Advancements in Nanomaterial-Based Electronics for Biosensing Applications: Electronic biosensing based on field-effect transistors (FETs) arrays

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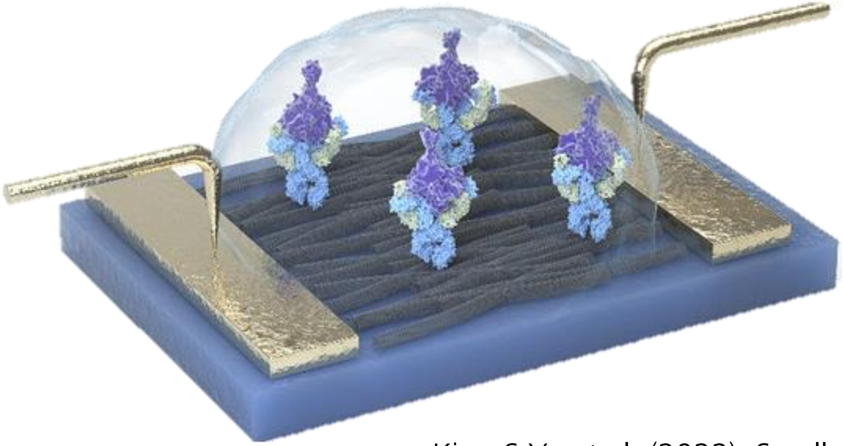
Competitive sensing approaches

Traditional biosensing technologies vs. FET-based electrical devices for biosensing

- RT-PCR Rapid antigen test, ELISA, microscopic techniques, and immunofluorescence → proved to be clinically significant, has limitations such as lower sensitivity, extensive manual work, low specificity, long time, etc



Kim, S.Y., et al, (2022), Small Sci., 2: 2100111.

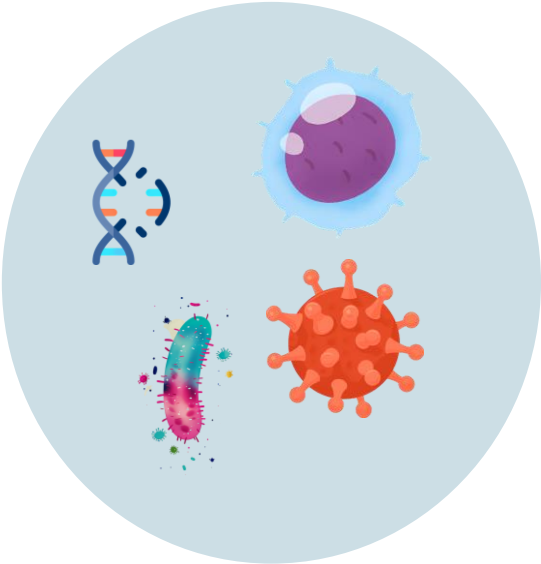
- **Rapid and label-free detection, highly sensitive, easy operation, and capability of integration of nanomaterials, scalable and fab-compatible.**

- **Applications in chemical sensing, biomarker detection, drug and pathogen screening, environmental control, continuous health monitoring, point-of-care testing (POCT) and remote healthcare.**

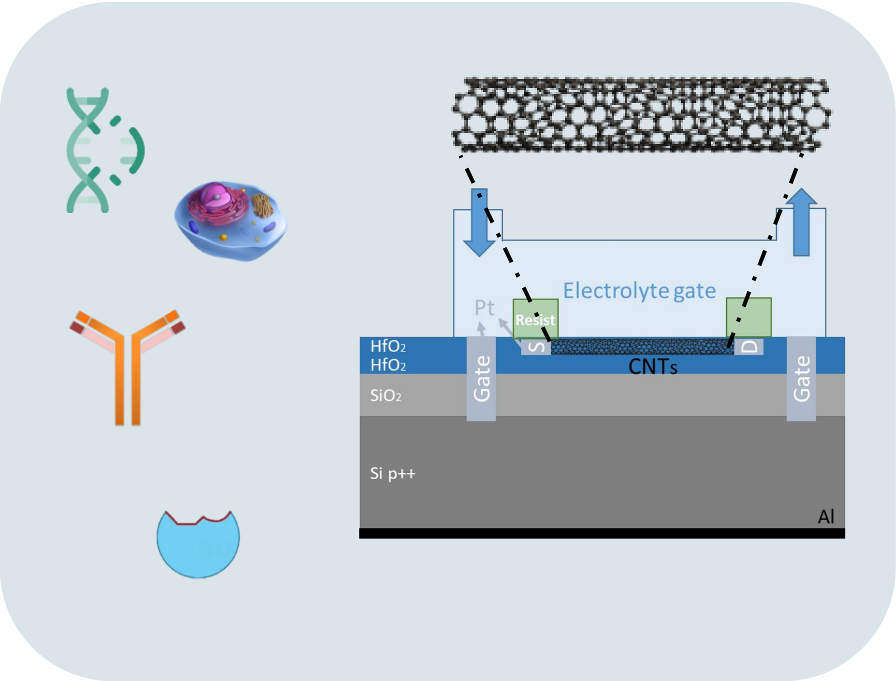
Carbon nanotubes field-effect transistors (CNT-FET) for electronic biosensing

