

Flow-through system based immunoanalytical devices for the diagnosis of viral-infections

Dr. Roman Viter

Vadošais pētnieks, Optisko biosensoru un funkcionālo nanomateriālu laboratorijas vadītājs



UNIVERSITY OF LATVIA
INSTITUTE OF
ATOMIC PHYSICS
AND SPECTROSCOPY





Partners

- Dr. Arunas Ramanavicius (Vilnius University)
 - electrochemical biosensors
 - surface functionalization
- Dr. Roman Viter (University of Latvia)
 - optical biosensors
 - surface functionalization
 - fluidic system
- Dr. Chien-Fu Chen (Taiwan National University)
 - paper based biosensors
 - Au-based nanoparticles
 - bioassays

Project goals (Latvian part)

- To develop optical transducers
- To form bioselective layer on the surface of ZnO
- To develop microfluidic system
- To investigate sensitivity to COVID antibodies
- To perform control measurements



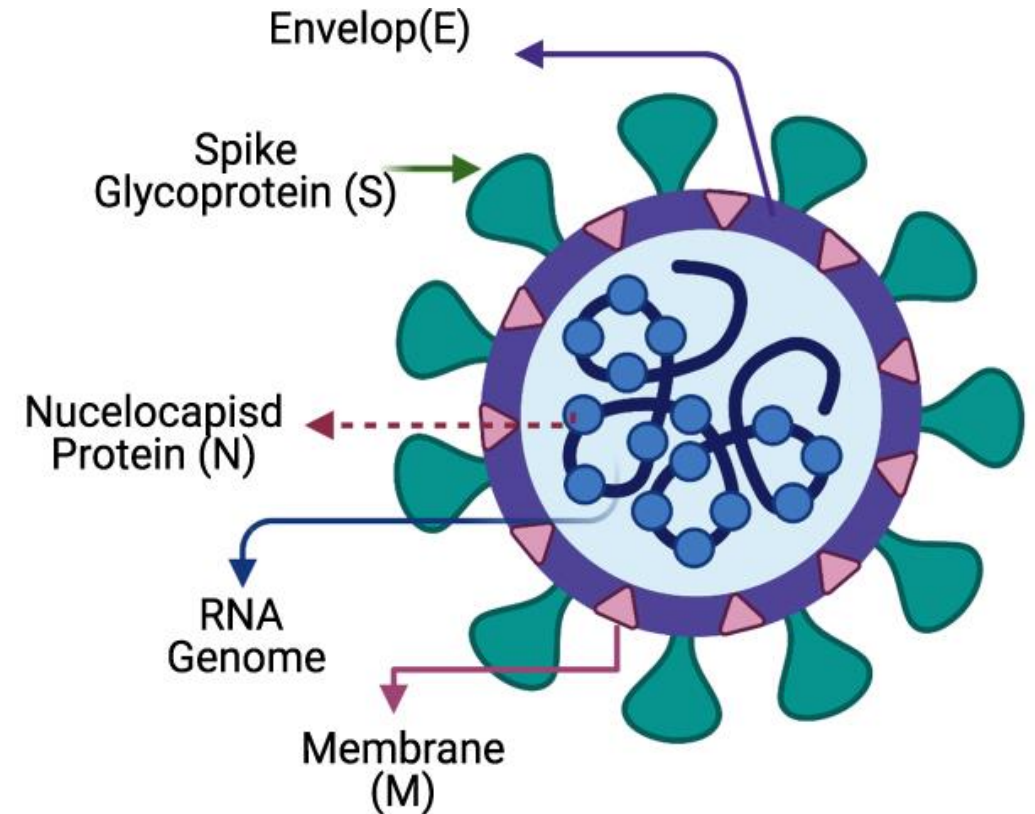
Materials developed

Material acronym	Material description	Potential application in optical biosensor
ZnO tp	ZnO tetrapods, formed by gas oxidation method	High photoluminescence (PL)
ZnOtp-PANI	ZnO tetrapods, coated by polyaniline (PANI) layer	PANI drastically reduced PL
ZnOtp-Au	ZnO tetrapods, coated by gold nanoparticles	PANI drastically reduced PL



Biomolecules used

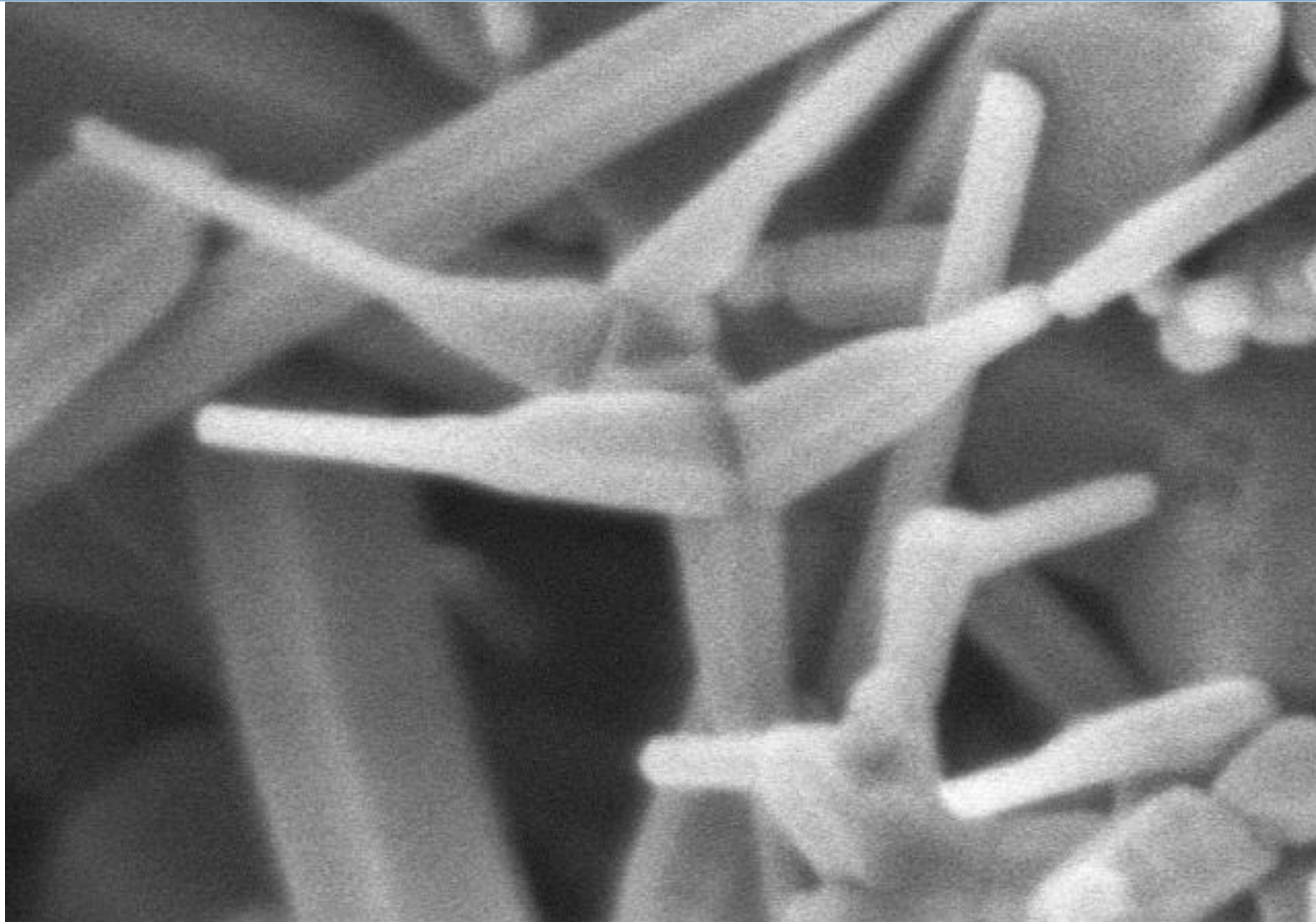
- Sars-COV-rS – spike protein
- Sars-COV-rN – nucleocapsid protein
- Antibodies were selected from COVID-19 positive blood serum probes
- Control measurements were the probes, taken from healthy person blood serum
- All probes were prepared by Vilnius University





