

MAY 06, 2020  
CONFERENCE  
ONLINE



INESC MN

Microsystems and  
Nanotechnologies

## MULTIANALYTICAL POINT-OF-CARE DEVICE FOR THE DIAGNOSIS OF VIRAL INFECTIONS

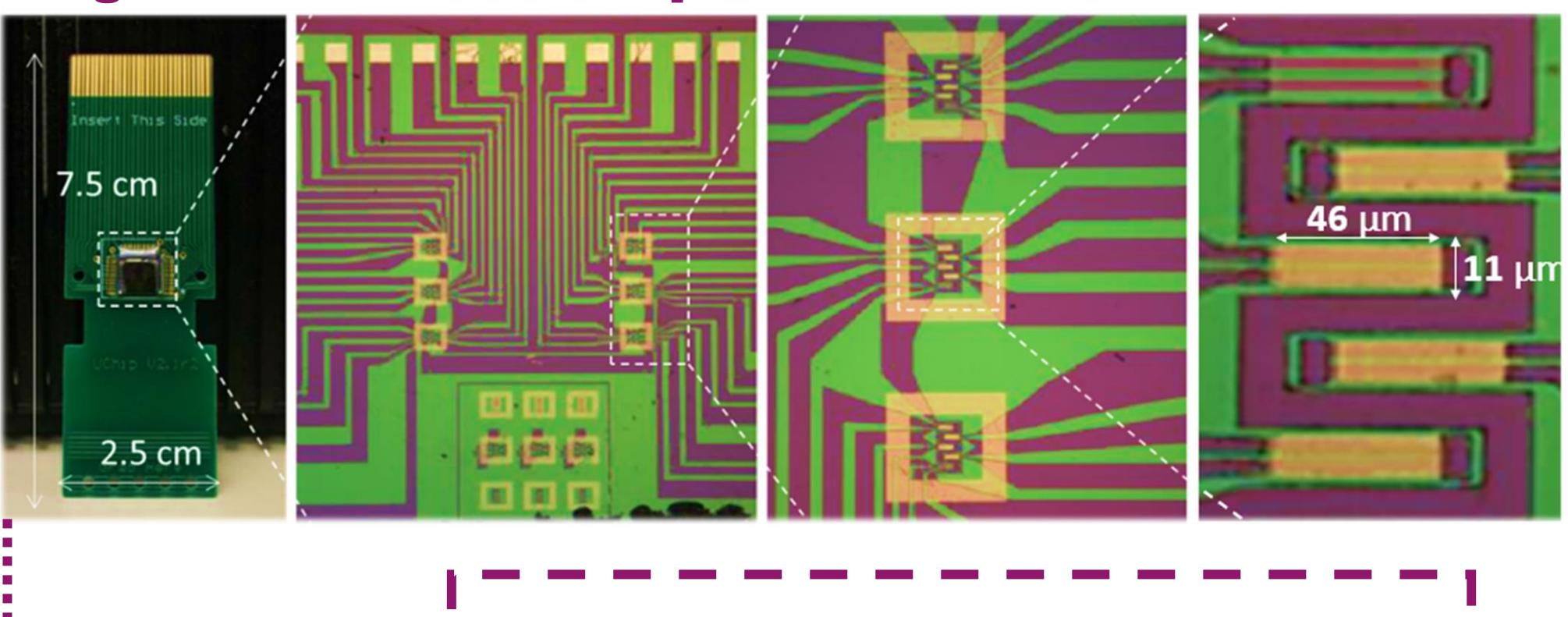
TÉCNICO  
LISBOA

Débora C. Albuquerque<sup>1,2</sup>, Verónica C. Martins<sup>1</sup>, Sofia A. M. Martins<sup>1</sup>, Sara Viveiros<sup>1,2</sup>, Susana Cardoso<sup>1,2</sup>, Paulo P. Freitas<sup>1</sup>

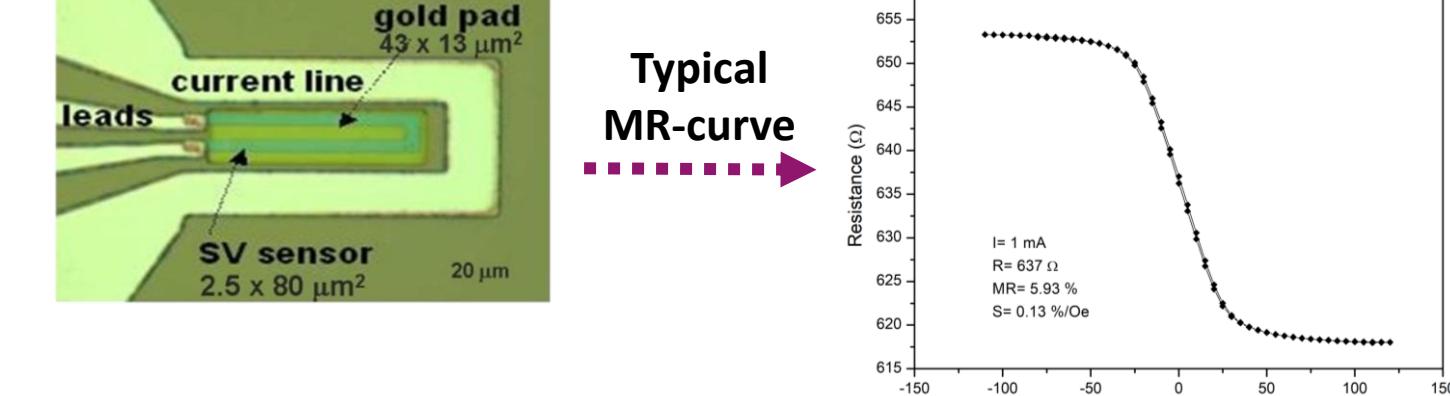
1 – INESC Microsystems and Nanotechnologies, Lisbon, Portugal – [www.inesc-mn.pt](http://www.inesc-mn.pt)  
2 – Instituto Superior Técnico, Universidade de Lisboa, Lisbon, Portugal

