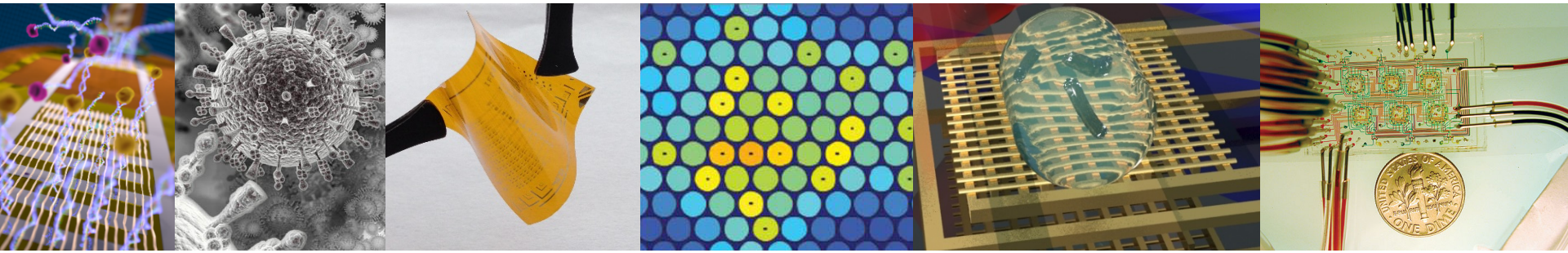
1st ICMA 22.04.2021

HZDR
HELMHOLTZ ZENTRUM
DRESDEN ROSSENDORF



Nanoscopic biosensors in microfluidics

High Potential Program supported by

Institute of Radiopharmaceutical Cancer Research

and

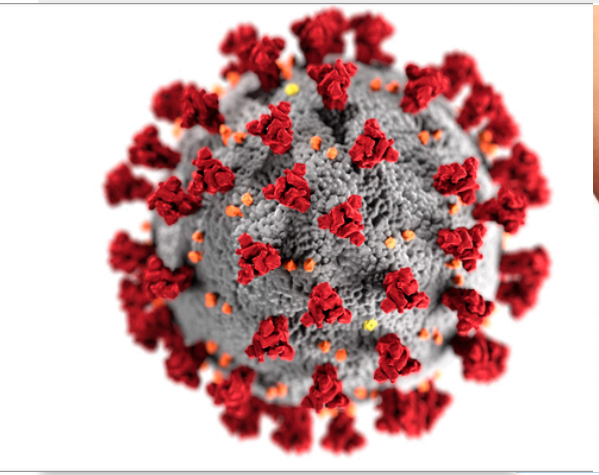
Institute of Ion Beam Physics and Materials Research, HZDR

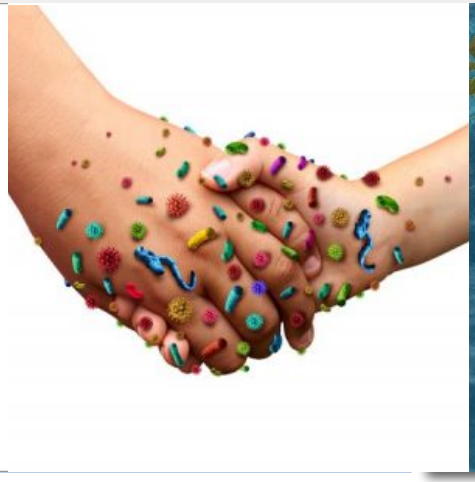
Larysa Baraban
HZDR

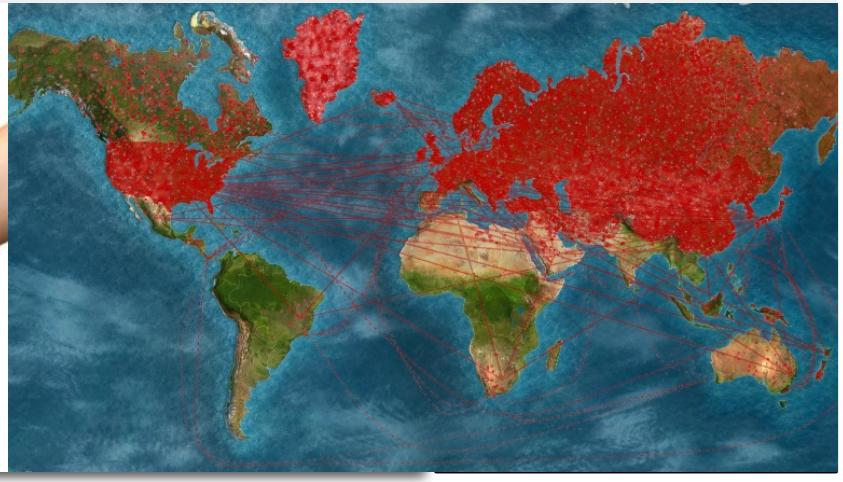
DRESDEN
concept

Dresden: Baroque and Hightech

New approaches for an early detection and therapy





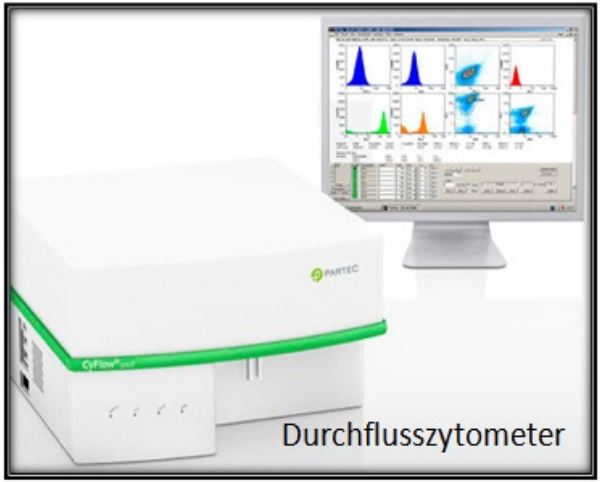


Challenge: low concentration of *e.g.* cancer cells circulating in the human blood; fast spreading diseases; time consuming clinical viral cell culture or antibody staining; global spreading of the microbes drug resistance