Elements of FET-based electrochemical biosensor

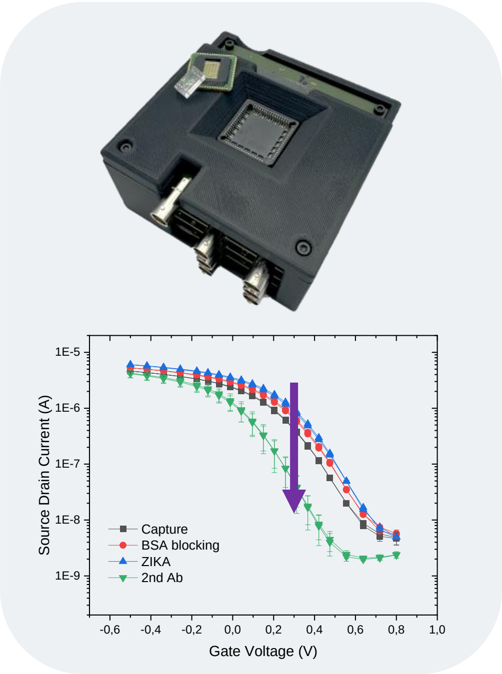
SAMPLE



TRANSDUCER

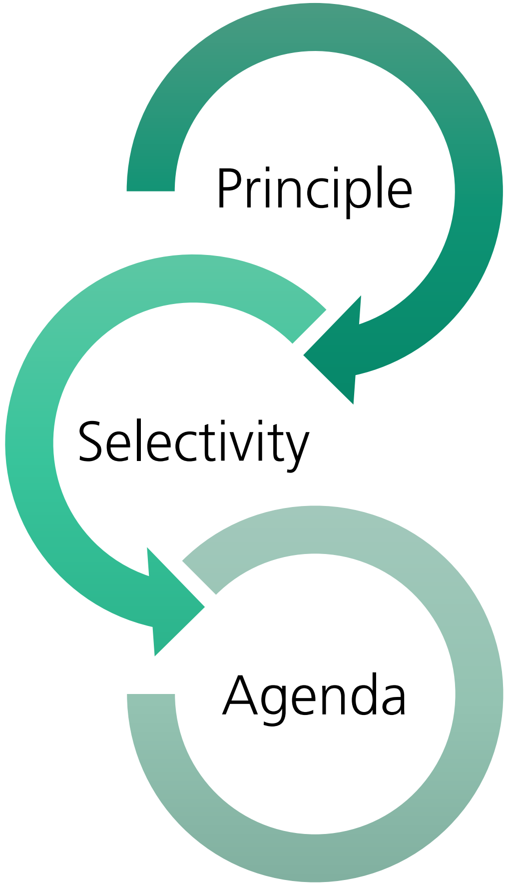


ELECTRONICS

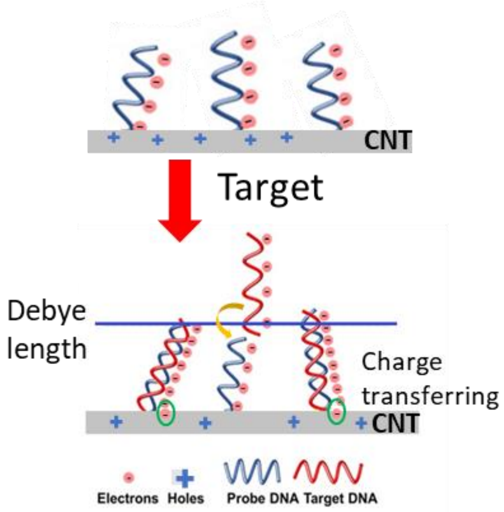


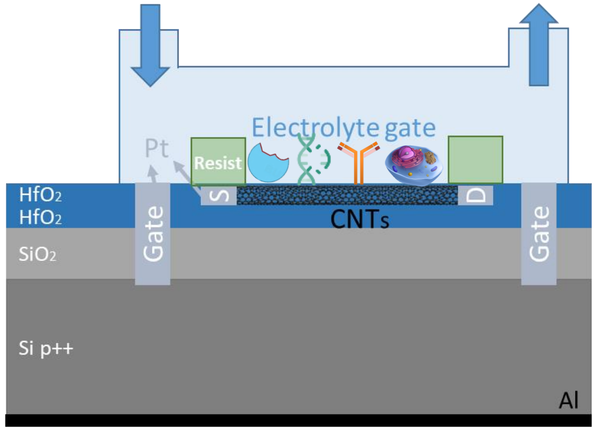
CNT-based bio-chemical sensor

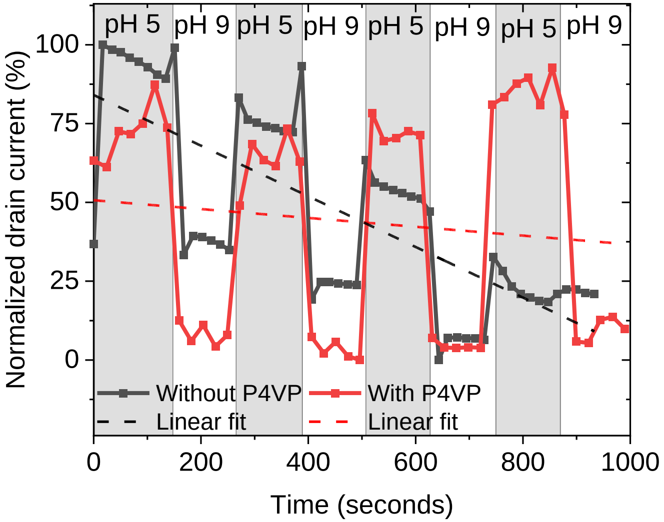
pH sensor, antibody and nucleic acid-based biosensors



- Detection of changes in FET channel potential → direct measurement of drain current
- Via functionalization and immobilization of specific biorecognition elements
- Establishment of wafer-level sensor technology & multiparameter sensing platform







P4VP enhanced pH Sensor
Alves da Silva, L. et al., Proceedings, 97, 216 (2024)

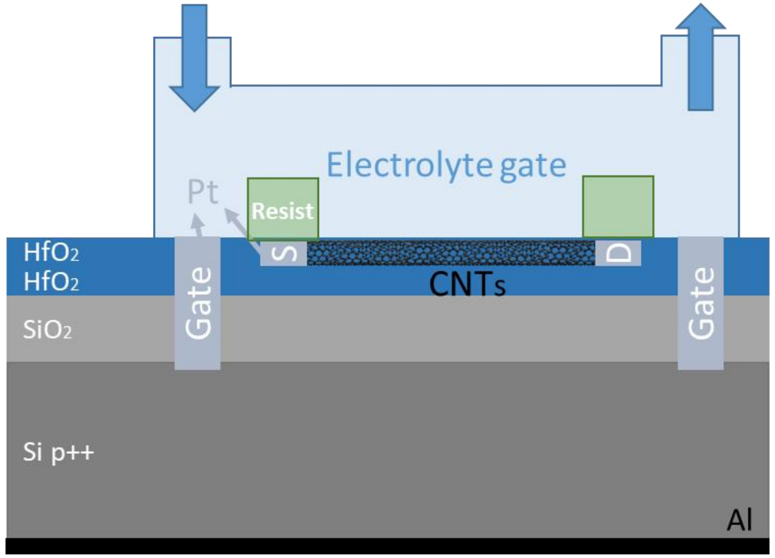
Tackled challenges on electronic biosensing