### 1 Magnetoresistive Biosensing Platform

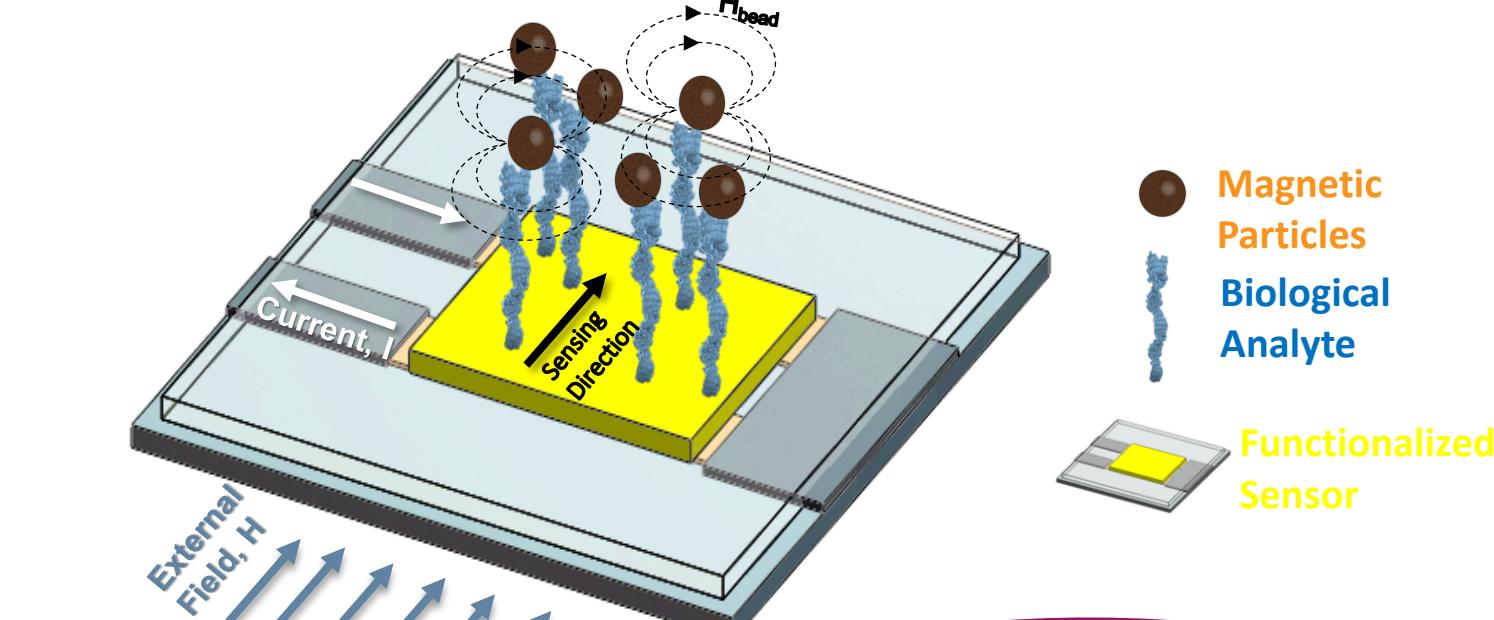
#### Magnetoresistive Biochips



#### Spin-valve sensors

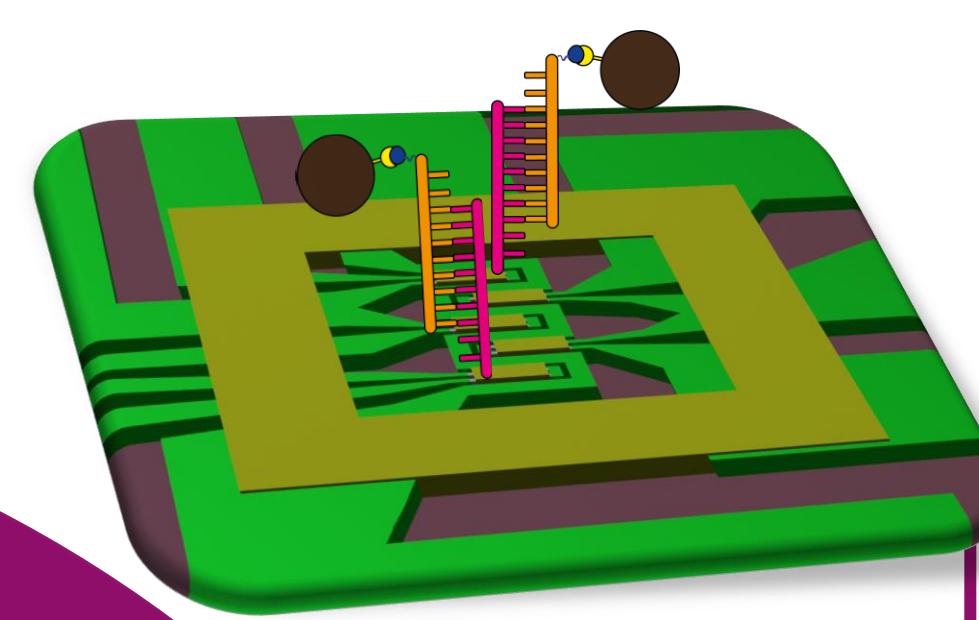


#### Working Principle

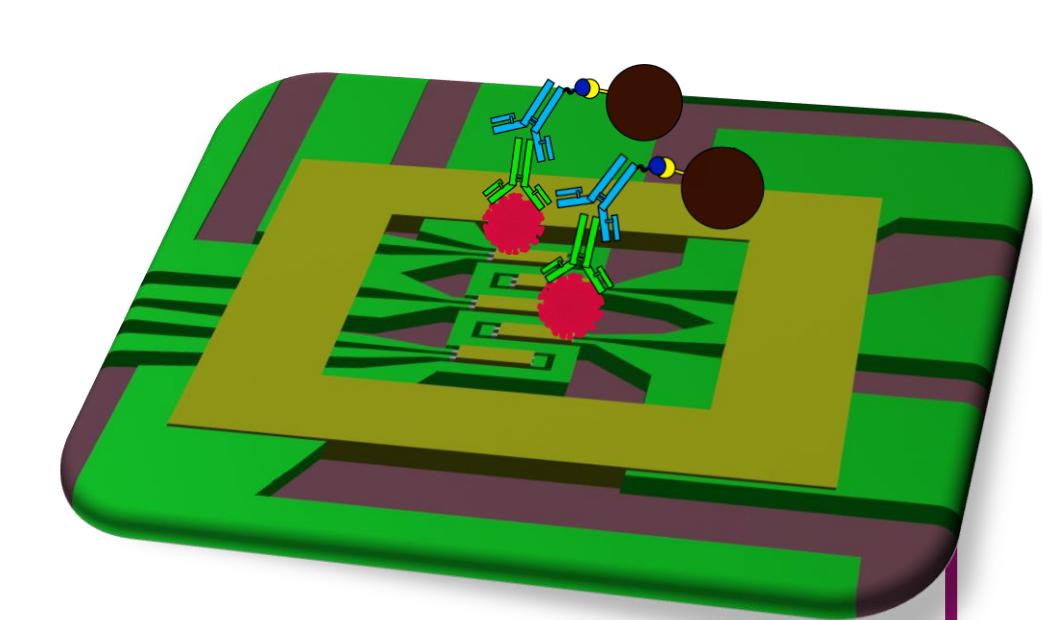


### 2 Two Parallel Detection Assays

#### DNA hybridization



#### Immunoassays