State of the art solutions available at the market


qRT-PCR

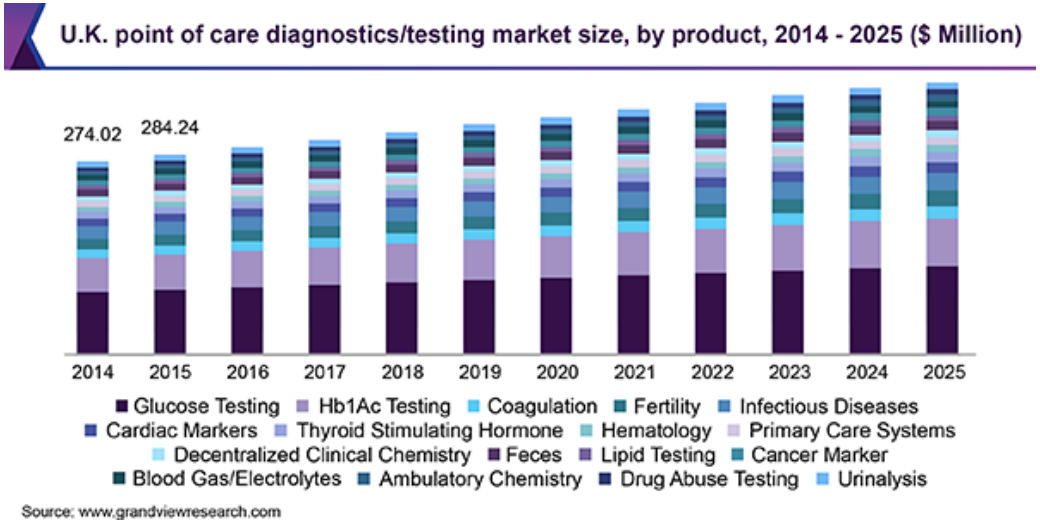
Immunoassay

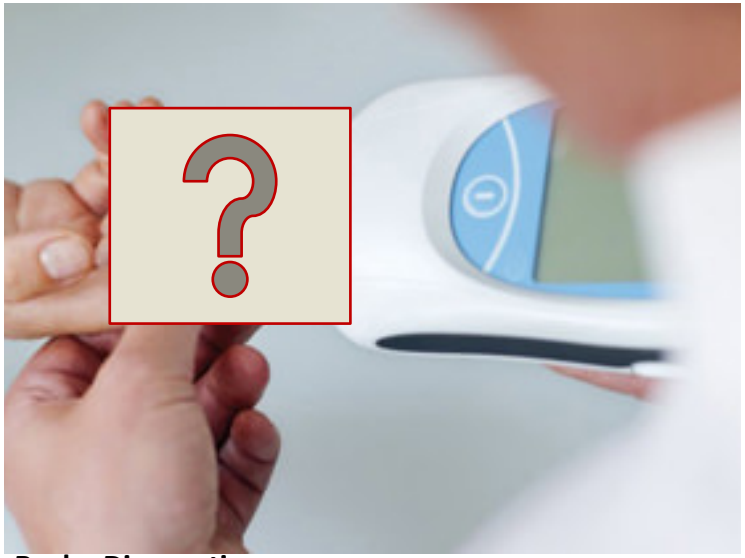


Durchflusszytometer

- Optical detection concepts are widely used
- Devices are bulky and relatively expensive
- New detection technologies are needed: **miniaturized and cost efficient**

