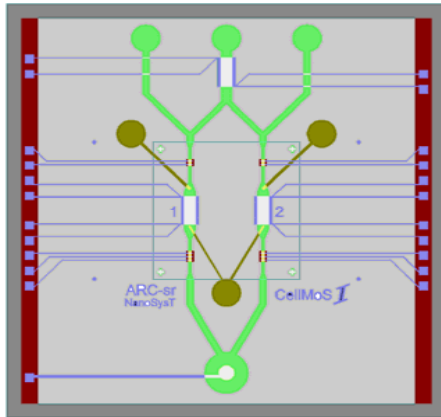
ARC  
NanoSysTech

Aureon  
Biosystems GmbH

Microinnova  
Dr. Kirschneck KEG



# From magnetic Lab-on-the-Chip to magnetic Lab-on-the-Bead



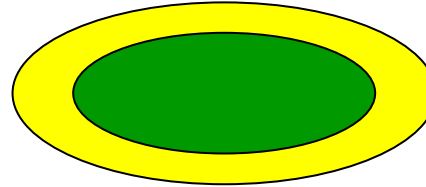
challenge:  
to get rid of substrate surface, microfluidic  
constriction, washing steps, PCR

vision: bead is reaction area & detection entity

- easier fabrication (no chip surface preparation)
- easier fluidics
- easier chip environment
- substrate-independent detection (no embedded sensors)



- **Vision of Lab-on-a-Bead** is possible with magnetic elliptical core/shell nanoparticles.



- **Technological challenge:**
  - There is a tremendous demand for **suitable magnetic particles** for all the different applications:
    - **in sufficient quality**
    - size homogeneity
    - core/shell
    - non-agglomerating
    - magnetic moment
    - anisotropy
    - toxicity
    - functionality (multifunctional)







# N.S. Kurnakov Institute of General and Inorganic Chemistry Russian Academy of Sciences



31, Leninsky Ave.,  
Moscow, Russia  
Tel. +7 (495) 952-39-48  
[www.ionh.ru](http://www.ionh.ru)



Founded: in **1934**

Number of employees: **~400**

Doctors of Sciences: **> 240**

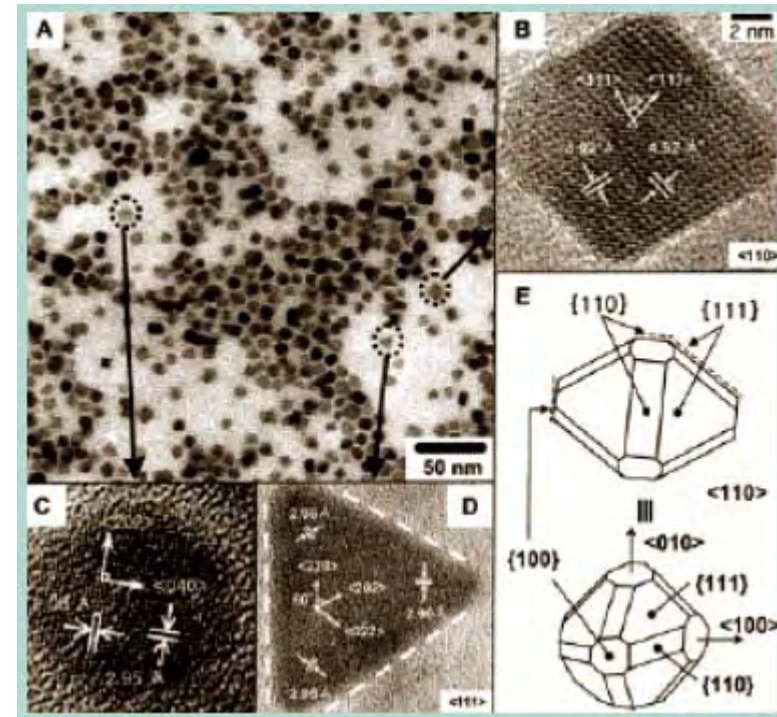
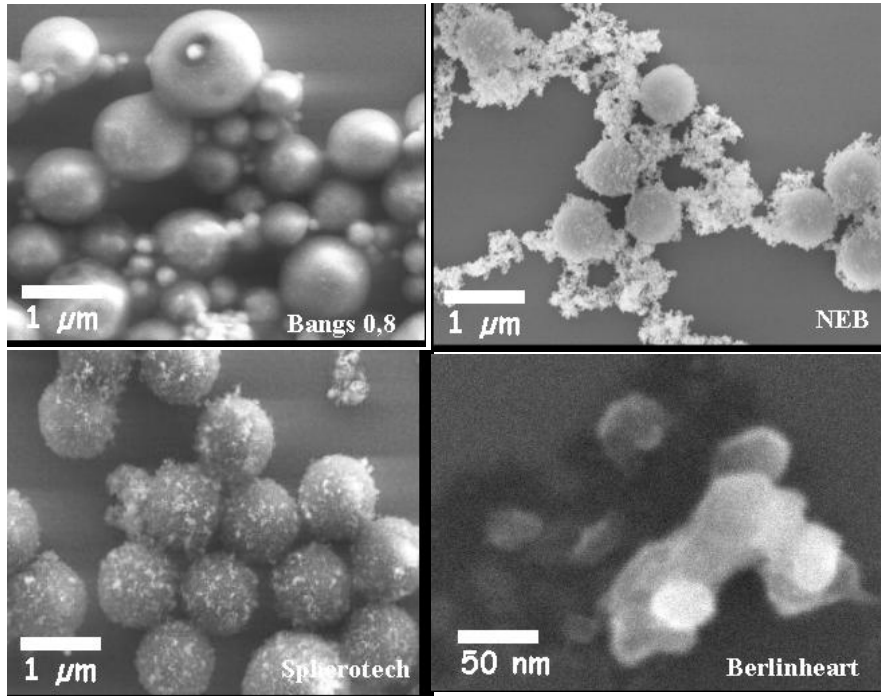
Academics and  
Corresponding members: **>20**