### PORTABLE PLATFORM



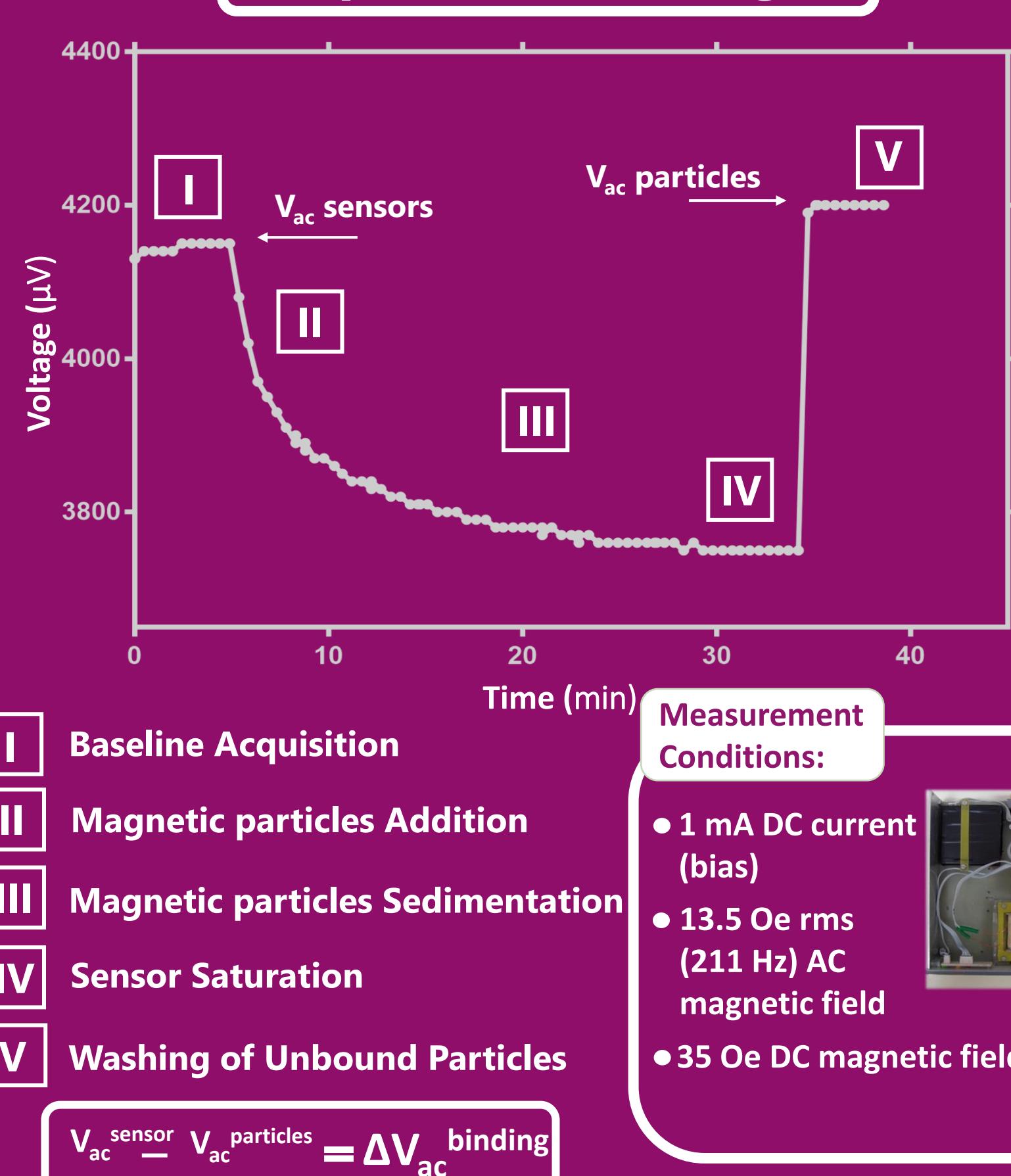
- ✓ Quantitative analytical performance
- ✓ Tailored dynamic range (up to 4 orders of magnitude)
- ✓ Assay time: 1 h

Measurement Conditions:

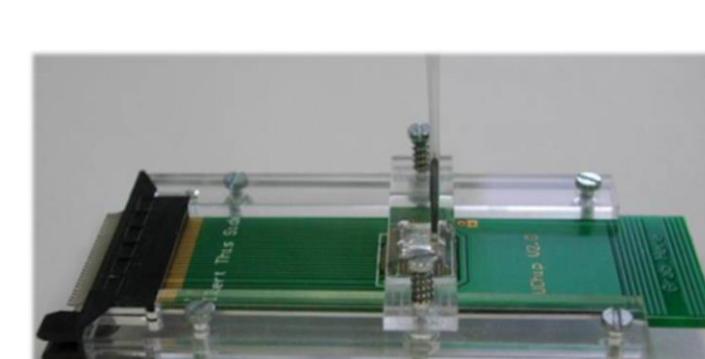
- 1 mA DC current (bias)
- 13.5 Oe rms (211 Hz) AC magnetic field
- 35 Oe DC magnetic field

$$V_{ac\text{ sensor}} - V_{ac\text{ particles}} = \Delta V_{ac\text{ binding}}$$

### Output Read-out Signal



### 5 Microfluidic System

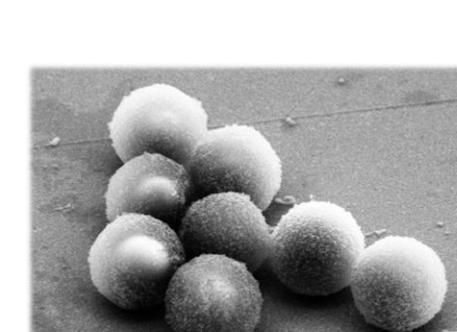


#### Microfluidics and Microelectronics Compatibility

Possible integration with sample preparation units and CMOS technology for high throughput analysis