Towards novel format of the molecular testing

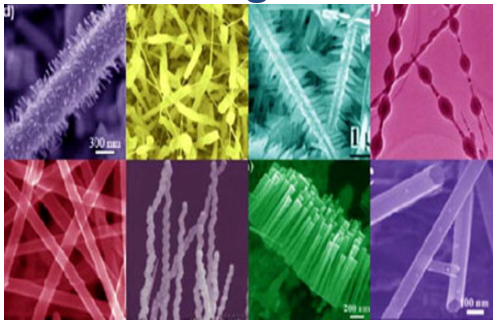




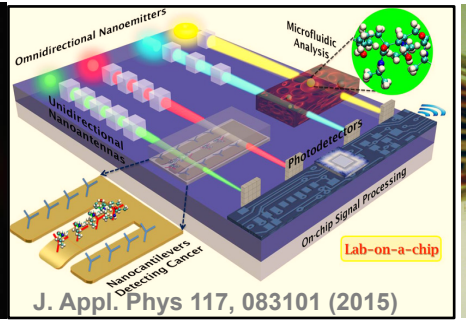
Roche Diagnostics

New technologies for future diagnostics

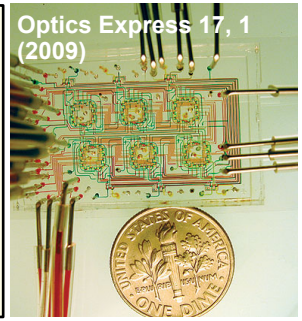
Nano and organic materials

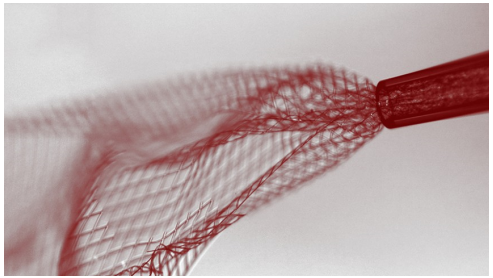


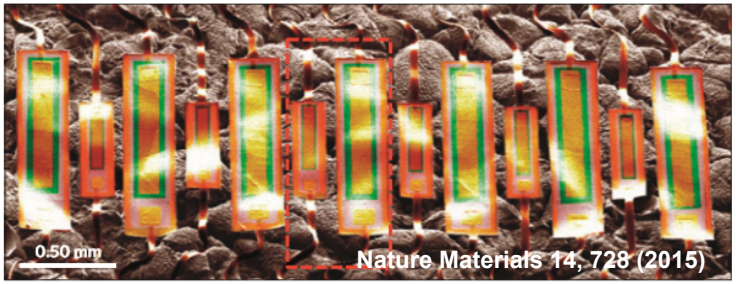
Bio-integrated electronics

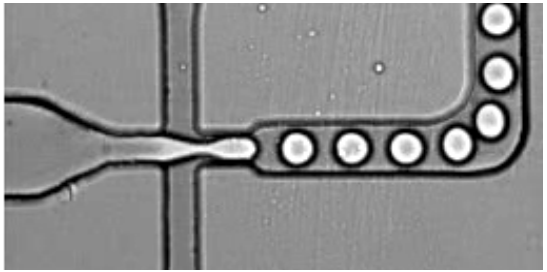


Microfluidics







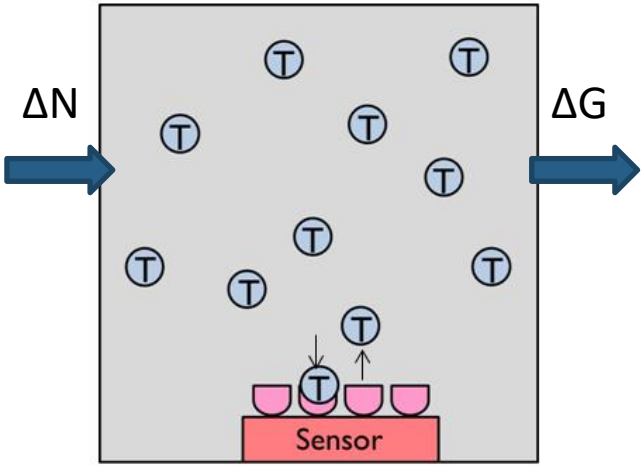


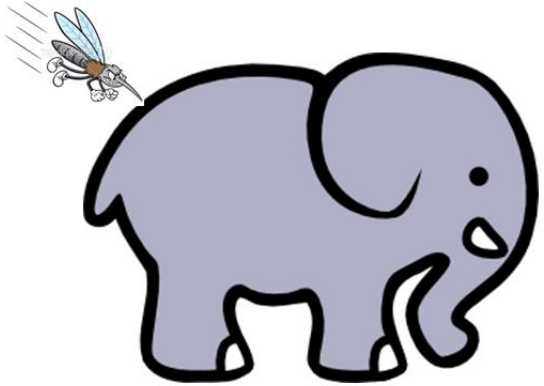
→ High sensitivity → Quick analysis → Portability → Cost efficiency

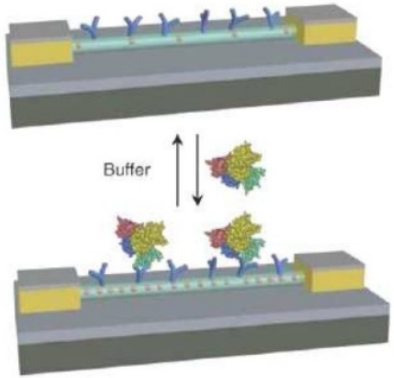
Why nanosensor?

Sensitivity issue

$\Delta G/\Delta N = ?$





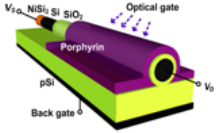


Limit of detection

Need for miniaturized sensors

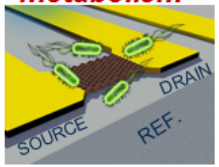
Point of care from the nanoscale

Bioelectronics

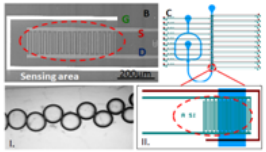


Nano Research December 2014

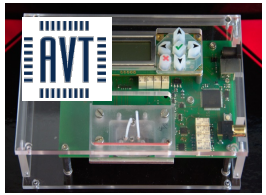
Bacteria Metabolism

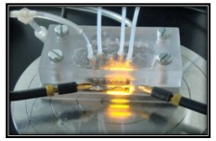


Droplets & FET sensor

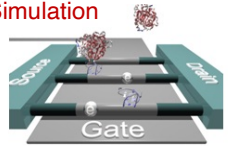


Electronics

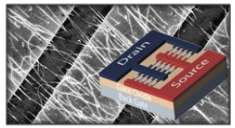


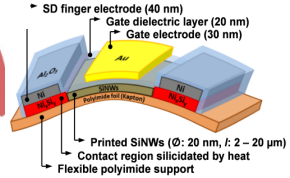


Simulation

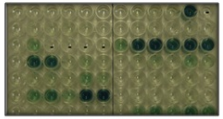


Micro- and Nanofabrication

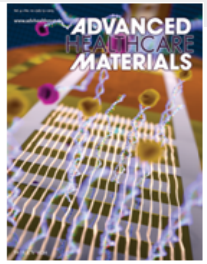


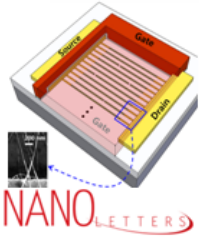


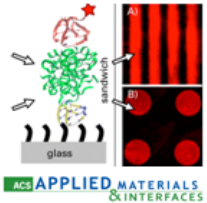
Microfluidics



Bioprocessing







M. M. Sanchez et al., *Nano Letters*, 16(7), (2016).
D. Karnaush., et al. *Adv. Health. Mater*., 4, (2015)
J. Schuett et al., *Nano Letters*, 16(8), (2016).
E. Baek et al., *Nano Letters*, 17(11) (2017).

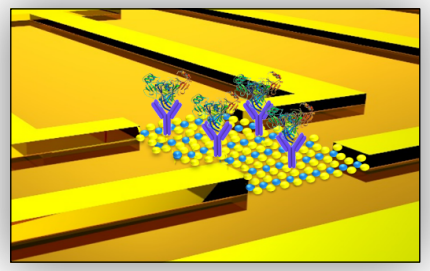
E. Baek at al., *Nature Electronics*, accepted.
P. Zhang et al., *Small*, 15 (23) (2019).
J. Schütt et al., *Nano Letters*, 20(9), 6572(2020).
T. Huang at al., *Adv. Func. Mater*., accepted.