Students: **~ 80**

Number of publications: **~ 400**  
articles/year

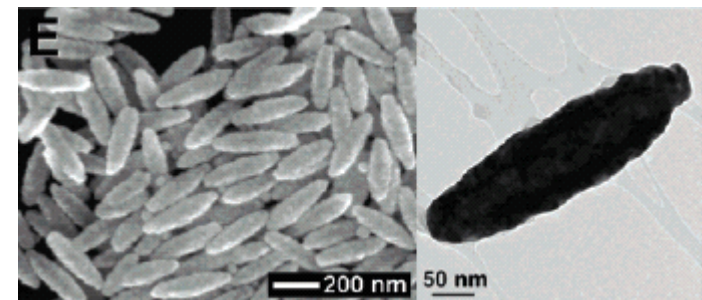
## The basic scientific fields of scientific activity of institute

- Synthesis and study of new substances and materials
- Chemical structure and reactionary ability of coordination compounds
- Theoretical fundamentals of chemical technology and development of effective chemical-engineering processes
- Methods of the chemical analysis and research of substances and materials



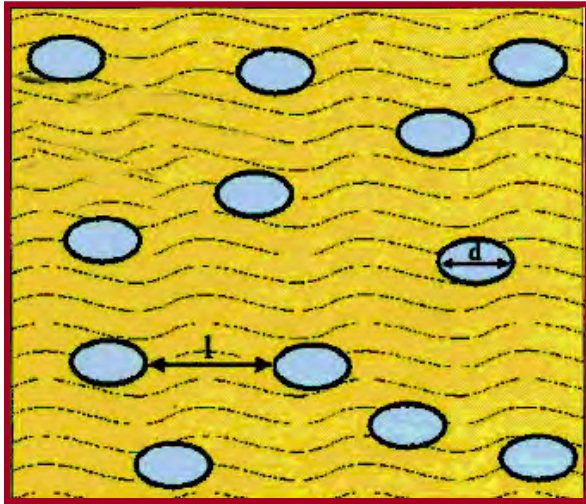
fm NP: J. Cheon et al., JACS 126, 1950 (2004)

- ferro- or paramagnetic beads, wires or rods in solvents
- size: few nanometers up to microns
- wide variety of materials (Co, Fe, Fe<sub>3</sub>O<sub>4</sub>, ..)
- chemical surface modification