CNT-FET sensor fabrication

Sensor **passivation**
Fully embbebed high κ ALD

Long-time stability
Over 2h with low drift

Large scale fabrication and **portable** system
> 70% yield + portable devices



pH sensing
50 mV/pH in an operation regime below 1 V

Versatile biosensing
DNA, antibody

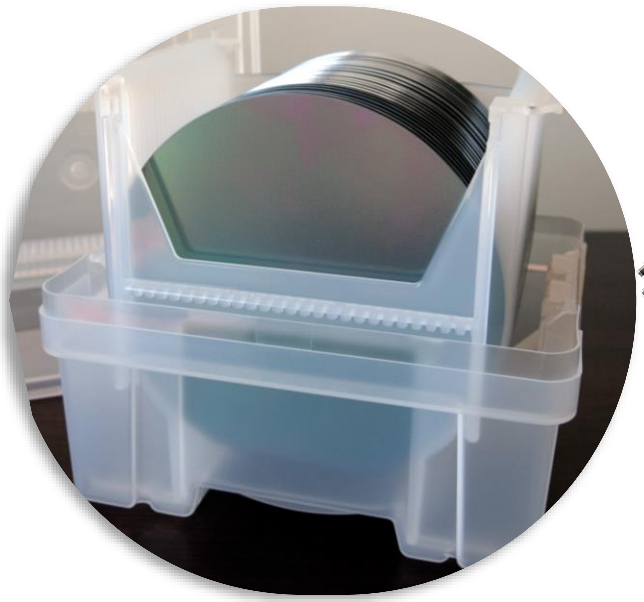
Low concentration analytes
Down to 0.1 pM tDNA

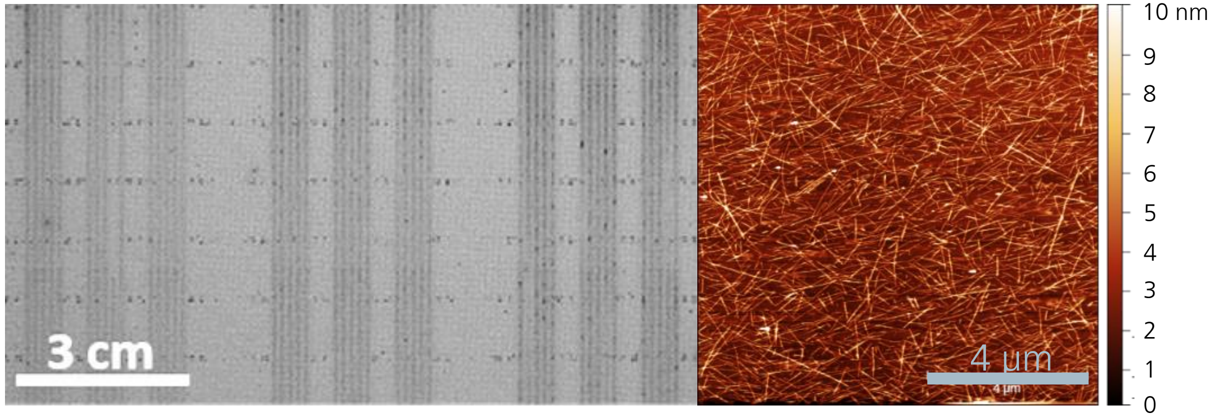
Sensing platform
CNT-FET sensor fabrication

- Wafer-level integration of CNT (200mm Ø)
- High purity semiconducting CNT dispersion
- CNT integration via printing technique with tunable density and alignment

- ALD-deposited HfO_2: high κ dielectric → lower gate leakage currents, and smaller drift and protects against electrical stress upon long-time measurements