L. Baraban et al., *Advanced Science*, 6 (15) (2019).
S.W. Park et al., *Angew. Chem. Int. Ed.*, (2020)
F. Zoergiebel et al., *Nano Research* , 7(2), (2014).
E. Baek, et al., *Nano Research* , 8(4), (2015).

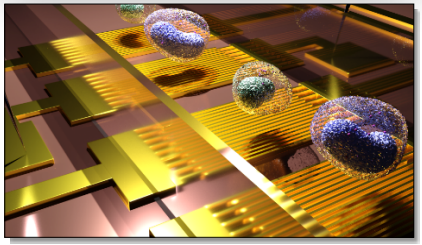
Outline

Development of new nanodevices and tools for lab on chip systems

✓ SiNW FET sensors and systems



✓ Gold nanowires based impedance sensors systems for blood analysis



Si-NW FET sensors and systems for molecular detection

J. Schuett et al., *Nano Letters*, 16(8), (2016).

E. Baek et al., *Nano Letters*, 17(11) (2017).

D. Karnaushenko, et al. *Adv. Health. Mater*., 4, (2015)

D. Y. Jeon, et al. *Nano Lett*., 15(7), (2015)

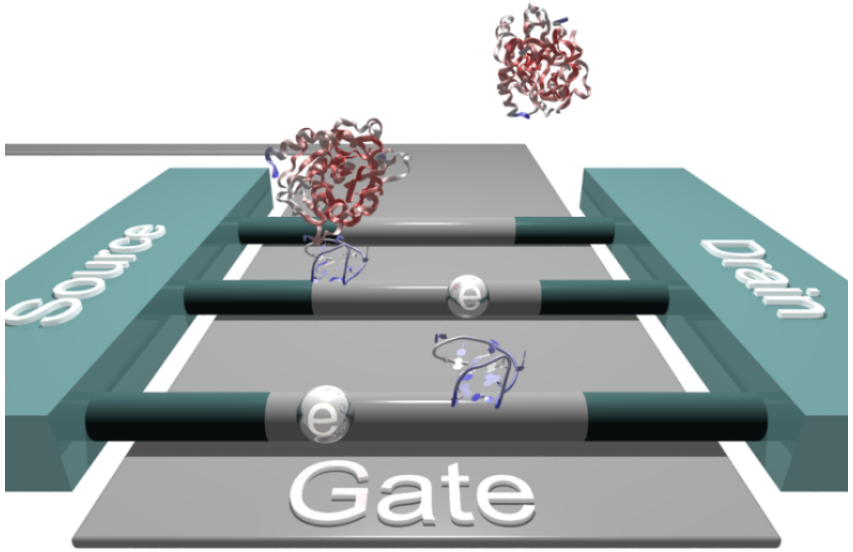
E. Baek, et al., *Nano Research ,* 8(4), (2015).

S. Pregl, et al., *Nano Research ,* 6(6), (2013).

Nanowire devices – label free devices

Potentiometric device: transforms the charge into the current

FET that is used to track analogue signal change



- ✓ **Higher surface to volume ratio**
- ✓ **Higher current modulation for the same active sensor area**

P. Bergveld, *IEEE Trans. Biomed. Eng*. **17**, 70 (1970).
D. Y. Jeon *et al*., *Nano Lett.* **15,** (2015).

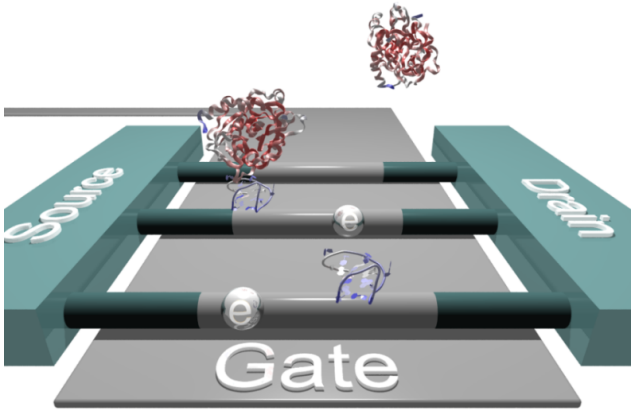
How does it operate?

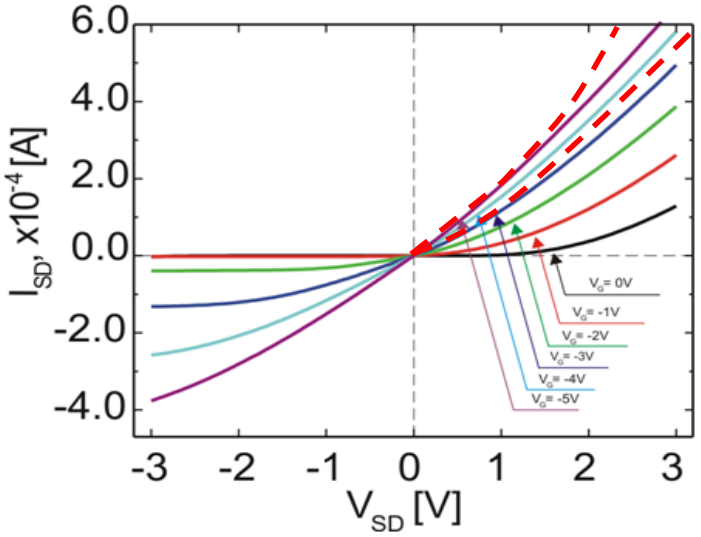
Concept of the sensor device:

(1) Silicon nanowires assembled as **field effect transistors** (FETs)