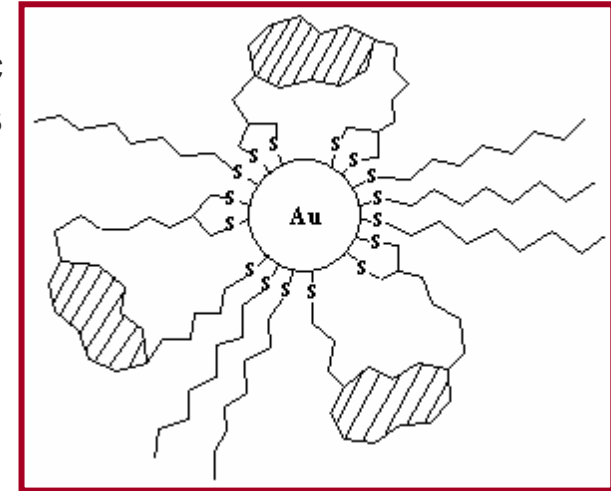
Hematite / Au

Hui Wang et al., Nanoletters 6, 827 (2006)



In the matrix

By organic ligands



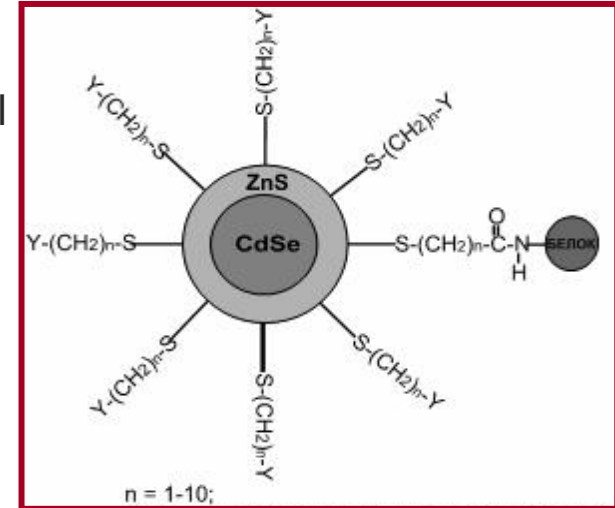
On the surface of nanogranules



Core/shell

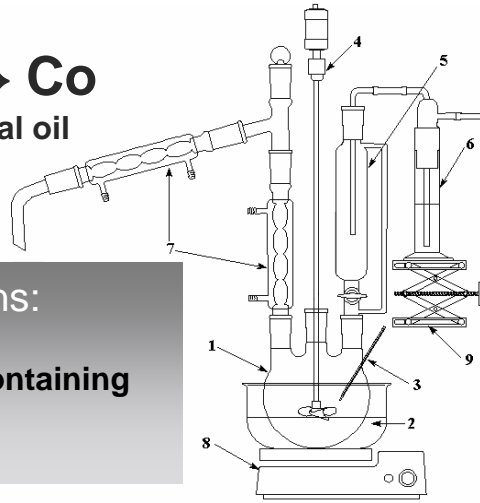
NG (nanogranules):  $\text{SiO}_2$ ,  $\text{Al}_2\text{O}_3$ , polymers, nanodiamonds, nanotubes and etc.

NP (nanoparticles): Ag, Au, Pd, Pt, Ni, Cu, Fe, Co,  $\text{MO}_x$ , CdS, CdSe and etc.





## Formation of Co-nanoparticles in mineral oil



Reaction conditions:

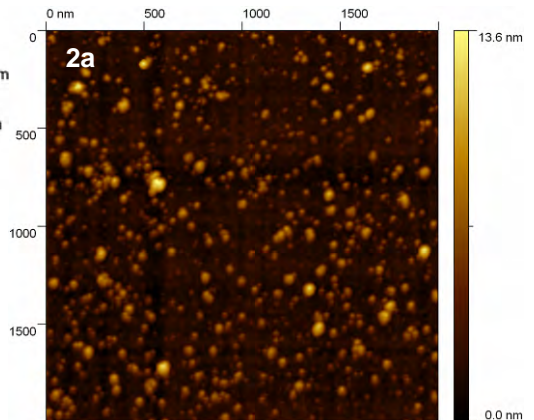
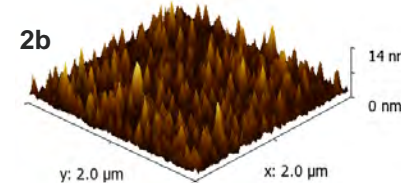
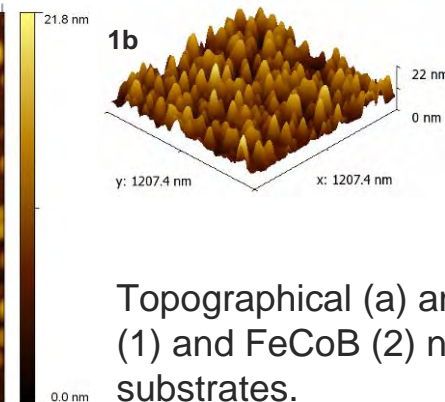
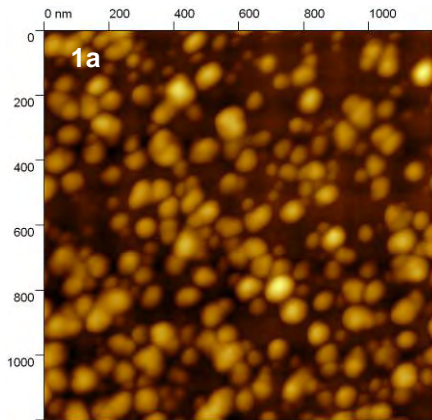
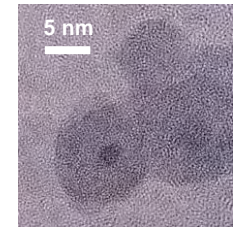
- Mineral oil
- Solution of metal containing compounds
- $t = 300 - 320 \text{ } ^\circ\text{C}$

## Formation of FeCoB-nanoparticles in water solution



Reaction conditions:

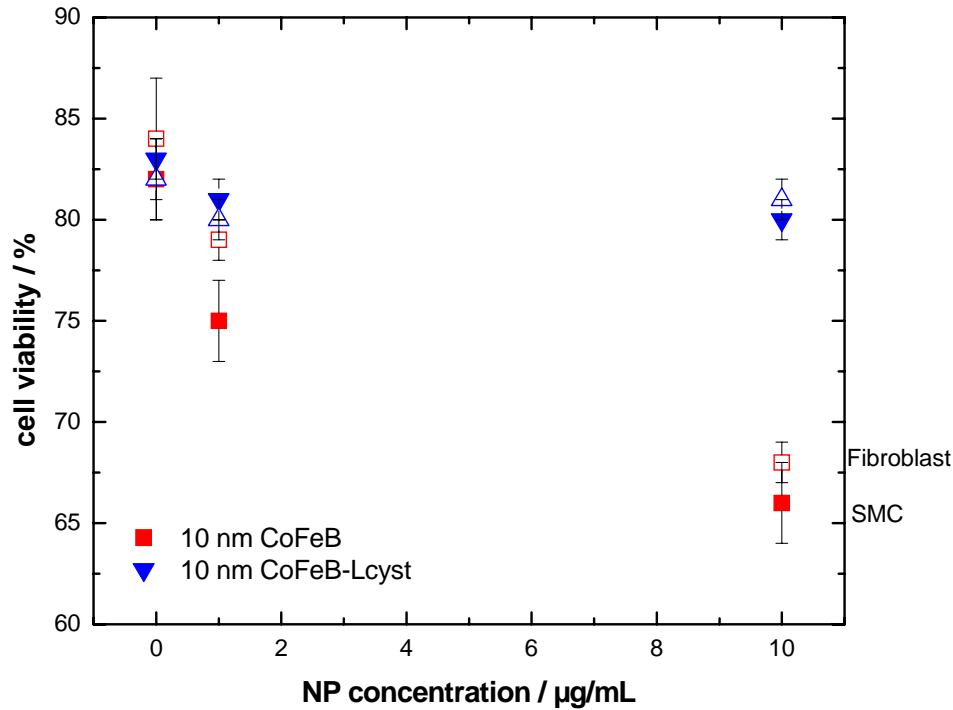
- Fe : Co = 1:1
- concentration of Fe- and Co-solution 0.05-0.2 M
- concentration  $\text{NaBH}_4$  0.5-2.0M