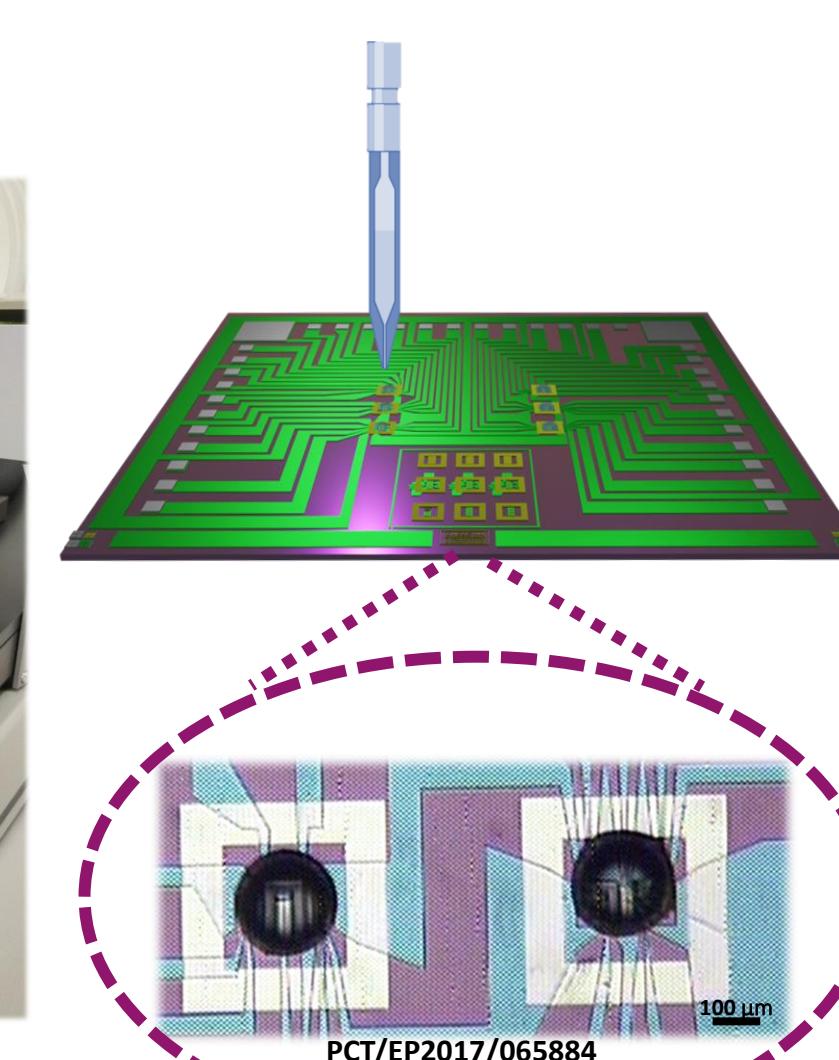
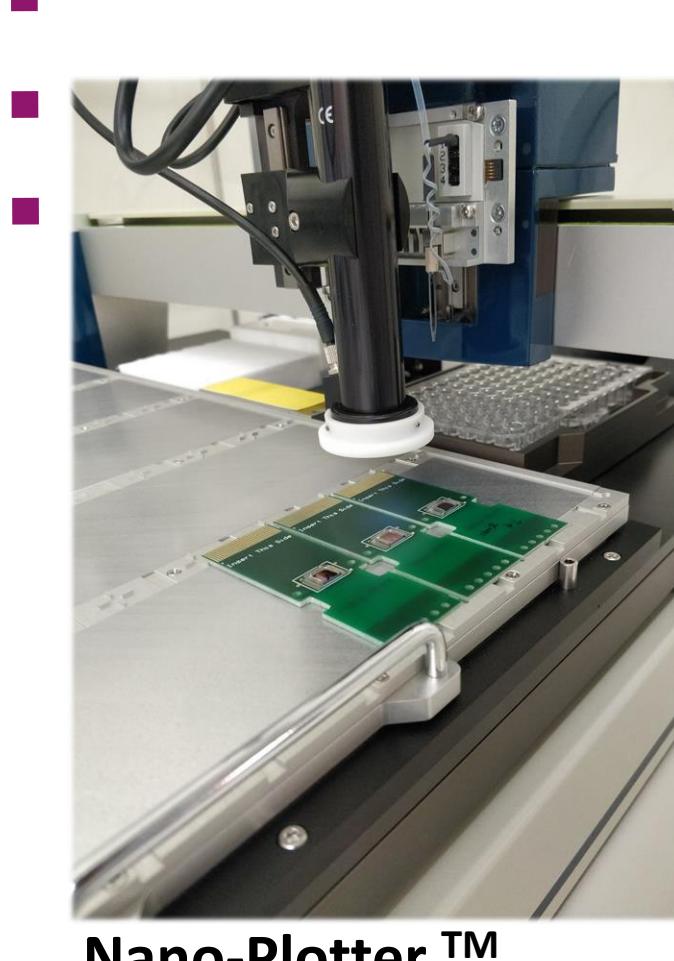
PDMS U-channel  
Channel Width: 800 μm  
Channel Height: 300 μm

### 4 Magnetic Labels



- Size: 250 nm
- Composition: 75-80% magnetite; dextran coated
- Modification: streptavidin
- Protein binding capacity: 450–500 streptavidin molecules per particle.
- Magnetic moment:  $1.6 \times 10^{-16} \text{ A.m}^2$  for  $H$  of 1.2 kA/m
- Susceptibility:  $\chi \approx 5$