(2) Surface of the NWs play crucial role in the **sensing the microenvironment**

(3) Changes of the surface charges: **gate effect**





✓ **Higher surface to volume ratio**

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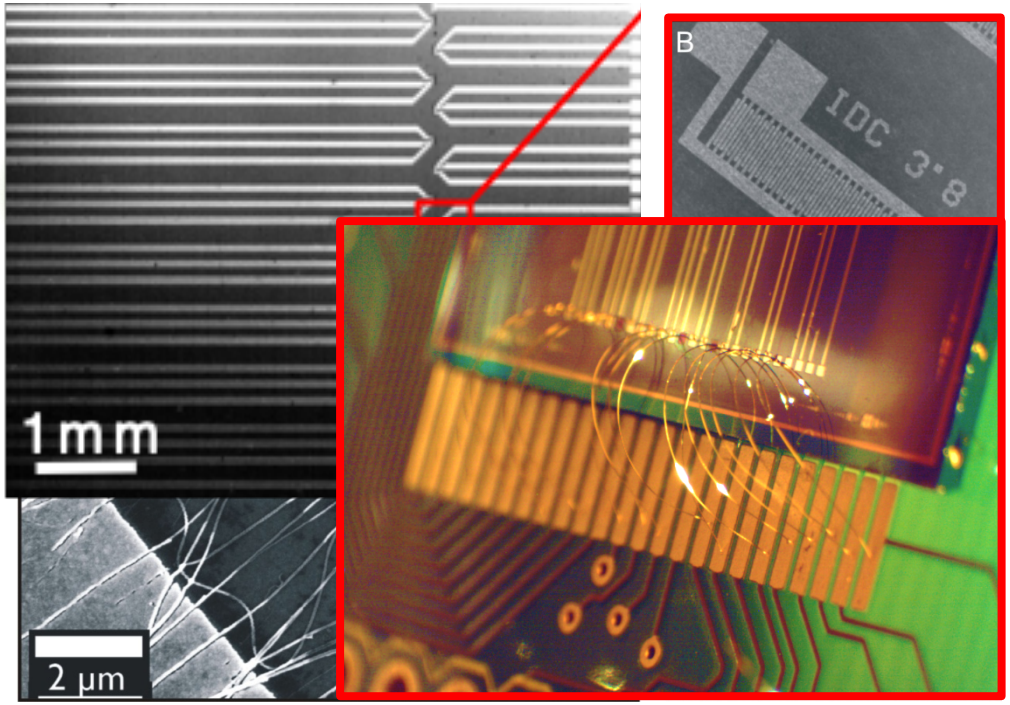
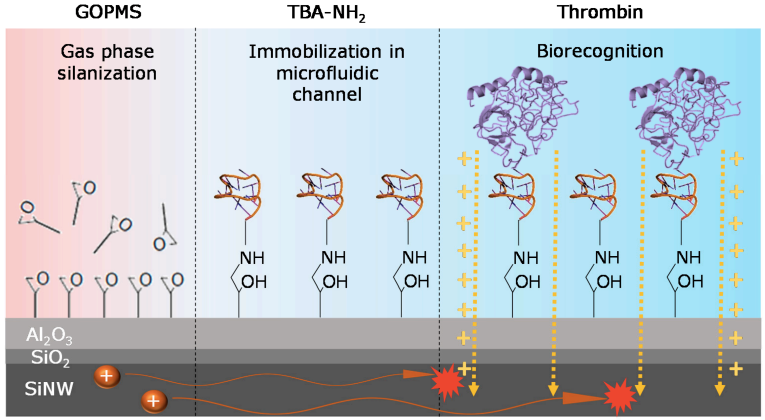
P. Bergveld, *IEEE Trans. Biomed. Eng*. **17**, 70 (1970).

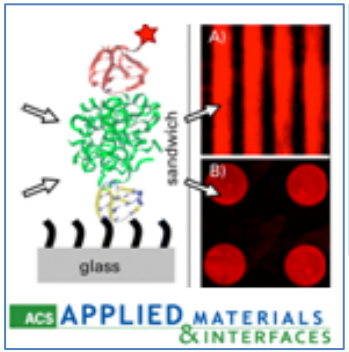
D. Y. Jeon *et al*., *Nano Lett.* **15,** (2015).