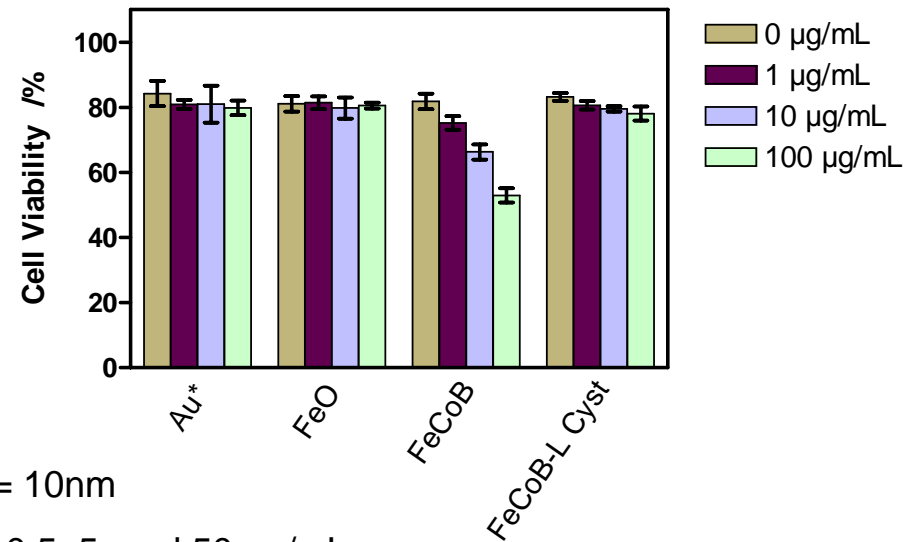
Topographical (a) and 3d (b) images of Co (1) and FeCoB (2) nanoparticles on mica substrates.



## Primary Human Cells Smooth Muscle Cells and Fibroblast Cells

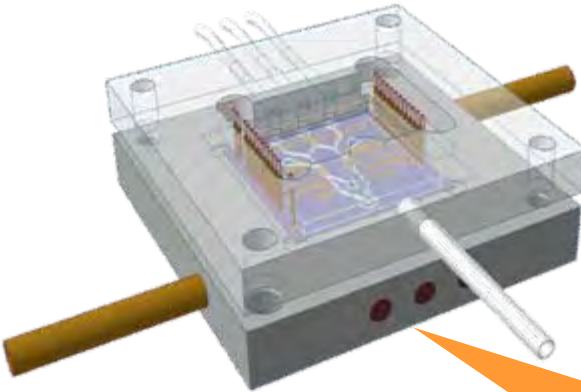


## Fibroblast



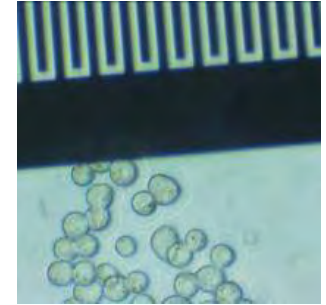
Diameter = 10nm

\* [Au nanoparticles] = 0, 0.5, 5, and 50 µg/mL

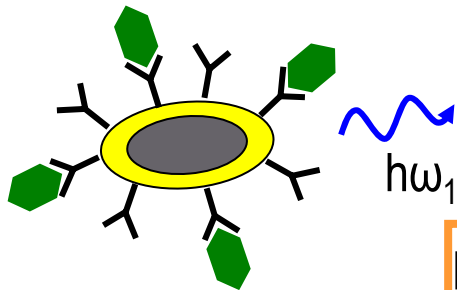


MagLab-on-a-Chip  
(Sepsis diagnosis)

Cell-Chip  
(risk assessment)

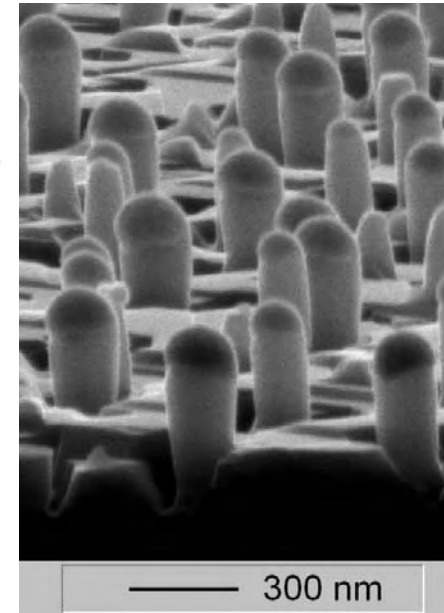


**magnetic nanoparticles  
at ARC, Nano-Systemtechnologies**



MagLab-on-a-Bead  
(pat. pend.)