- **Yield of >70% achieved!**

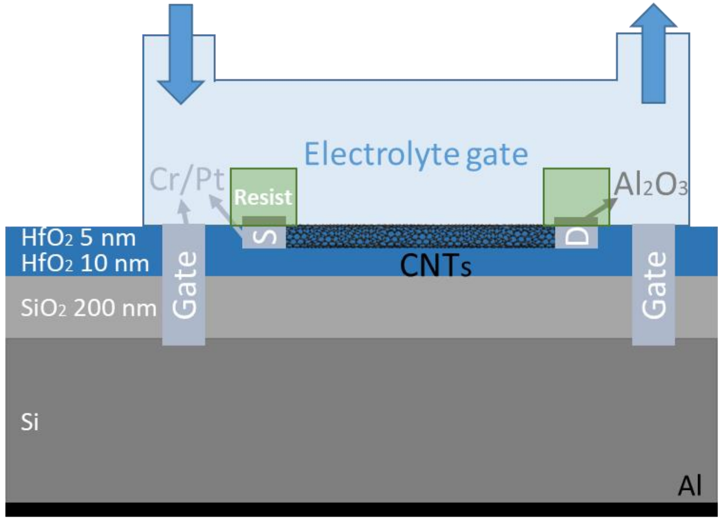


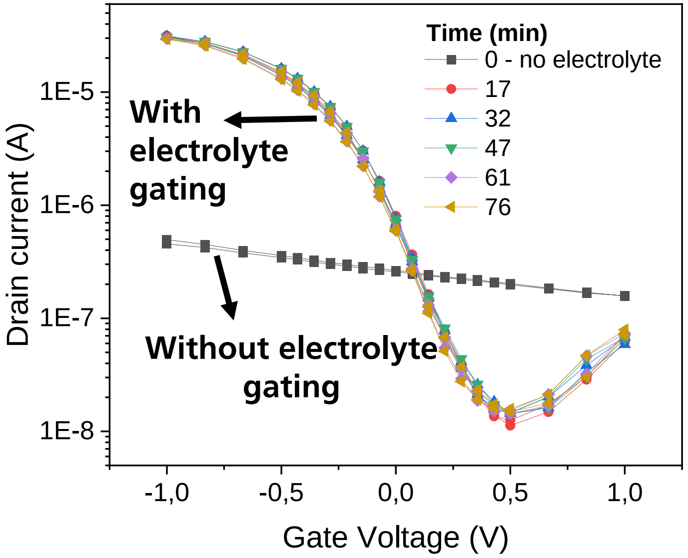


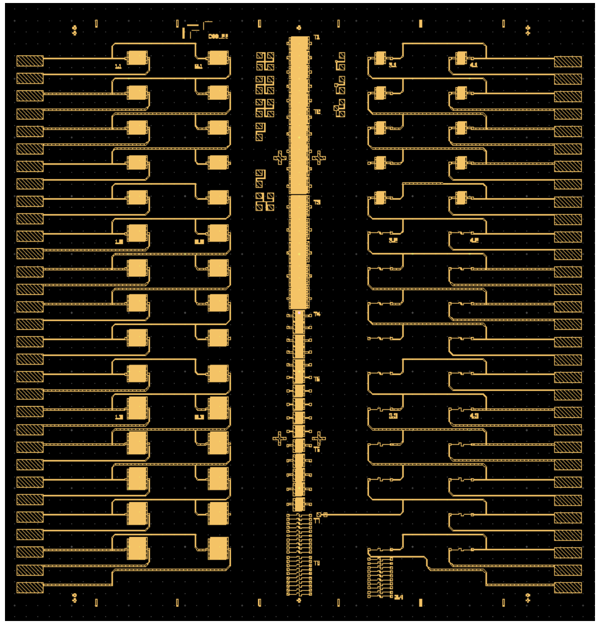
Sensing platform

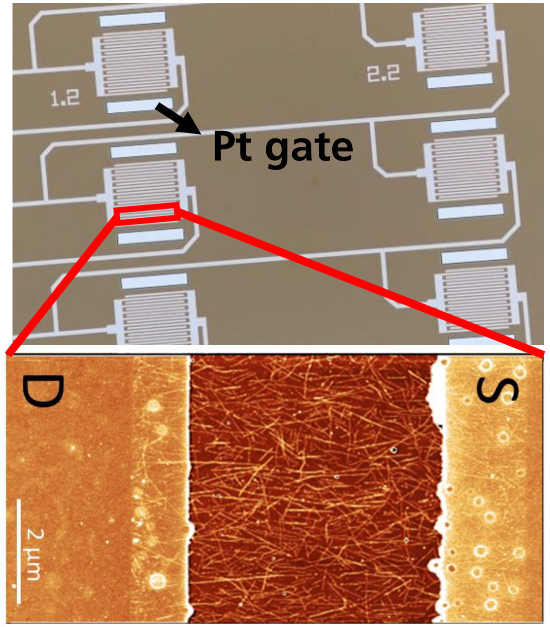
CNT-FET electrolyte gating

- 5 nm thin ALD-HfO_2 channel passivation: fully embedded transistor (SiO_2/ HfO_2/CNT/HfO_2)
- SU-8 contacts passivation
- Device structure optimized for **liquid gating**
- Liquid testing range: below 1 V → avoid electrochemical reactions within the liquid/contacts/biological species









Sensing platform and miniaturization possibilities

Measurement setup

High-precision liquid dispensing onto the fluidic channels

- Possible combination with microfluidic pumps for combination of solutions

Multi-sensor/parallel reading

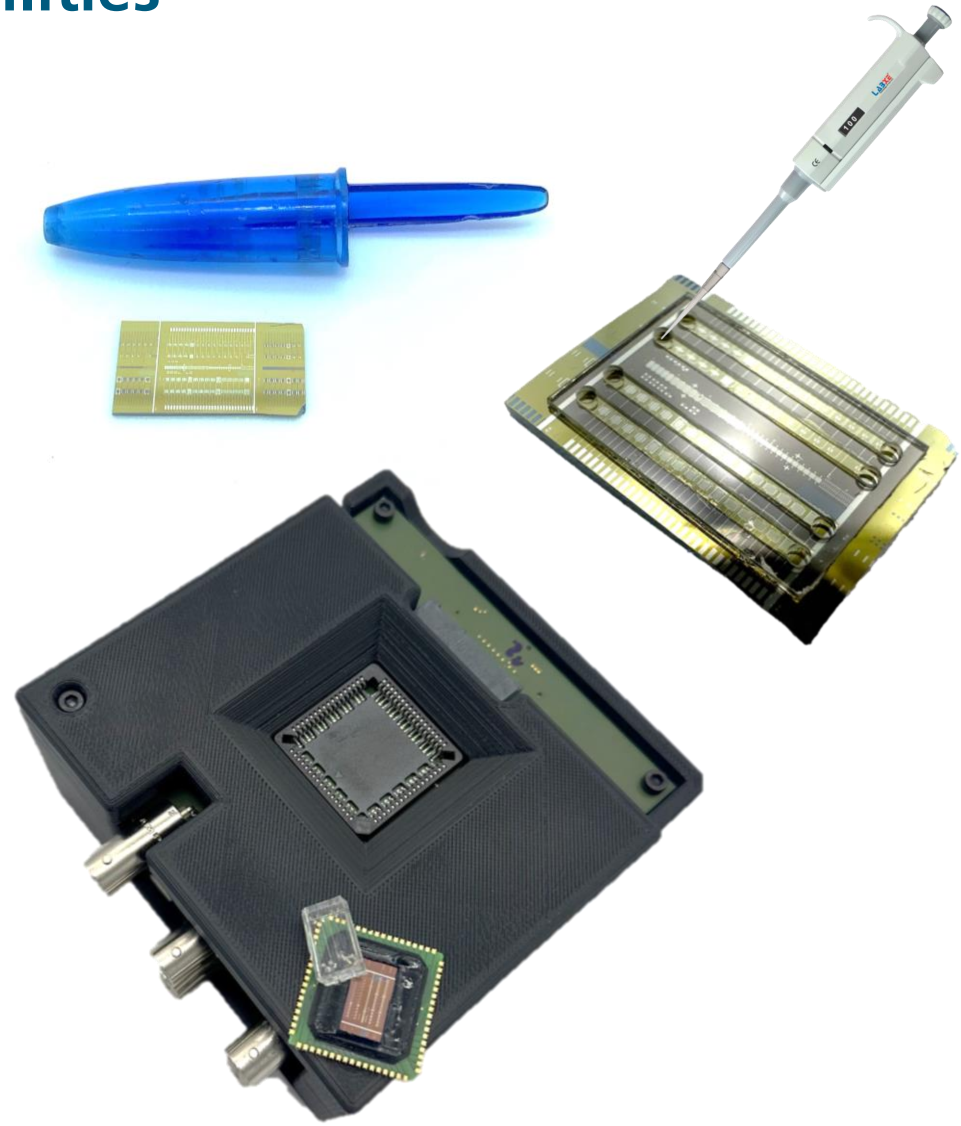
- Switch matrix and probe card for many devices monitoring
- Automatic in-line monitoring of sensor arrays and stability analysis