Si NW devices for sensor platform



E. Baek, et al., *Nano Research* , 8(4), (2015).
F. Zoergiebel et al., *Nano Research* , 7(2), (2014).

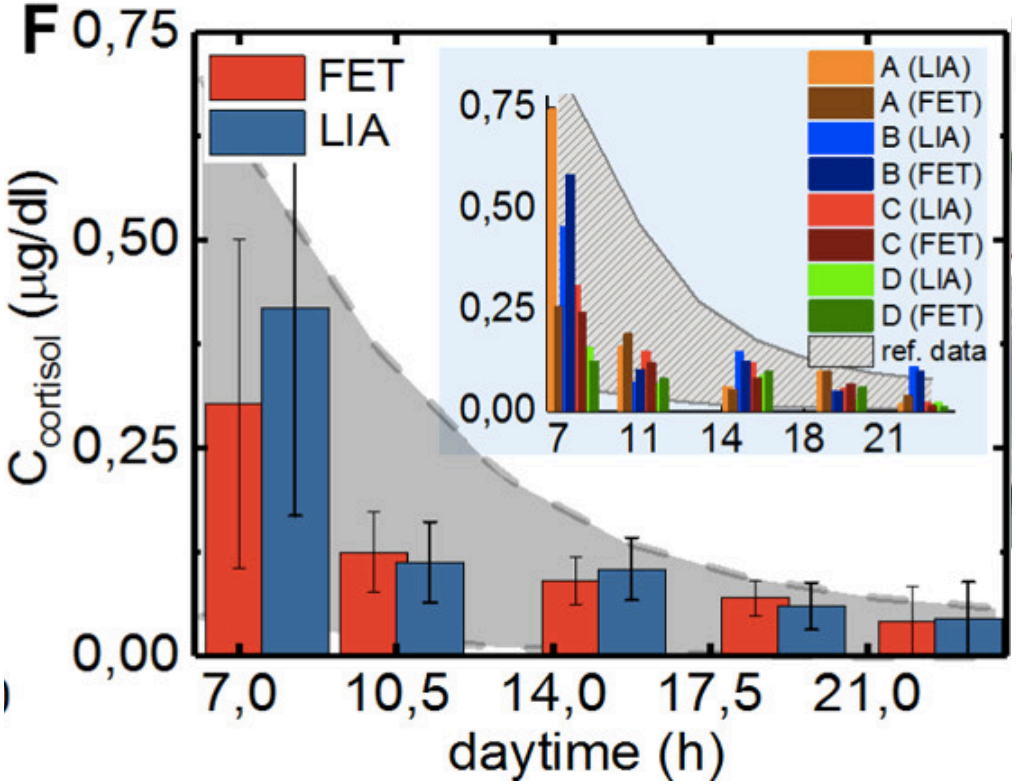


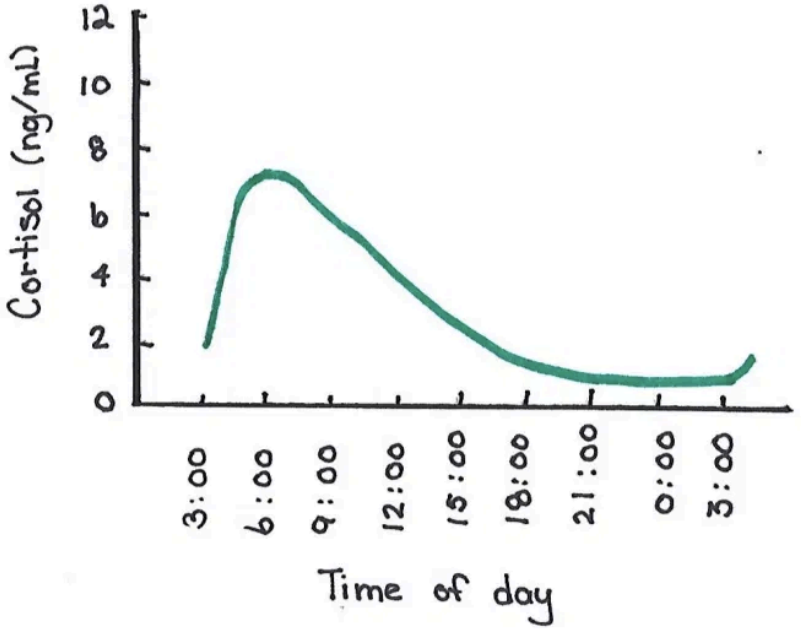


S. Pregl, et al., *Nano Research* , 6(6), (2013).
D. Y. Jeon, et al. *Nano Lett*., 15(7), (2015)

Clinical applications

Real time monitoring of stress biomarkers: human testing

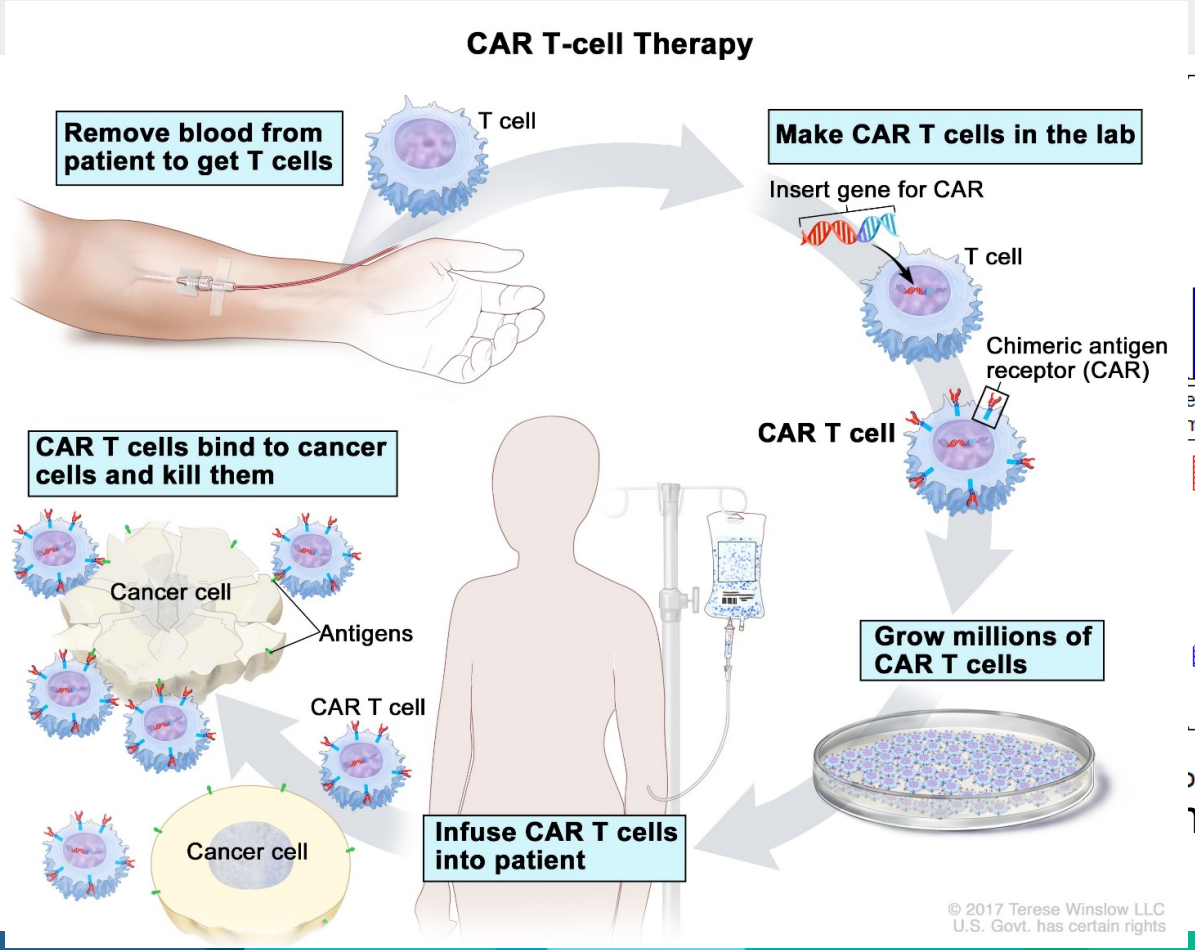


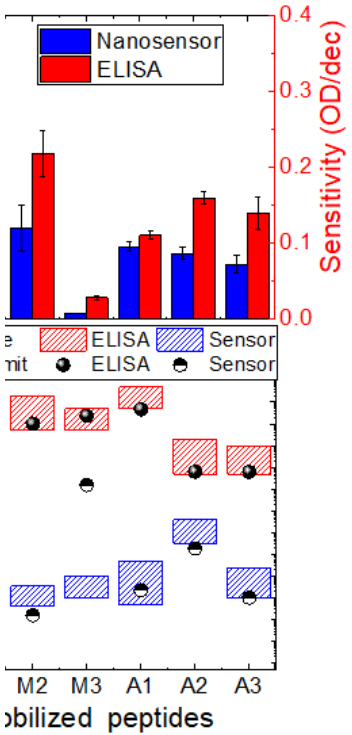


Cooperation: Clemens Kirschbaum, Biopsychology

S Klinghammer, et al. ACS Sensors, 2020.