### 3 Micro-spotting

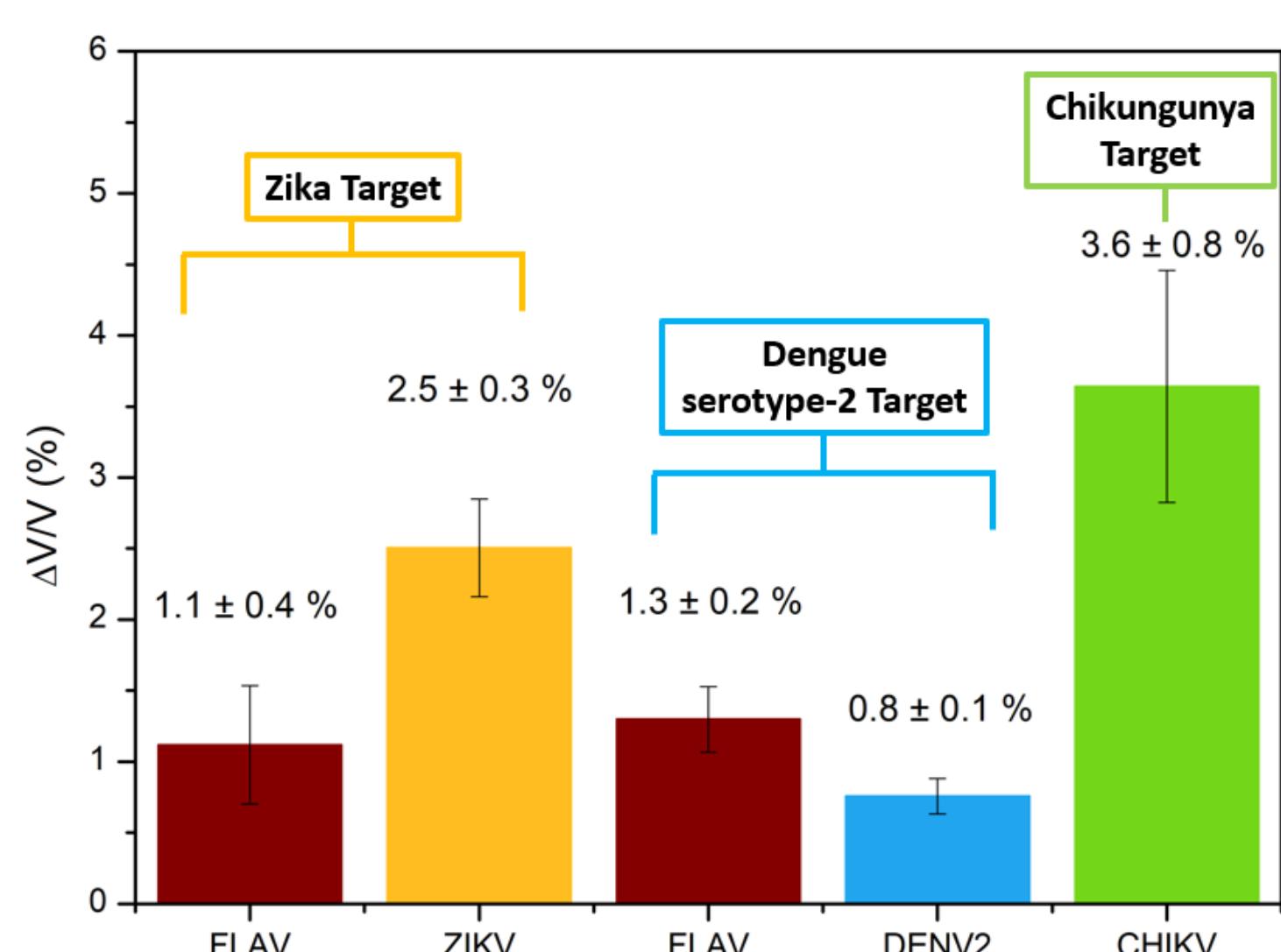
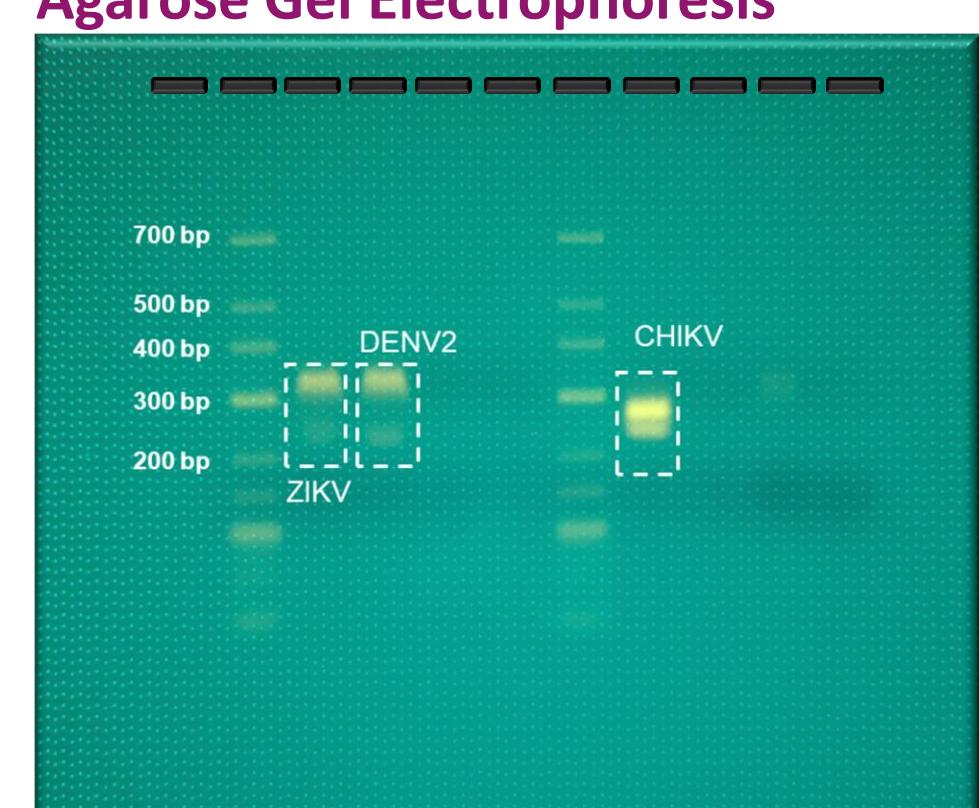