bio-inspired  
acceleration sensor





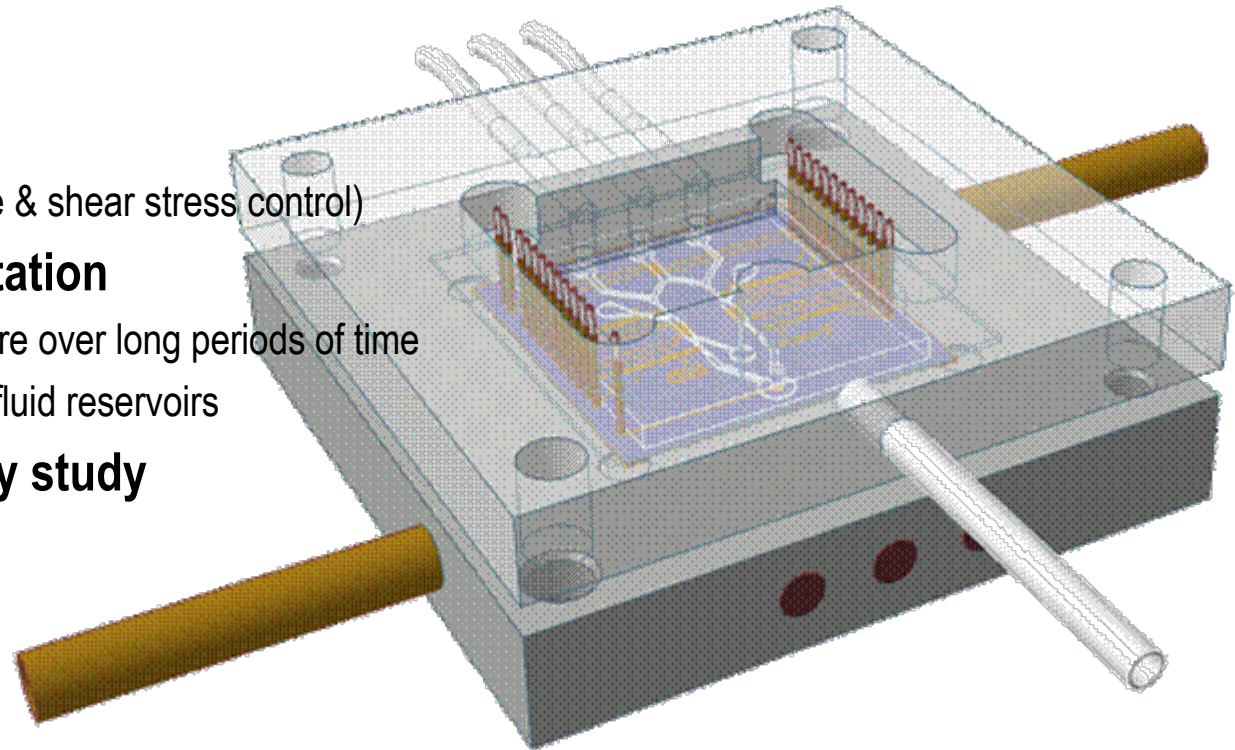
---

Any questions ?