Microfluidic with PDMS channels

- ↓ volume and ↑ interaction to sensor platform

Portable sensing unit

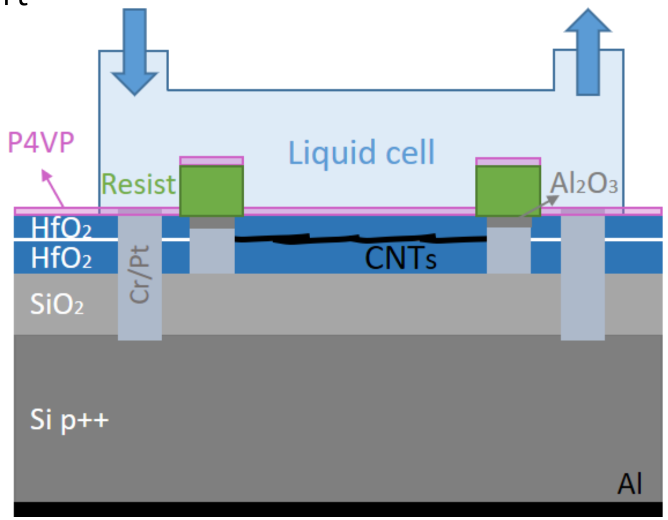
- Bonded wired chips
- *Packaging for distribution*

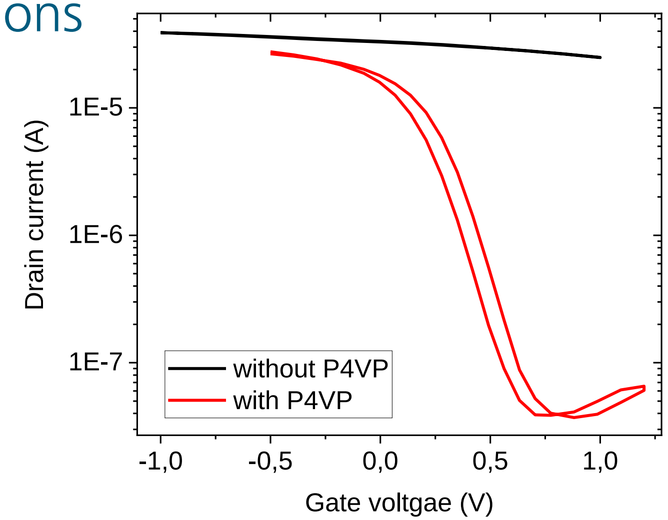


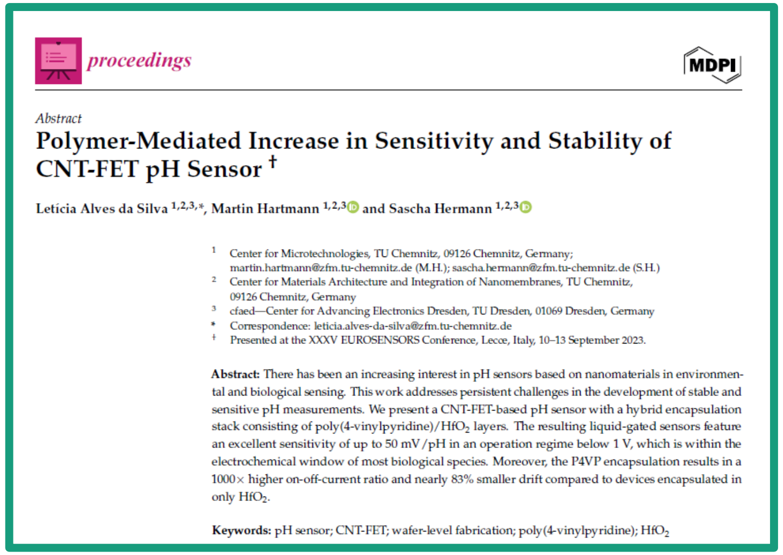
pH sensing

Encapsulated CNT-FET for sensing applications

- ✓ Polymer coating → reduced signal drift and sensor response increase in x1000
- ✓ Improved device characteristics: protection against unintended doping effects, providing enhanced electron transfer kinetics and higher device stability
- ✓ Shift of the operation point to below 1 V, sensitivity of 50 mV/pH unit and 82,5% smaller drift







Abstract

Polymer-Mediated Increase in Sensitivity and Stability of CNT-FET pH Sensor †

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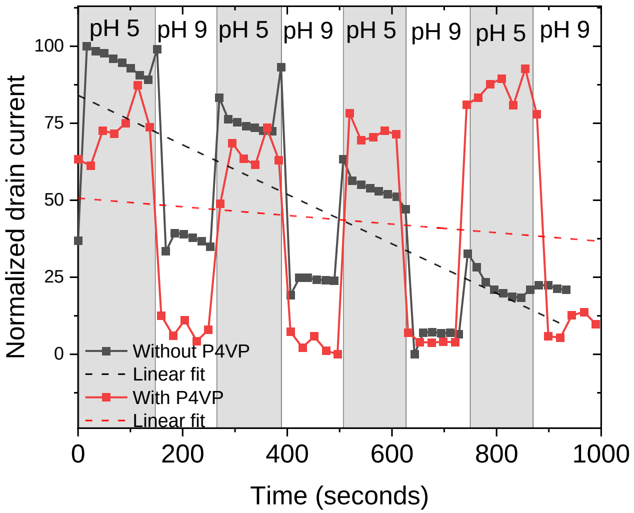
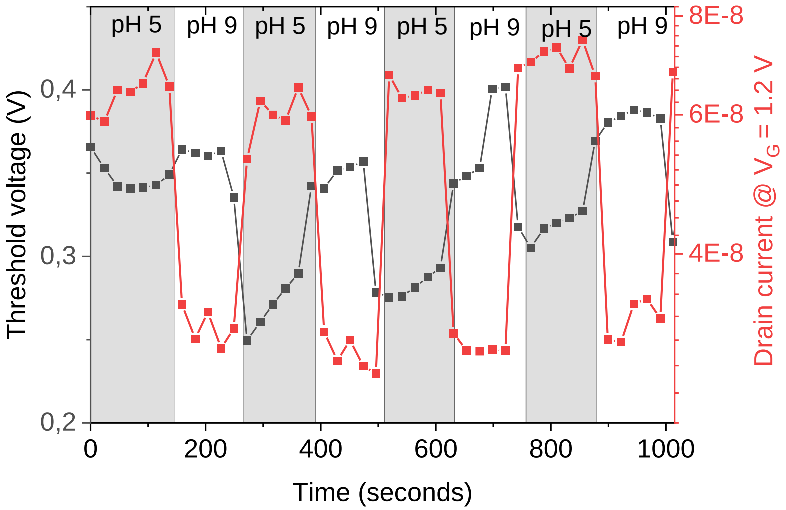
† Presented at the XXXV EUROSENSORS Conference, Lecce, Italy, 10–13 September 2023.