- Micro-spotting of specific probes (e.g. DNA oligos, antibodies, antigens)
- Multiplexing: up to 6 different probes can be immobilized
- Spot droplets with diameter of ~200 μm

### Proof of Concept: Magnetoresistive Detection of ① Viral genome & ② Antigens

#### 1 Zika (ZIKV), dengue (DENV) and chikungunya (CHIKV) RNA detection (after RT-PCR amplification)

##### Agarose Gel Electrophoresis



Specific probes for species and genus (Zika virus (ZIKV), Dengue virus (DENV), Chikungunya virus (CHIKV), and Flavivirus genus (FLAV)).

The platform has also been validated for detection of bacterial, microvesicles, other nucleic acids and serum protein biomarkers in ischemic stroke patients.

Levels of sensitivity in the order of  $10^{-15}$  mol/L and ng/mL for nucleic acid hybridization and immunoassays, respectively, are reported.

- Low cost (< 10€/test)
- Multiplex (6 probes/test)
- Fast time to results (< 1 h)
- Portable and user-friendly
- Quantitative Assay (ng/ml/fM)

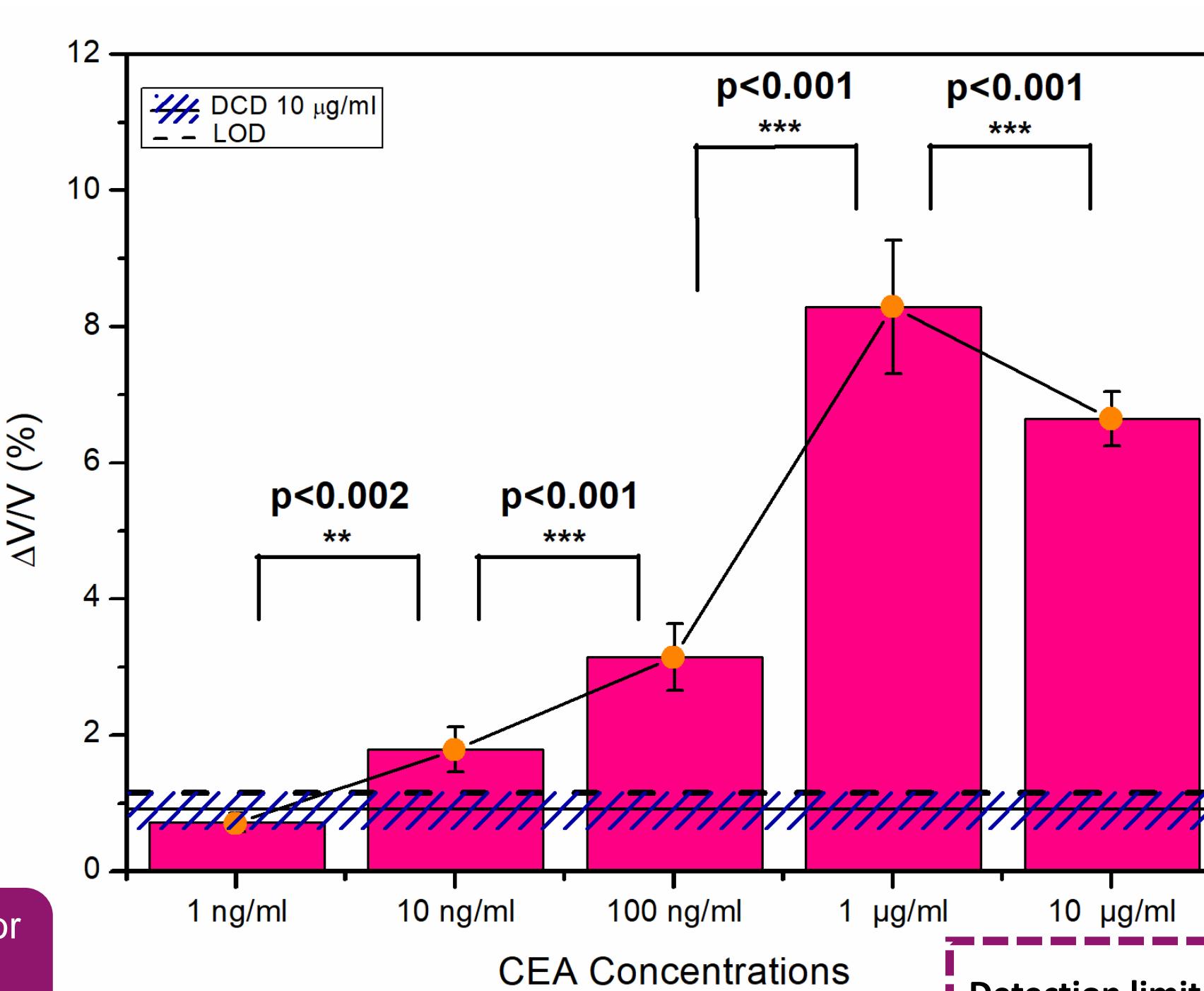
This technology shows great potential for the double diagnostic of Covid-19 by molecular and serological assays.