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SEM of ZnO tetrapods

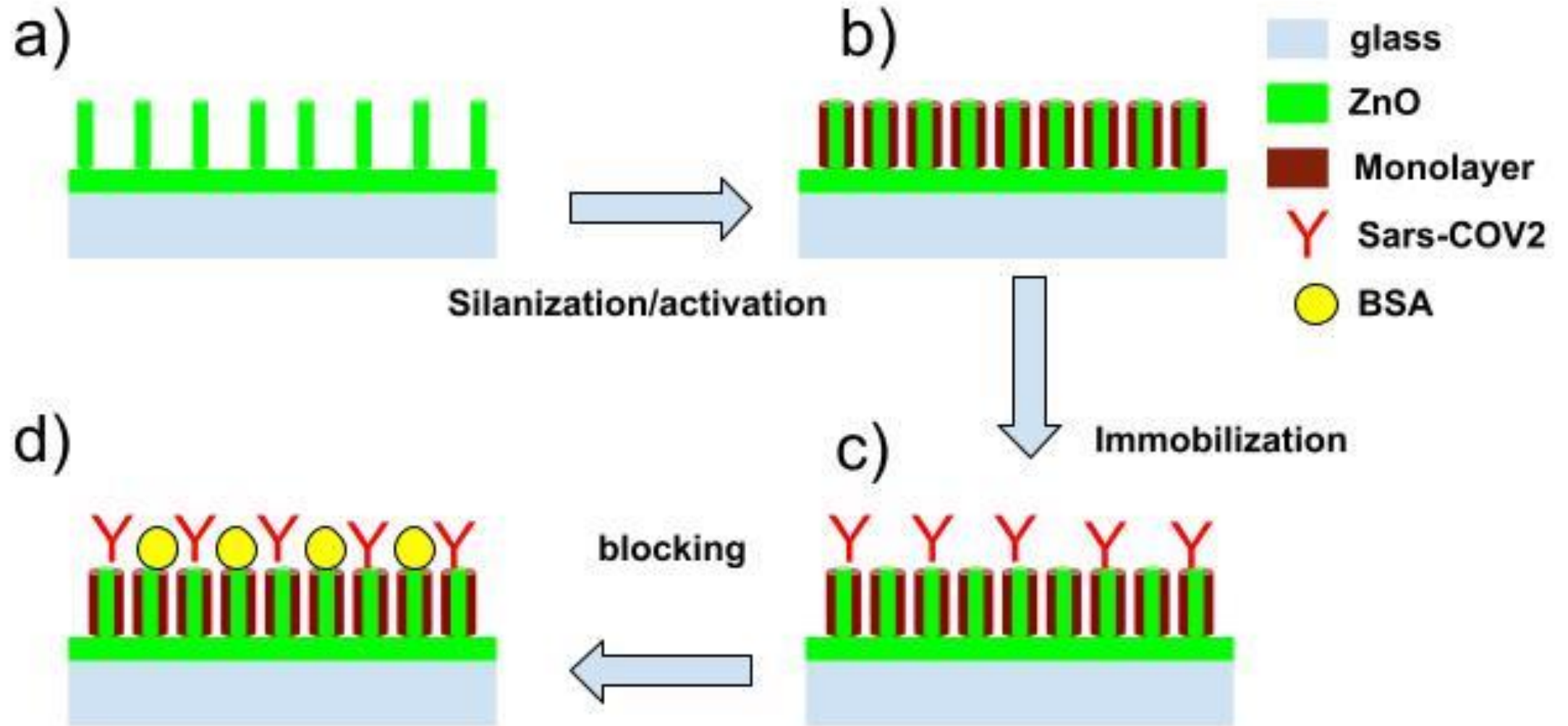


S4800 2.0kV 2.5mm x200k SE(U)