Immunotherapy monitoring

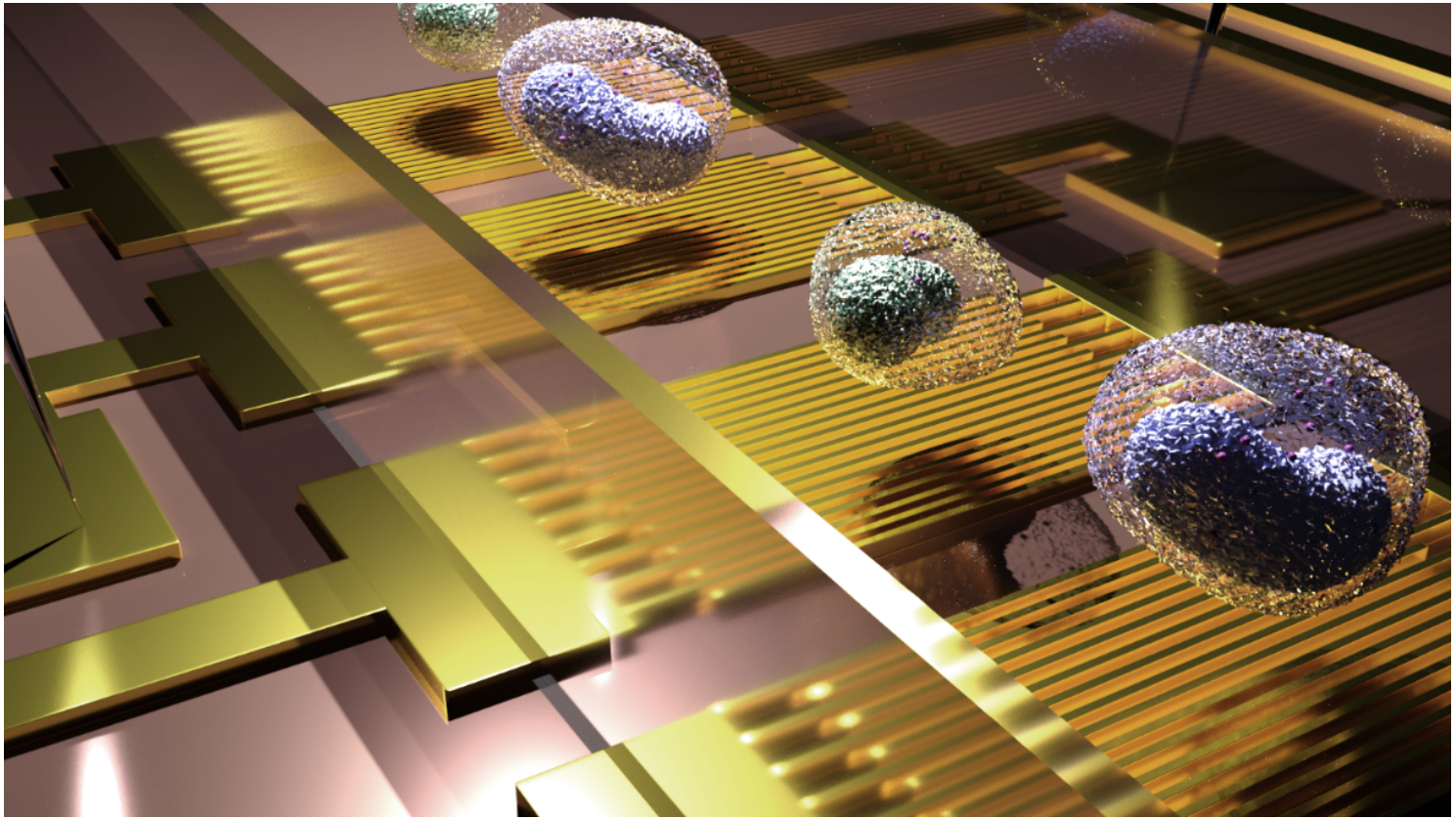




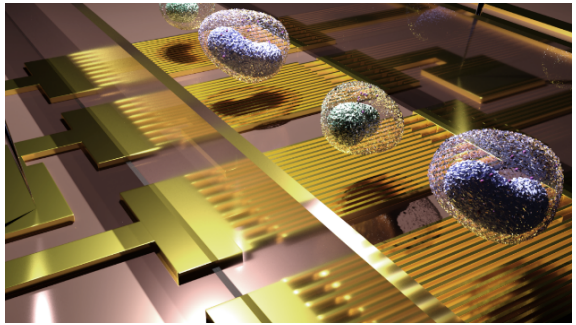
n: Michael Bachmann (HZDR),

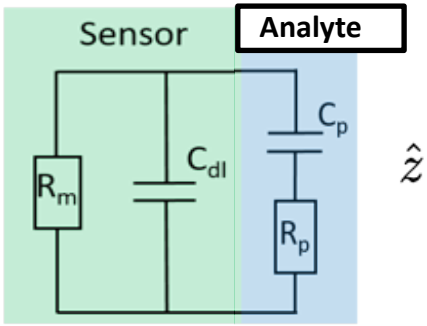
Ahn Trang Nguyen-Le et al., submitted

Metal nanowire based impedance sensors



Metal nanowires impedance based system





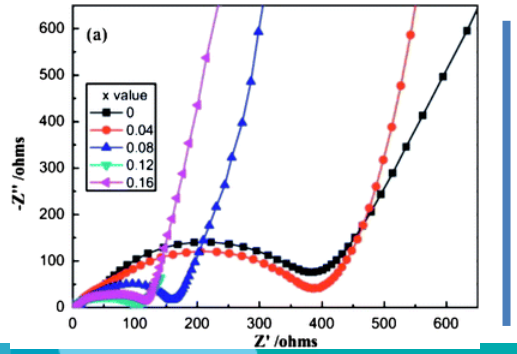
$$\hat{z}(j\omega) = R + \frac{1}{j\omega C} + j\omega L$$

Dynamic mode!

Impedance spectroscopy

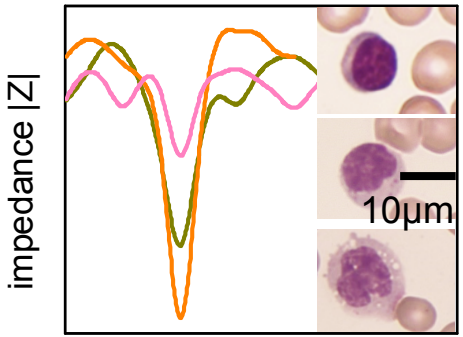
Scan of the frequencies to detect analyte

Static mode!



Impedance cytometry

Constant frequency in time domain

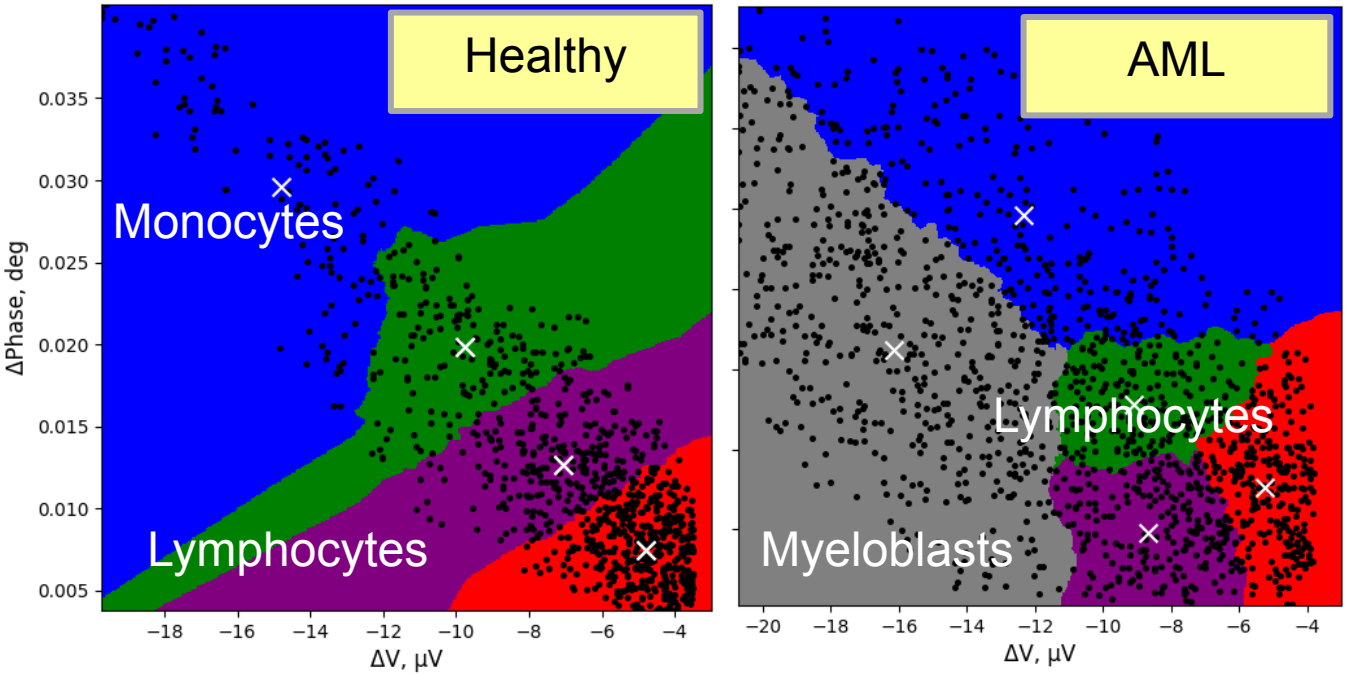


Monocytes

T-cells

NK-cells

Nanocytometer: Metal nanowires impedance based system + machine learning



Cooperation: Martin Bornhäuser,
Uni Klinik, Oncohematology

J. Schütt et al., *Nano Letters*, 20(9), 6572–6581 (2020).

Summary and Outlook

- Electronic nanobiosensors
- Microfluidic analysis

- Towards complex nanosystems for analysis of the biological systems

Thanks

Thank to all collaborators:

Walter M. Weber, TU Wien

Thomas Mikolajick , TU Dresden

Oliver G. Schmidt , Leibniz IFW

Gianaurelio Cuniberti, TU Dresden

Denys Makarov, HZDR

Arben Merkoci, Barcelona

Samuel Sanchez, Barcelona

Martin Bonhäuser, Uni Klinik Dresden (Hematooncology)

Michael Bachmann, HZDR

Peter Spieth, Uni Klinik Dresden (Anesthesiology)

Juergen Weitz, Uni Klinik Dresden (Surgery)

Clemens Kirschbaum, TU Dresden, (Biology)

Arjan de Visser, Wageningen

Joost de Graph, Utrecht

Thanks to the group

Thanks for your attention!