#### 2 Carcinoembryonic antigen detection by immunoassay

Negative Control (Goat E.coli as Detection Antibody)

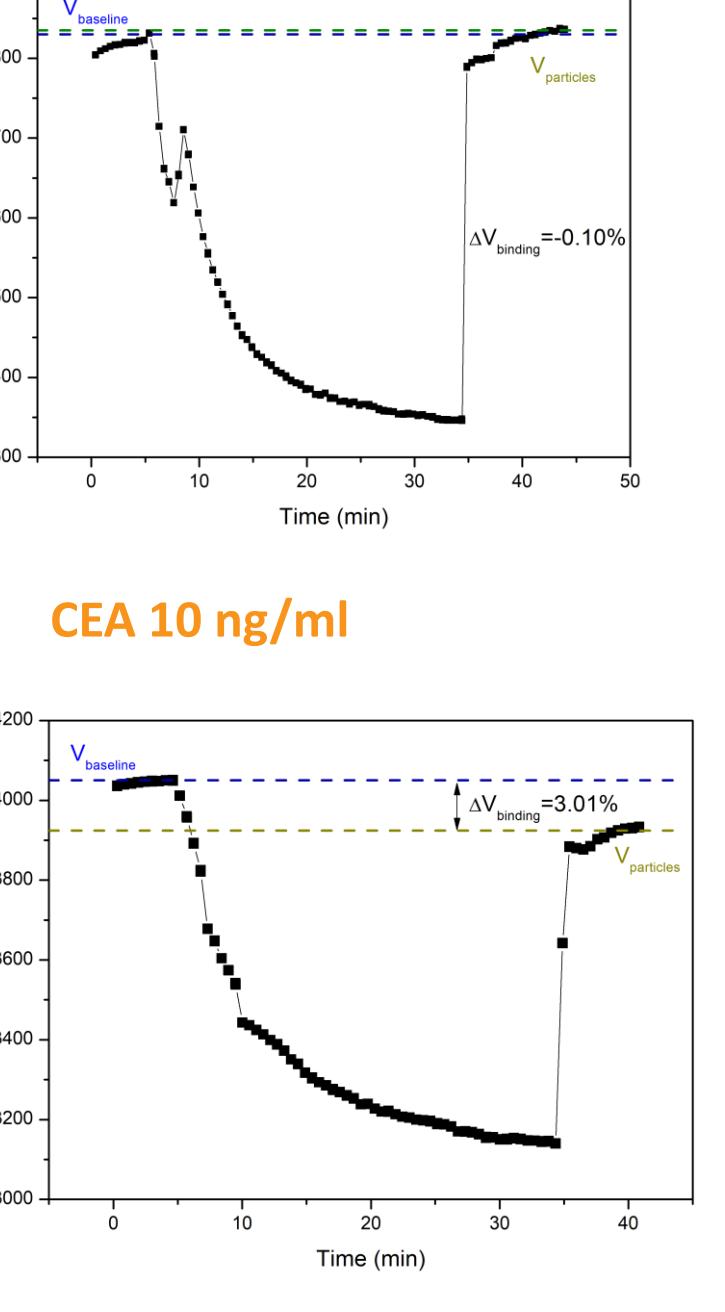
DDC 10 μg/ml

LOD



$\Delta V_{ac\text{ binding}} = 0.10\%$

CEA 10 ng/ml



p < 0.01

Detection limit: 5 ng/ml

### CONTACT PERSON

Verónica C. Martins: [vromao@inesc-mn.pt](mailto:vromao@inesc-mn.pt)  
Sofia A. M. Martins: [sammartins@inesc-mn.pt](mailto:sammartins@inesc-mn.pt)

Acknowledgements: FCT grant with ref. PD/BD/143024/2018 for Doctoral Program AIM- Advanced Integrated Microsystems. INESC-MN acknowledges Fundação para a Ciência e a Tecnologia (FCT) funding from the Pluriannual Funding model for R&D units and financial support from Project PO NORTE-01-0145-FEDER-22090.

### REFERENCES

1. Germano, J., Martins, V. C., Cardoso, F. A., Almeida, T. M., Sousa, L., Freitas, P. P., Piedade, M., Sensors, 6 (2009) 4199
2. Martins, V. C., Cardoso, F. A., Germano, J., Cardoso, S., Sousa, L., Piedade, M., Freitas, P. P., Fonseca, L., Biosens. Bioelectron 8 (2009) 2690
3. Fernandes, E., Martins, V. C., Nóbrega, C., Carvalho, C. M., Cardoso, F. A., Cardoso, S., Dias J., Deng, J., Luskens, L.D. Azeredo, J., Biosens. Bioelectron 15 (2010) 239
4. Albuquerque, D. C., Martins, V. C., Cardoso, S., IEEE Magnetic Letters 10 (2019)
5. Martins, V. C., Martins, S. A. M., Germano, J., Cardoso, F. A., Cardoso, S., Sousa, Freitas, P. P., ACS Nano 11 (2017) 10659



MAY 06, 2020 CONFERENCE ONLINE