200nm

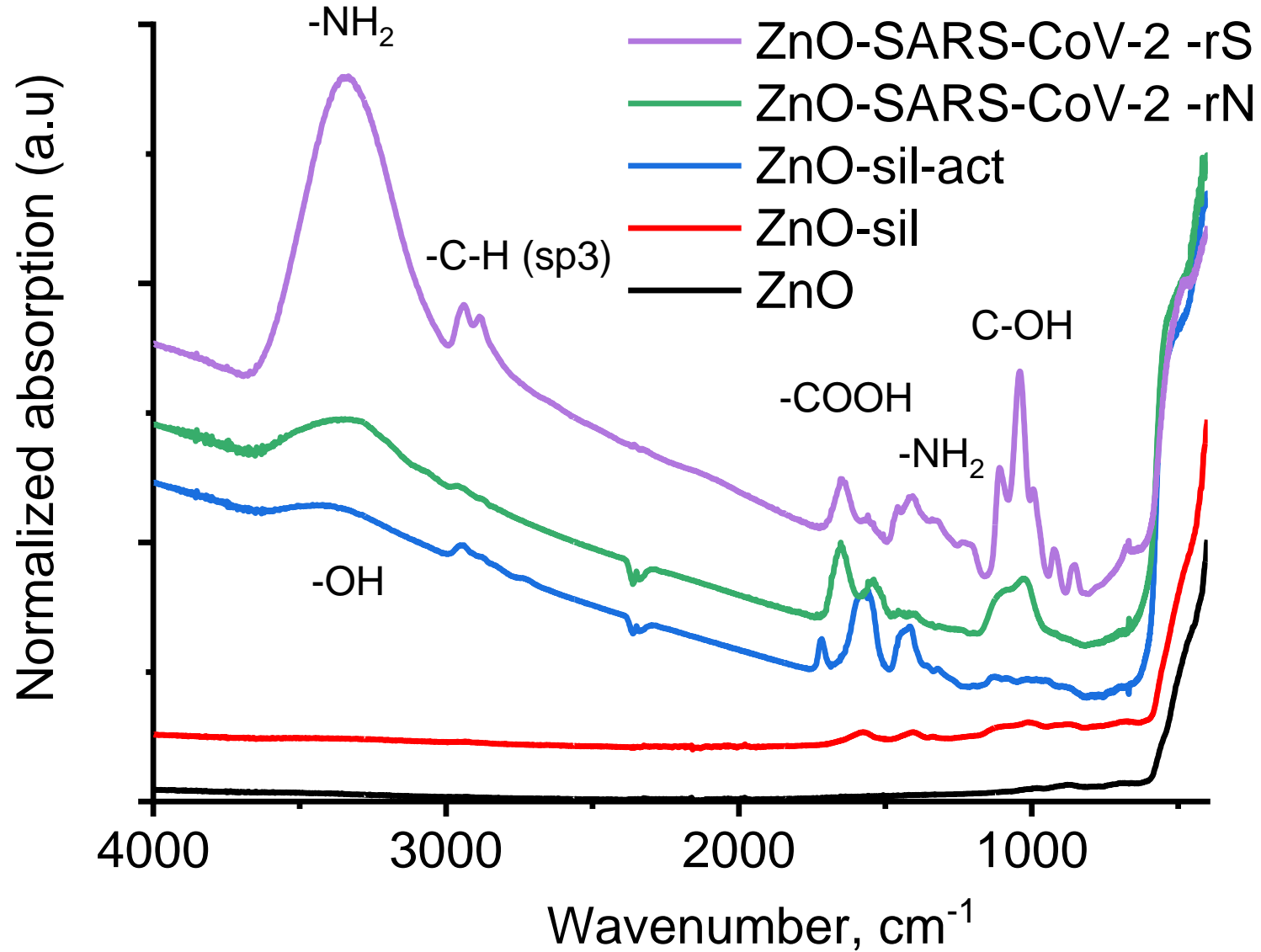


Biofunctionalization of the ZnO-tp surface



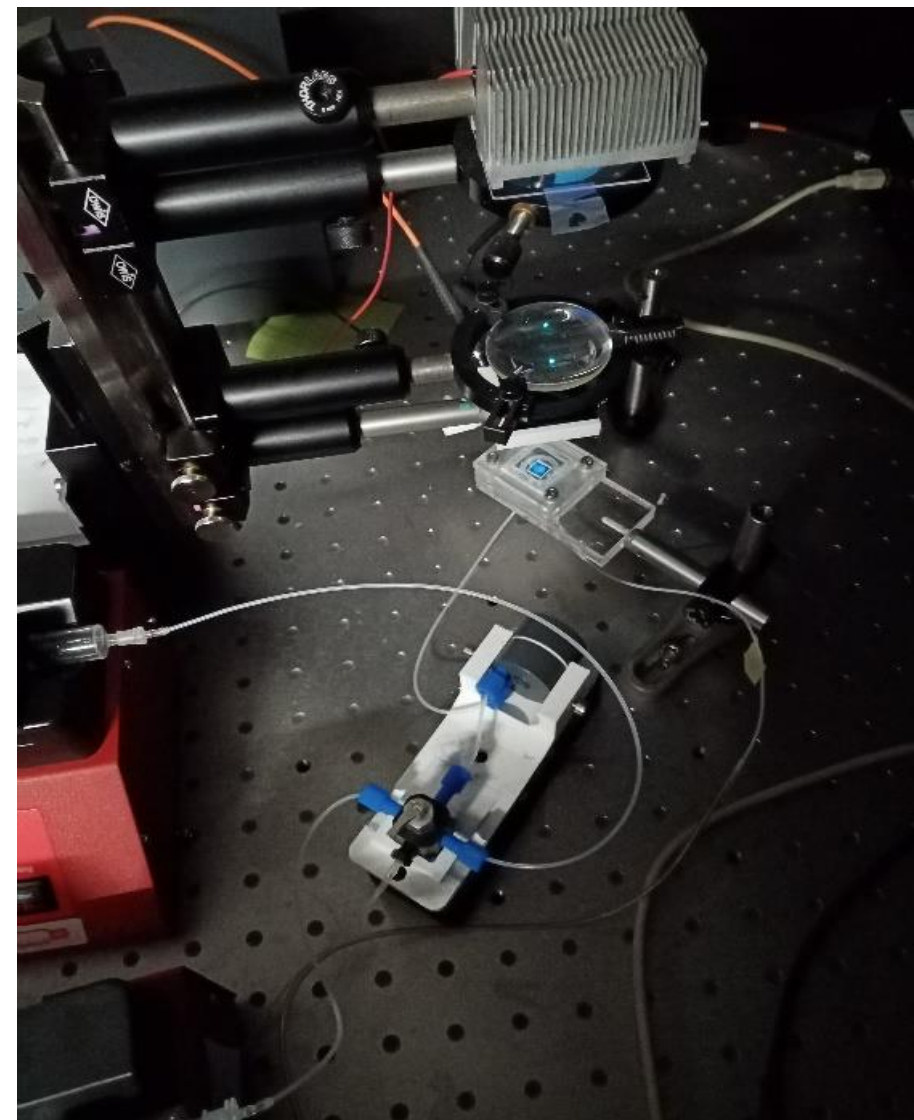
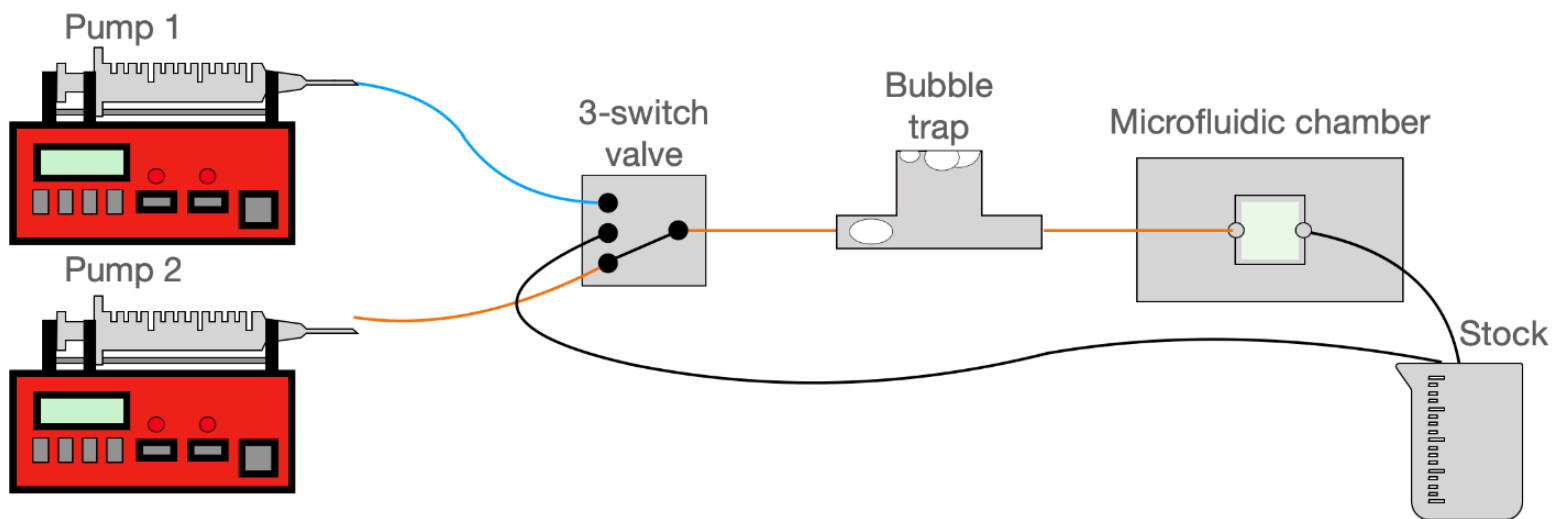