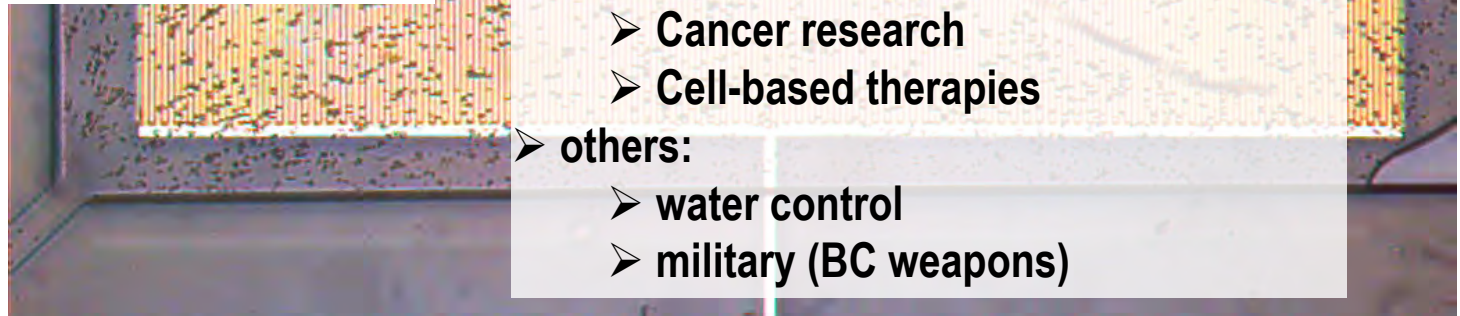
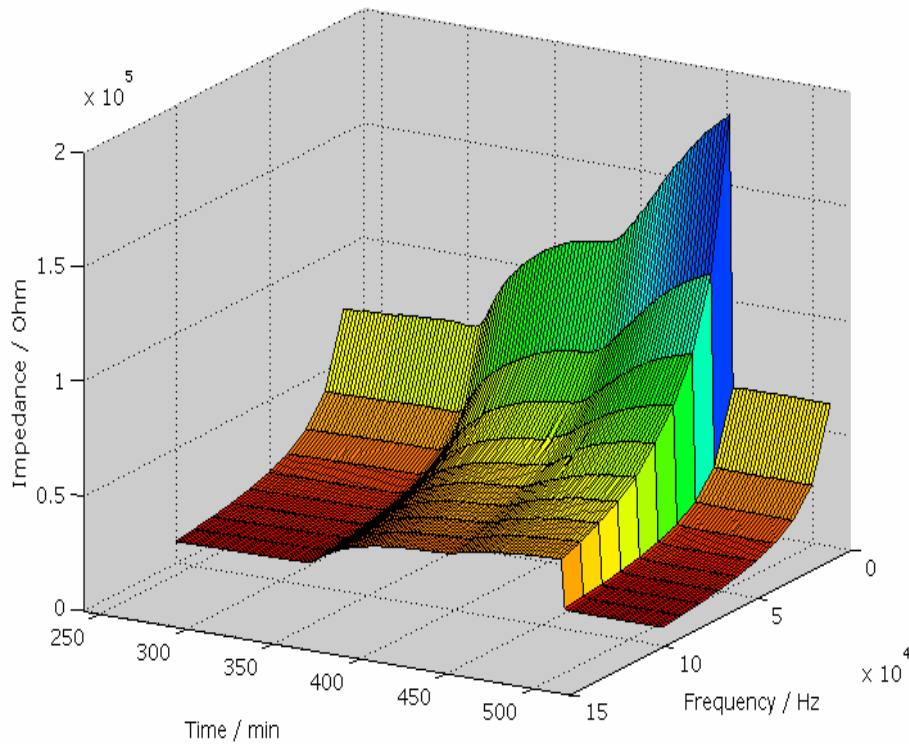


- **Micro-electromechanical systems (MEMS) Technology**
  - Two-component chip using different materials (glass & polymer)
- **Multiparameter detection platform**
  - High-density interdigitated capacitors ( $\mu$ IDC) and band electrodes: contactless
  - Optical window for microscopy
  - Integrated reference sensors
- **Integrated microfluidic system**
  - Three input reservoirs (flow rate & shear stress control)
- **Heating system and pumping station**
  - Maintaining constant temperature over long periods of time
  - Three individually addressable fluid reservoirs
- **Continuous & long-term viability study**





On-chip growth of candida albicans



## Main applications:

### ➤ Biotechnology

- Pharmaceutical development
- Strain selection with best qualities
- Lead finding
- Screening for drug performances

### ➤ Health care

- Toxicology
- Alternative to animal testing
- Medical diagnostics
- Detection & monitoring of diseases

### ➤ Biomedical research

- Cell responses to pH, ions, stress...
- Stem cell research
- Cancer research
- Cell-based therapies

### ➤ others:

- water control
- military (BC weapons)