Abstract: There has been an increasing interest in pH sensors based on nanomaterials in environmental and biological sensing. This work addresses persistent challenges in the development of stable and sensitive pH measurements. We present a CNT-FET-based pH sensor with a hybrid encapsulation stack consisting of poly(4-vinylpyridine)/HfO_2 layers. The resulting liquid-gated sensors feature an excellent sensitivity of up to 50 mV/pH in an operation regime below 1 V, which is within the electrochemical window of most biological species. Moreover, the P4VP encapsulation results in a 1000× higher on-off-current ratio and nearly 83% smaller drift compared to devices encapsulated in only HfO_2.

Keywords: pH sensor; CNT-FET; wafer-level fabrication; poly(4-vinylpyridine); HfO_2





Contribution @ Eurosensors 2023

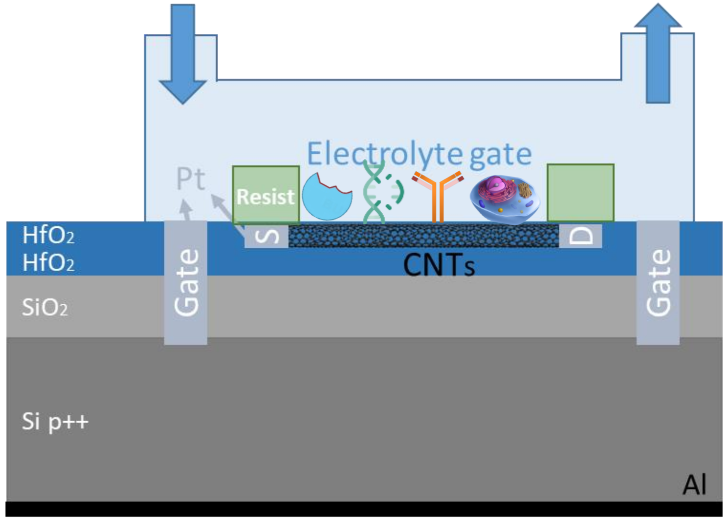
ZfM Zentrum für Mikrotechnologien
TECHNISCHE UNIVERSITÄT CHEMNITZ

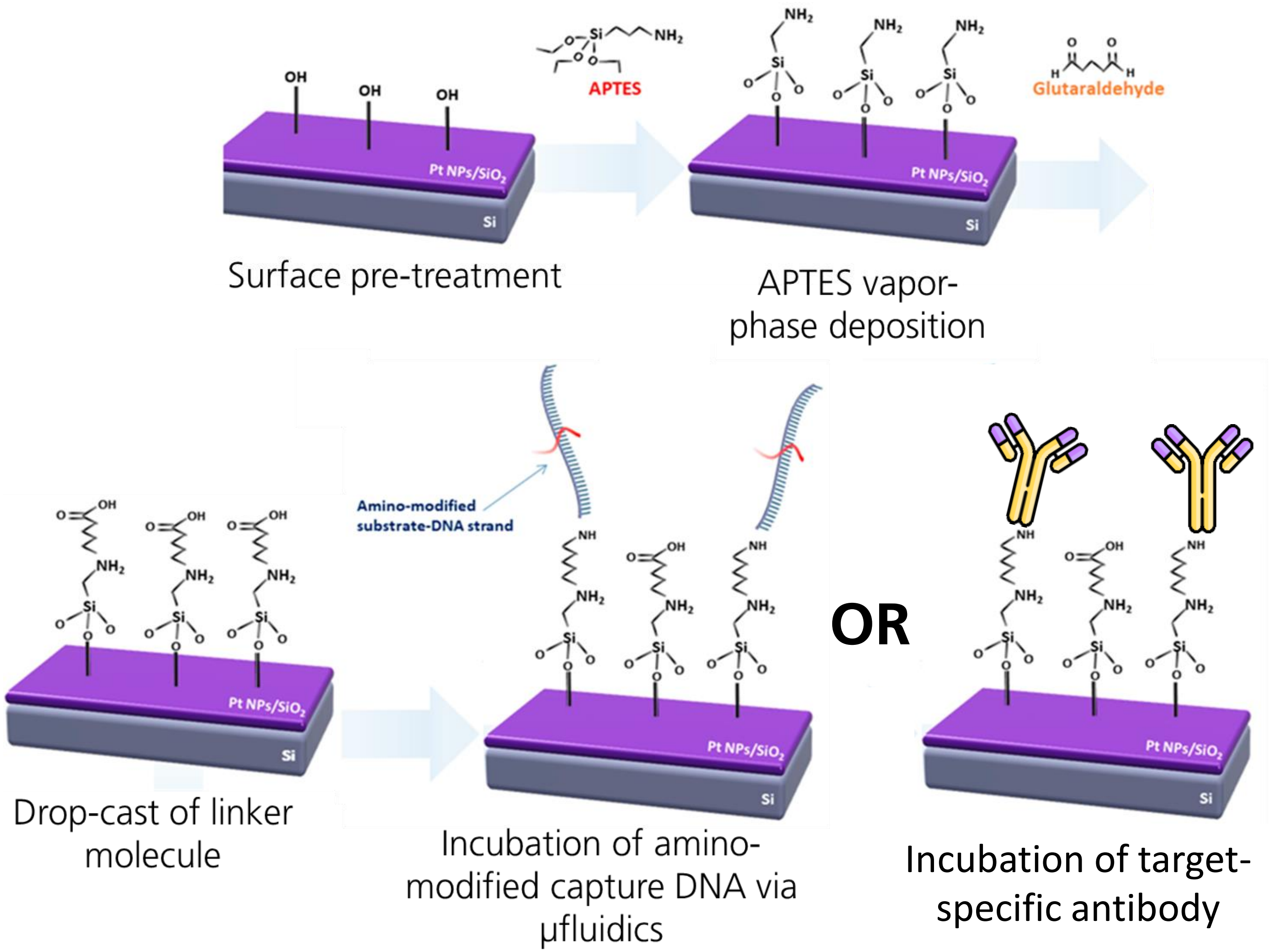
Sensor fabrication

Surface functionalization

Surface preparation

- Surface pre-treatment with UV – ozone
- APTES as encapsulation layer
- Glutaraldehyde: linker molecule
- Capture molecule: cDNA or antibody