ZnO surface functionalization



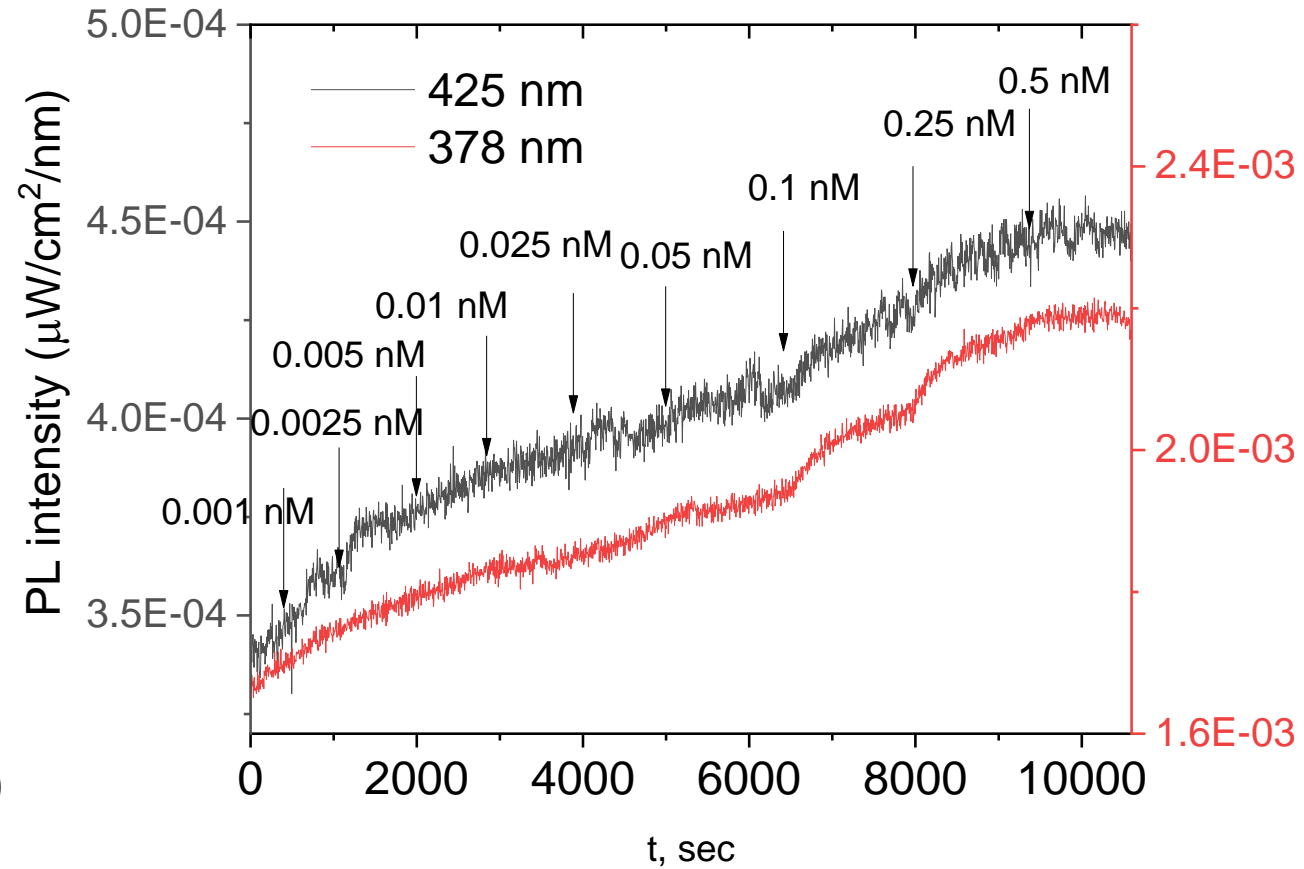
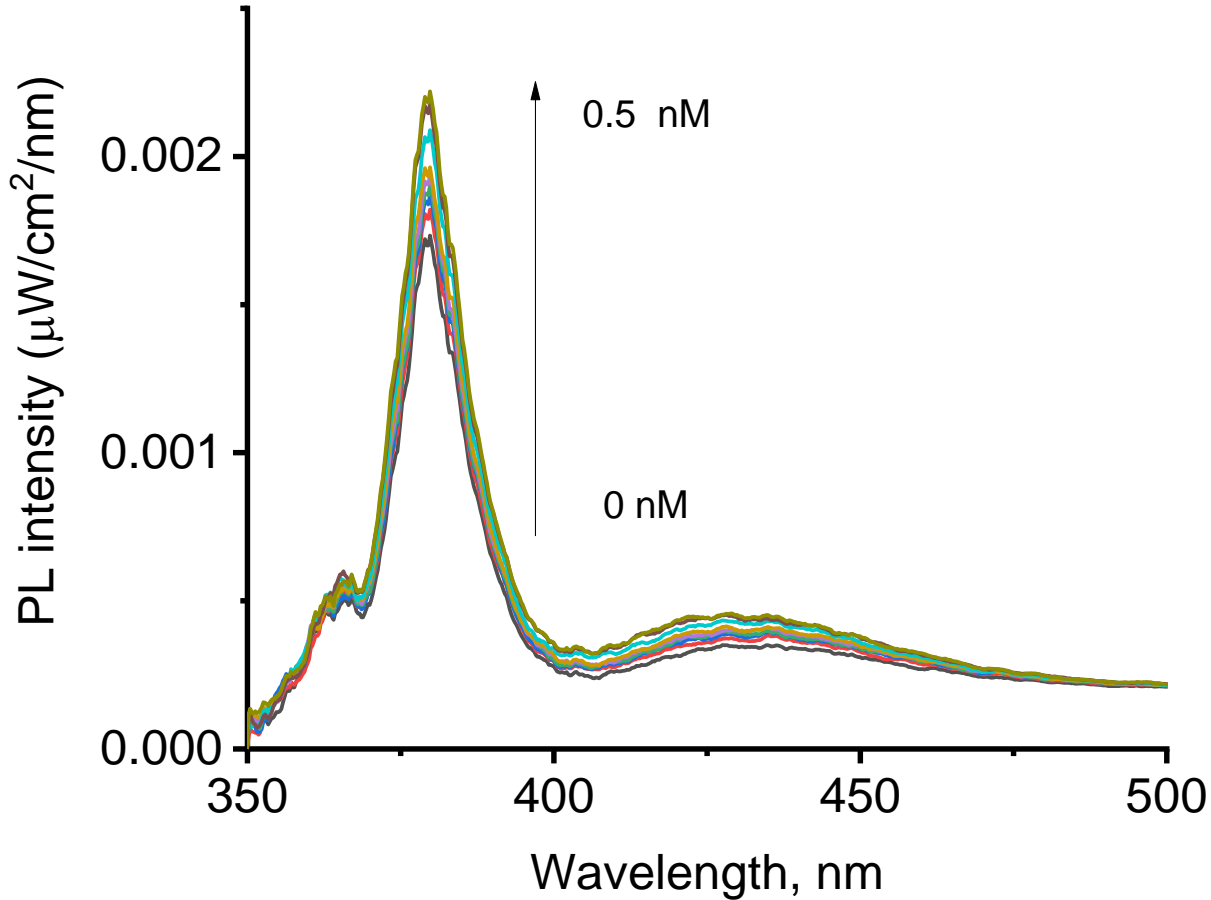


Design of fluidic system



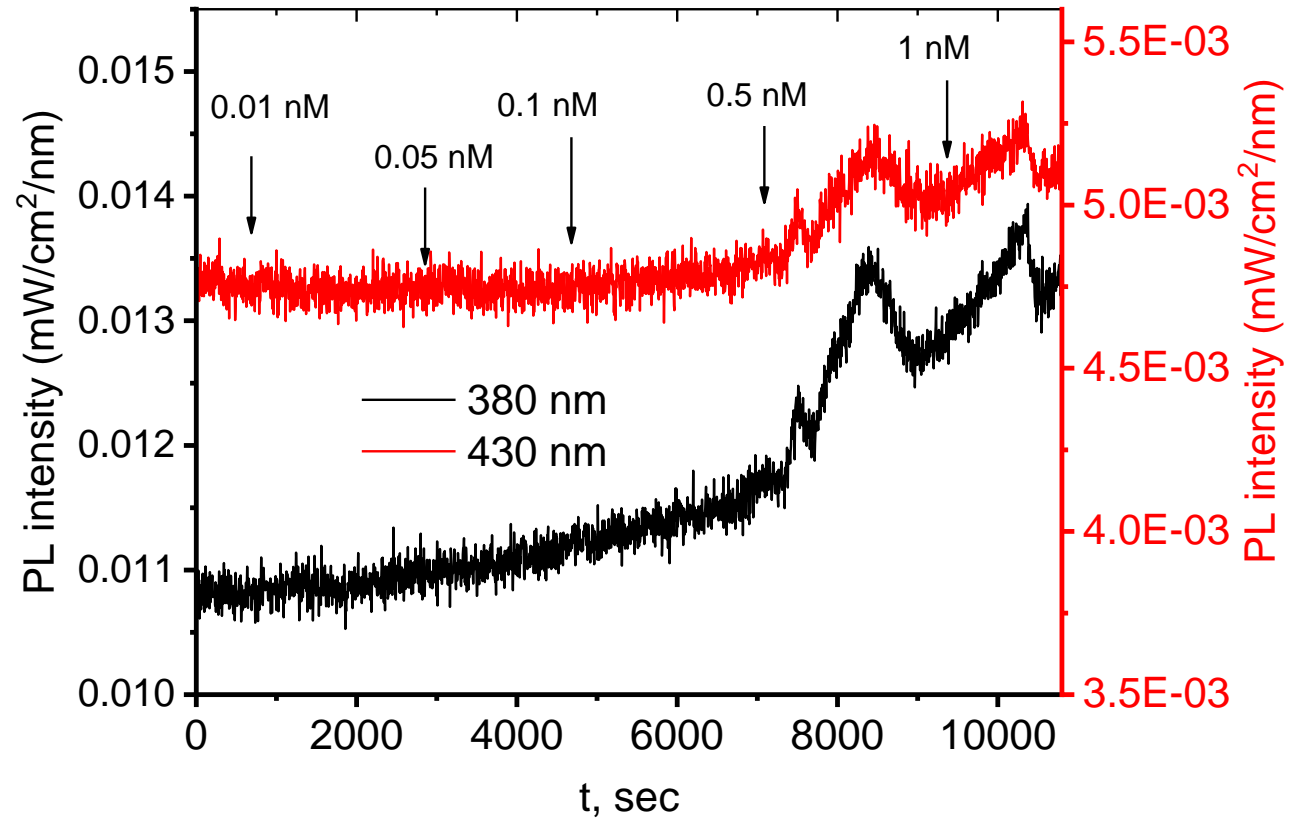
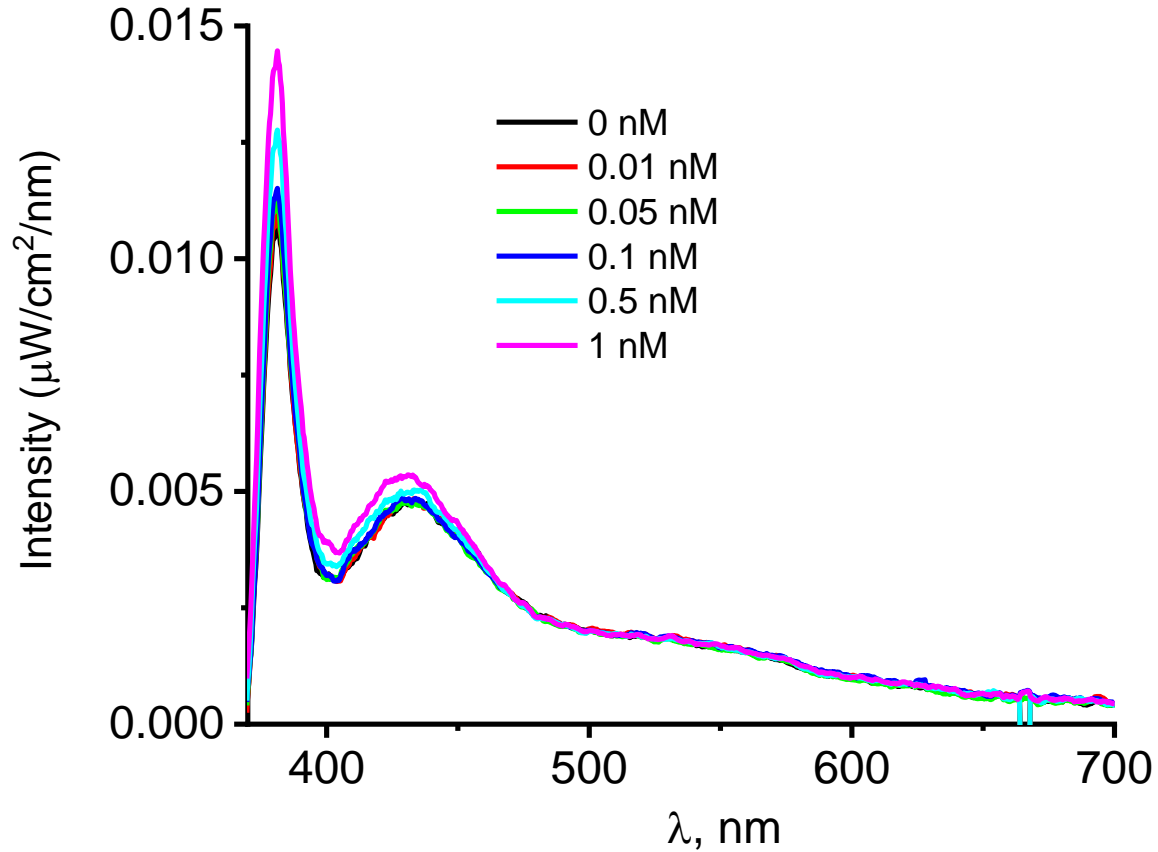