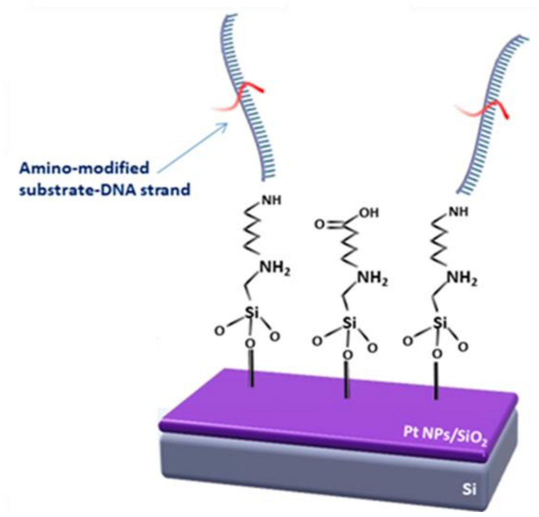


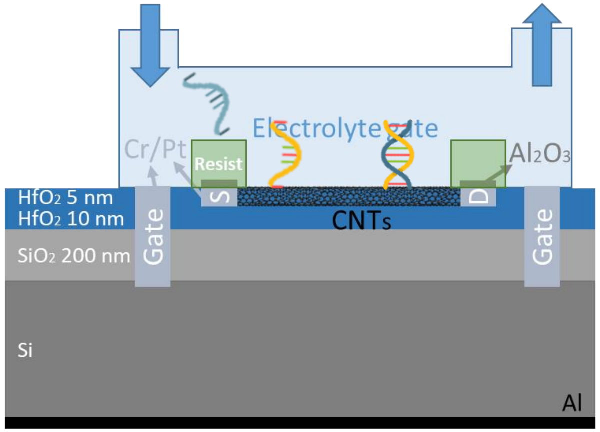
Adapted from: Skotadis, E. Et et al., Sensors 2023, 23, 7818

Sensor analysis

Target DNA detection

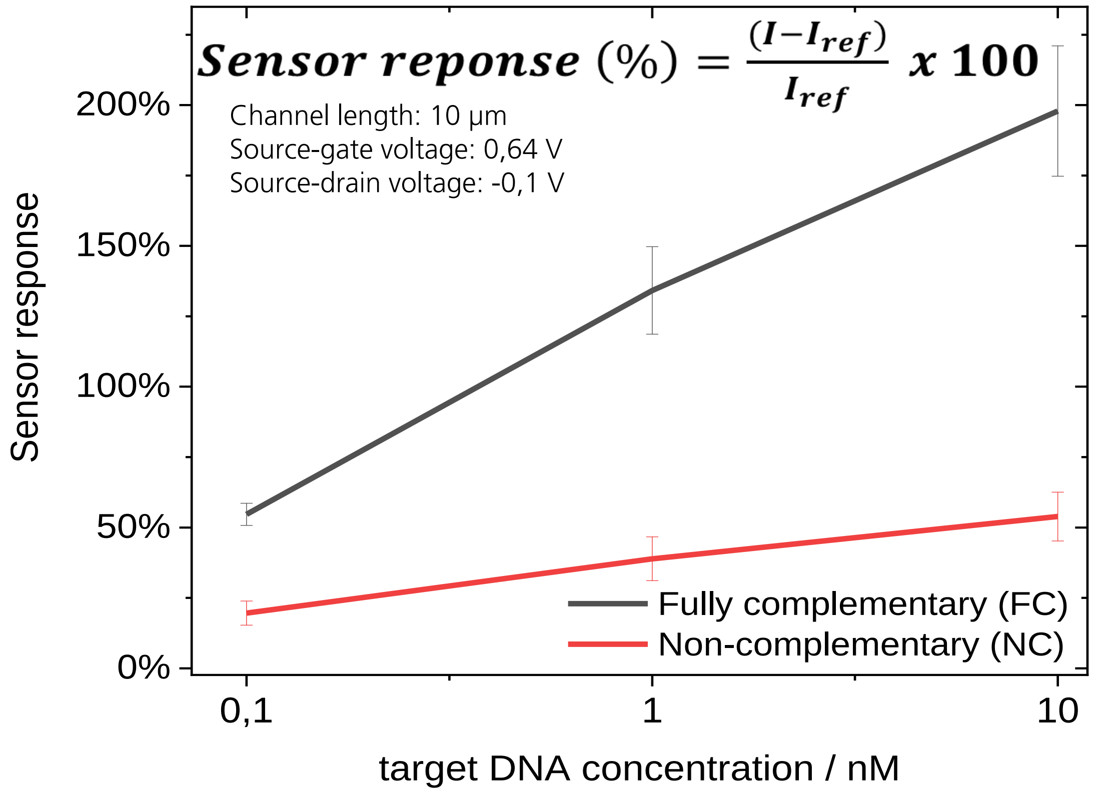
- Target detection with FET:
  - Negatively charged DNA change potential on the sensor surface → change in electrical response
- tDNA detection within 10 minutes
- Response 3.6x higher than current change for long-time measurements of the non-complementary tDNA
- **Proven response down to 0.01 nM tDNA**





Sensor response

tDNA (nM)	FC tDNA	NC tDNA
0,1	55 ± 4 %	20 ± 4%
1	134 ± 16 %	39 ± 8%
10	198 ± 23 %	54 ± 9%