Sensor test to COV-2 of ZnO-Sars-COV2-rS



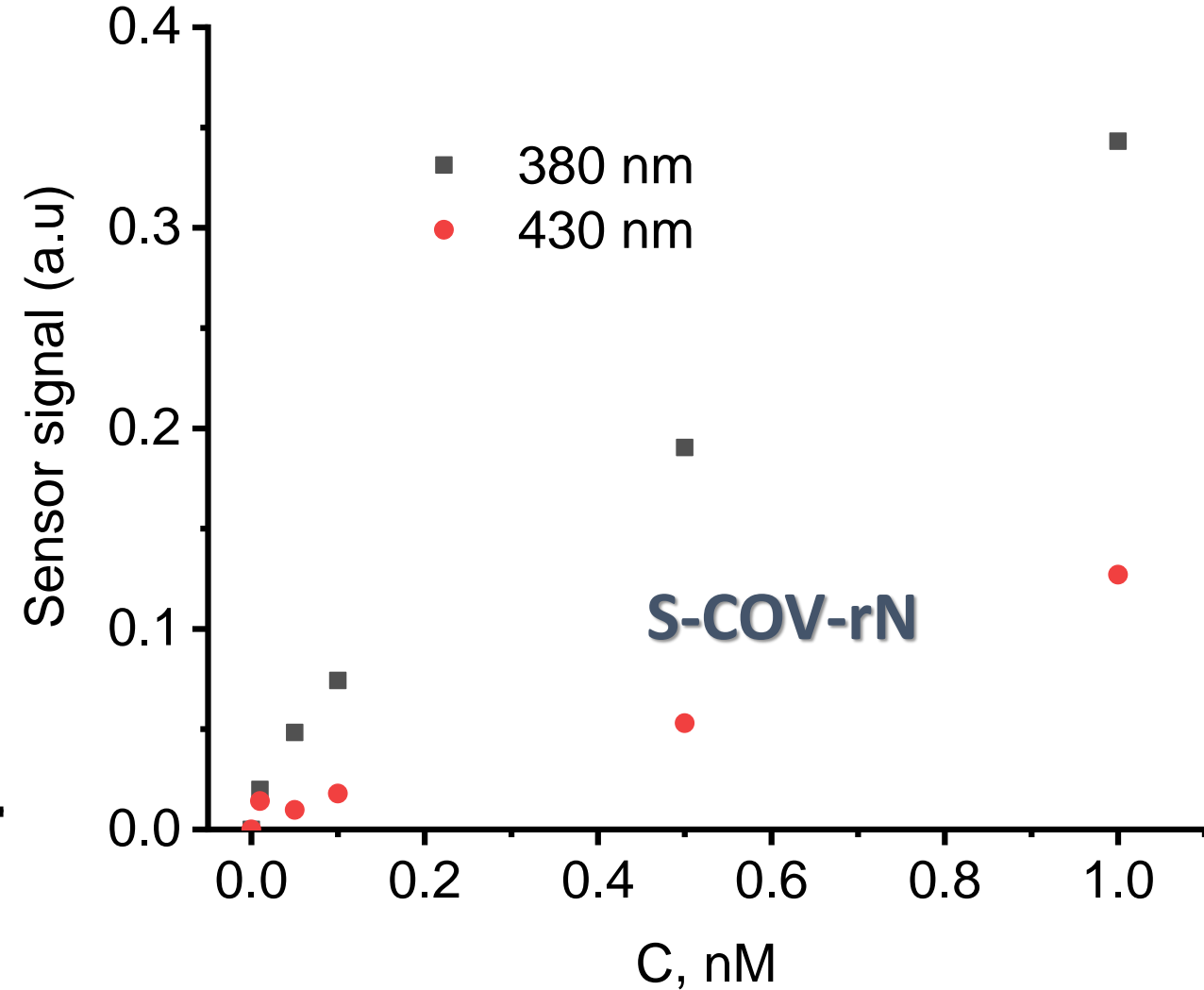
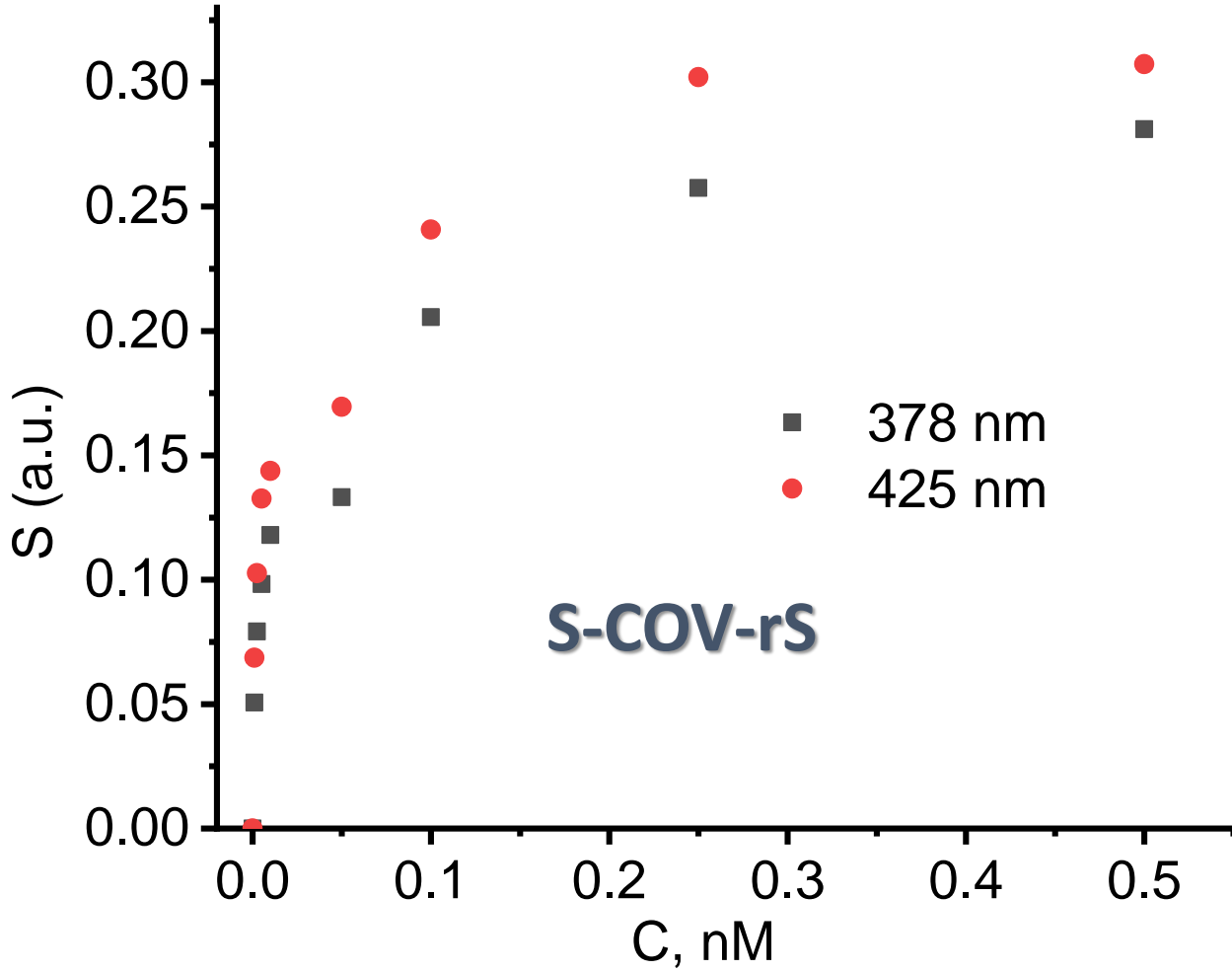


Sensor test to COV-2 of ZnO-Sars-COV2-rN



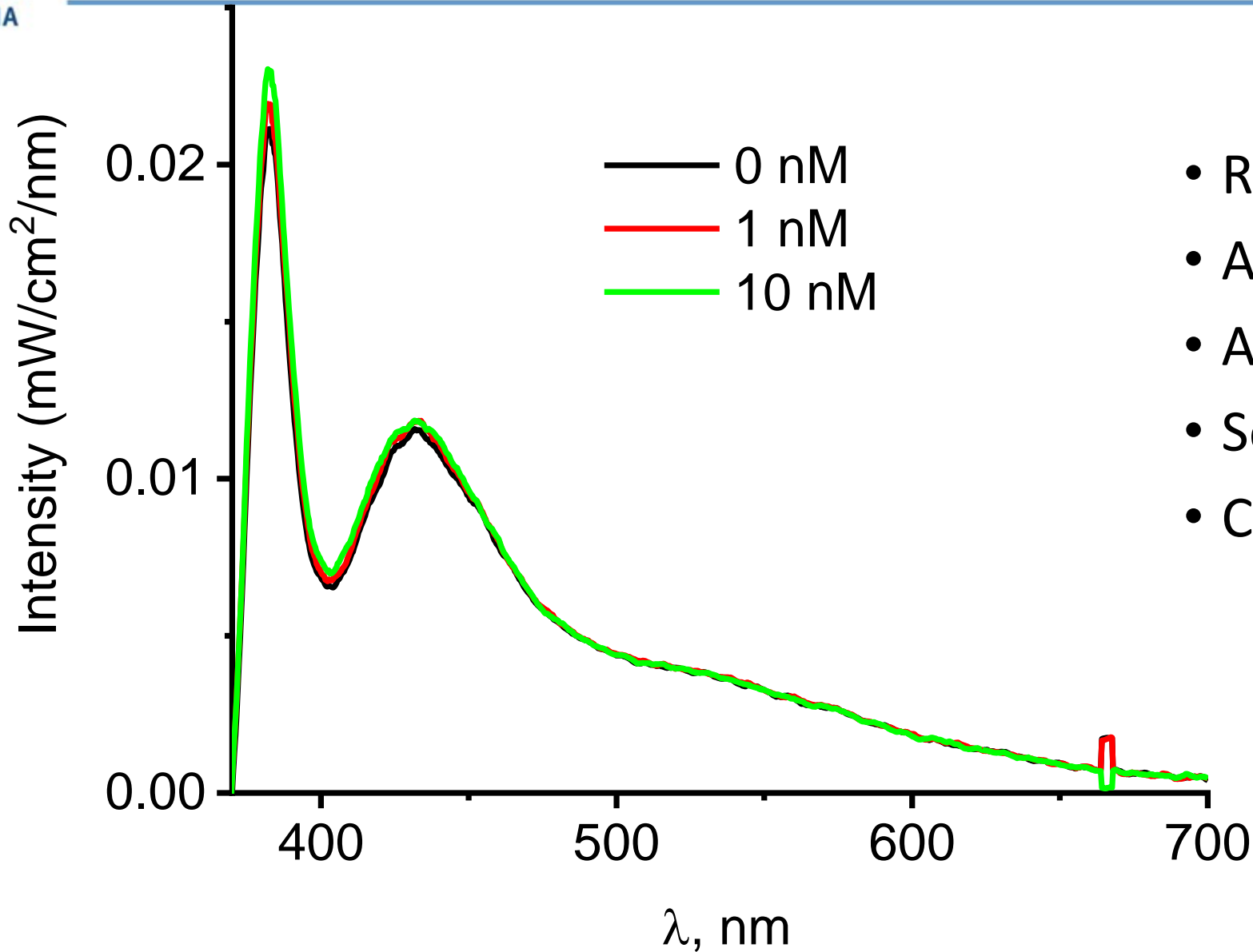


Sensor response





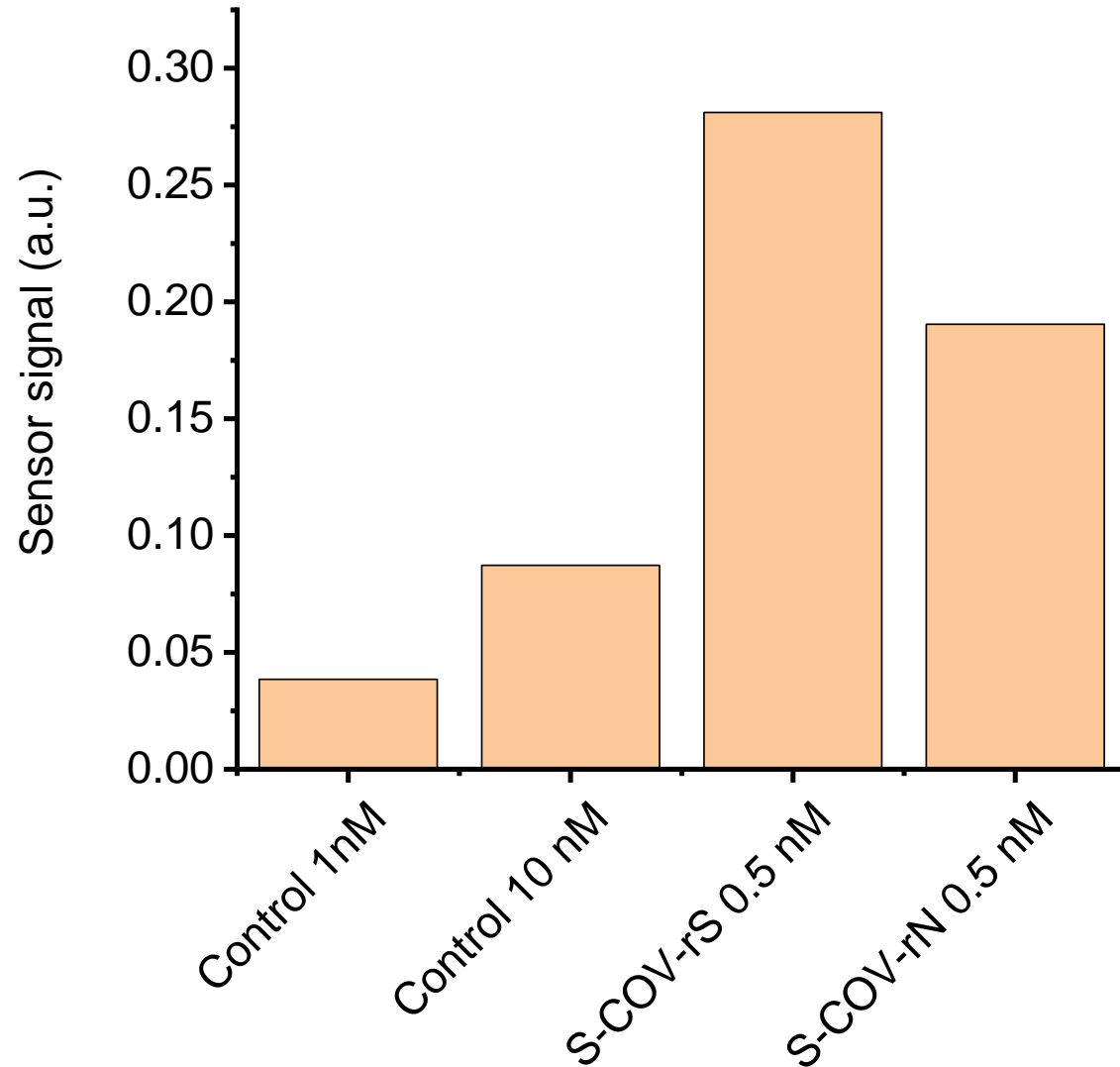
Control tests



- Repeatability
- Analysis of isotherms
- Affinity constants
- Sensitivity analysis
- Control measurements



Selectivity of the sample



- Sensitivity range
- ZnO-S-COV-rN: 0.1-1 nM, LOD=0.1 nM
- ZnO-S-COV-rS: 0.01-0.1 nM, LOD=0.05 nM



Conclusions

- Between Sars-COV-rS and Sars-COV-rN, the first has more stable layer on the ZnO surface
- PL signal increased in all cases under interaction with COVID-19 antibodies
- Sensitivity range for COVID-19 was 0.01-0.1 nM and 0.1-1 nM for Sars-COV-rS and Sars-COV-rN, respectively
- Bioselective layer of Sars-COV-rS has higher affinity to COVID-19 in the optical biosensor
- Developed fluidic system has good potential for Covid-19 detection.



Dissemination and mobility

- 1) M. Drobysh, A. Ramanaviciene, R. Viter, C.-F. Chen, U. Samukaite-Bubniene, V. Ratautaite, A. Ramanavicius. Biosensors for the Determination of SARS-CoV-2 Virus and Diagnosis of COVID-19 Infection. *International Journal of Molecular Sciences* 2022, 23, 666. <https://doi.org/10.3390/ijms23020666> Q1
- 2) S. Ramanavičius, I. Morkvėnaitė-Vilkončienė, U. Samukaitė-Bubnienė, V. Ratautaitė, I. Plikusienė, R. Viter, A. Ramanavičius. Electrochemically deposited molecularly imprinted polymer based sensors. *Sensors* 2022, 22, 1282. <https://doi.org/10.3390/s22031282> Q2
- 3) V. Liustrovaite, M. Drobysh, A. Rucinskiene, A. Baradoke, A. Ramanaviciene, I. Plikusiene, U. Samukaite-Bubniene, R. Viter, C.-F. Chen, A. Ramanavicius. Towards an electrochemical immunosensor for the detection of antibodies against SARS-CoV-2 spike protein. *Journal of The Electrochemical Society* 2022, 169, 037523. <https://doi.org/10.1149/1945-7111/ac5d91> Q1- Q2
- 4) M. Drobysh, V. Liustrovaite, A. Baradoke, A. Rucinskiene, A. Ramanaviciene, V. Ratautaite, R. Viter, C.-F. Chen, I. Plikusiene, U. Samukaite-Bubniene, R. Slibinskas, E. Ciplys, M. Simanavicius, A. Zvirbliene, I. Kucinskaite-Kodze, A. Ramanavicius. Electrochemical determination of interaction between SARS-CoV-2 spike protein and specific antibodies. *International Journal of Molecular Sciences* 2022, 23, 6768. <https://doi.org/10.3390/ijms23126768> Q1
- 5) M. Drobysh, V. Liustrovaite, A. Baradoke, R. Viter, C-F. Chen, A. Ramanavicius, A. Ramanaviciene. Determination of rSpike Protein by Specific Antibodies with Screen-Printed Carbon Electrode Modified by Electrodeposited Gold Nanostructures. *Biosensors*, 2022, 12, 593. <https://doi.org/10.3390/bios1208059> Q1-Q2
- 6) M. Drobysh, A. Ramanaviciene, R. Viter, A. Ramanavicius. Affinity sensors for the diagnosis of COVID-19. *Micromachines*, 2021, 12, 390. DOI: 10.3390/mi12040390 Q2