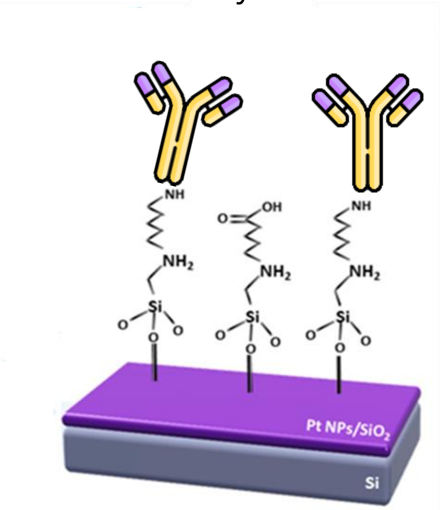
Contribution @ NT 2024

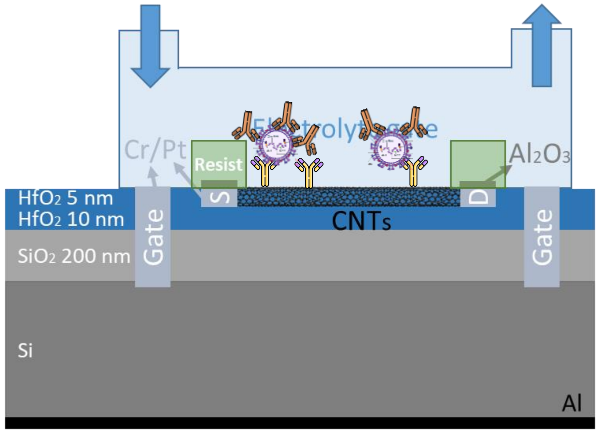
Sensor analysis

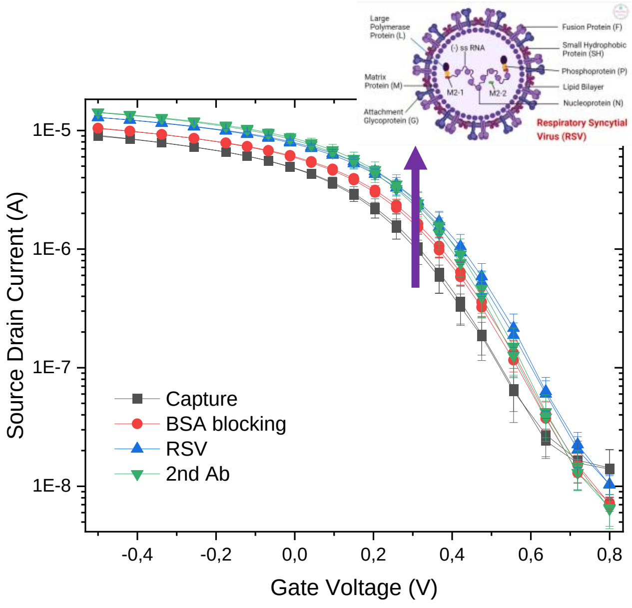
Respiratory Syncytial Virus (RSV) detection

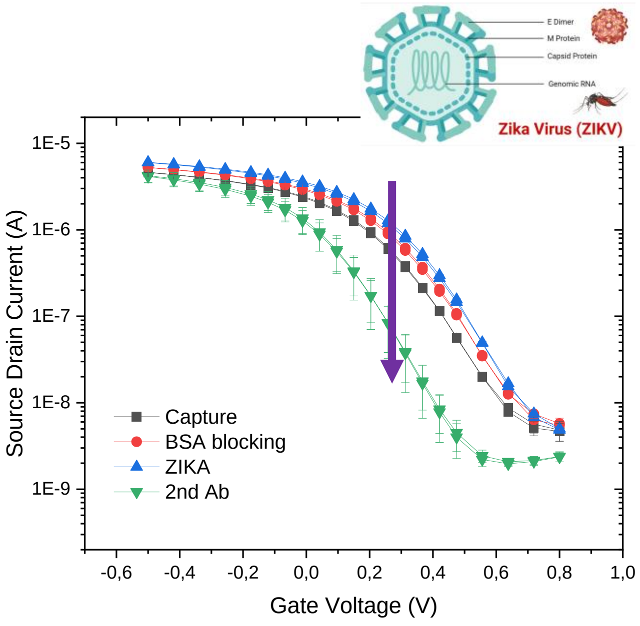
- Target-specific antibody surface coating
- Change potential on the sensor surface upon binding
  - Respose: change in electrical response
- Proof of concept for antibody-based CNT-FET biosensors

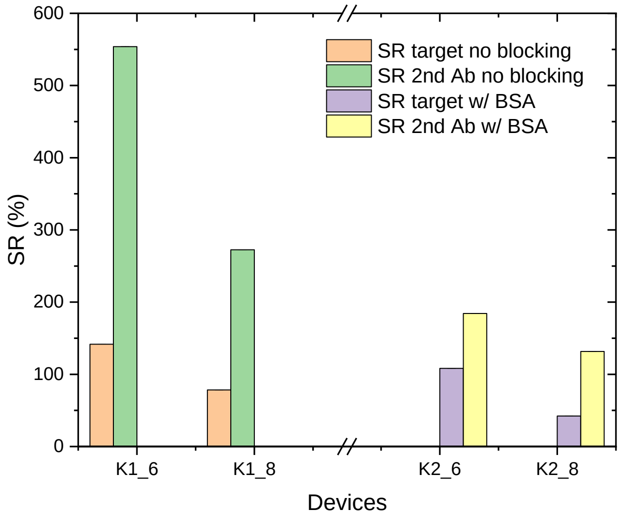
- Specificity: upon incubation with the secondary antibody

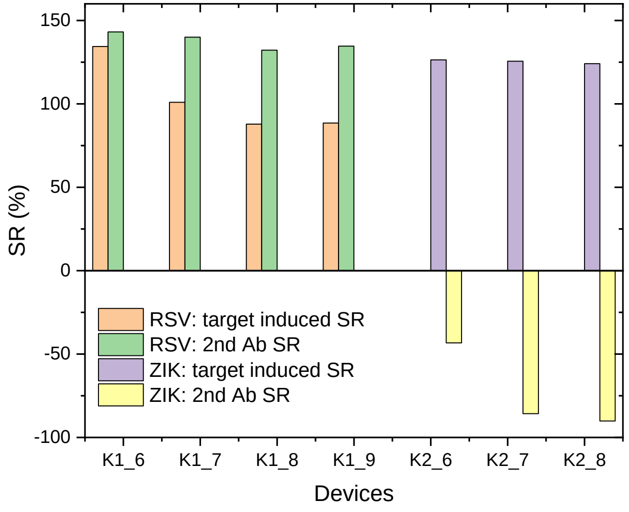












Collaboration with Fraunhofer IZI - Leipzig

Takeaways

- Wafer-level clean room compatible high-yield device fabrication
- Portable and multi-parametric switch matrix measurement platform for electrical sensing
- Development of surface modification approaches for enhanced biomarker detection
- Successful CNT-based sensing platform for DNA and proteins
- Encapsulated chip for on-site measurements and distribution for partners

Thank you for your attention.

Questions?