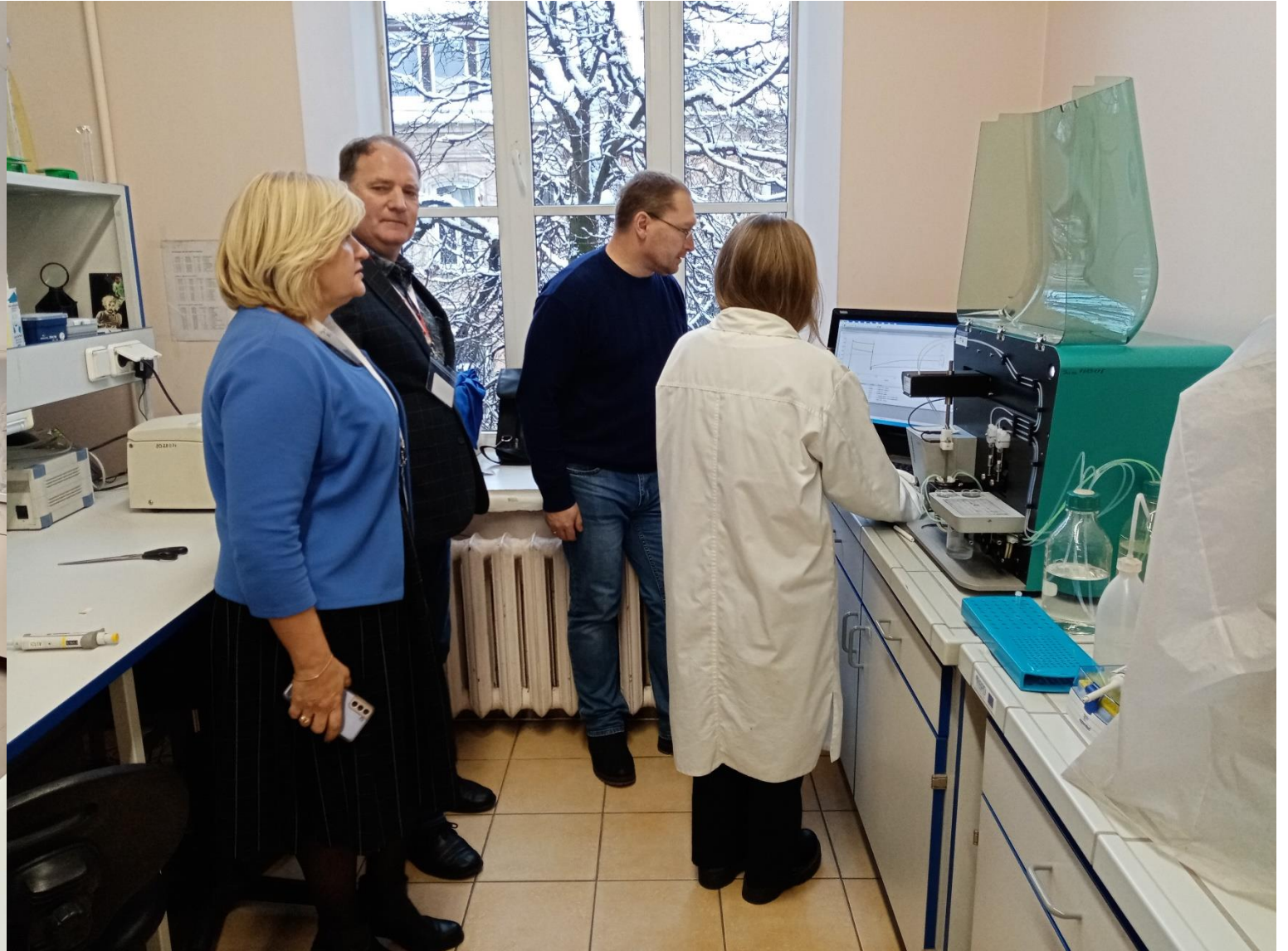
Dissemination and mobility

- 1) M. Drobysh, V. Liustrovaitė, A. Ručinskienė, M. Simanavičius, A. Žvirblienė, R. Slibinskas, I. Plikusienė, E. Ciplys, R. Viter, C.F. Chen, A. Towards electrochemical affinity sensors for the COVID-19 diagnosis. "Advanced materials and technologies 2021" International conference, August 23-27, 2021 Palanga, Lithuania: abstract book.
- Kaunas University of Technology, 2021. p. 34.
- • 2) M. Drobysh, A. Ramanavičiene, R. Viter, A. Ramanavičius. The review of affinity sensors for the diagnosis of COVID-19. "Chemistry and chemical technology 2021" International conference, September 24, 2021 Vilnius, Lithuania: abstract book. 2021. p.22.



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Signal Enhanced Lateral Flow Immunoassay

Second amplification
First amplification
Hybridization reaction

Sample pad Conjugate pad Nitrocellulose membrane Absorbent pad

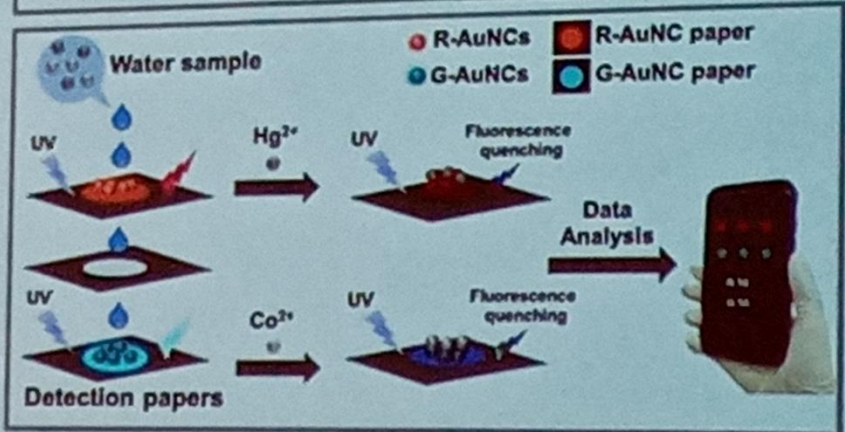
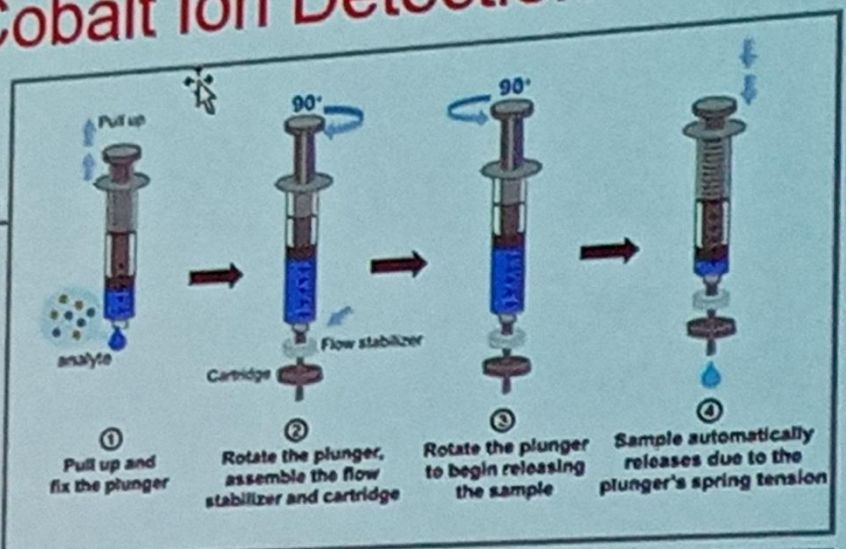
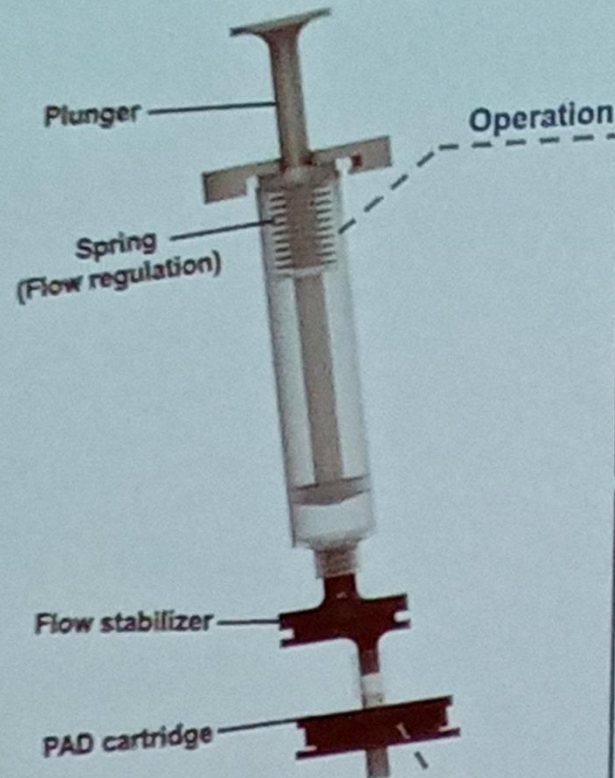
Hybridization	First signal amplification	Second signal amplification

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A Semi-Automatic Environmental Monitoring Device for Mercury and Cobalt Ion Detection





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Thank you