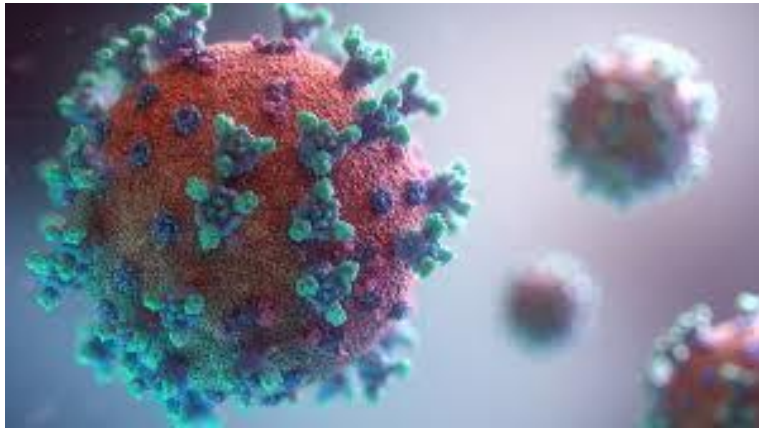


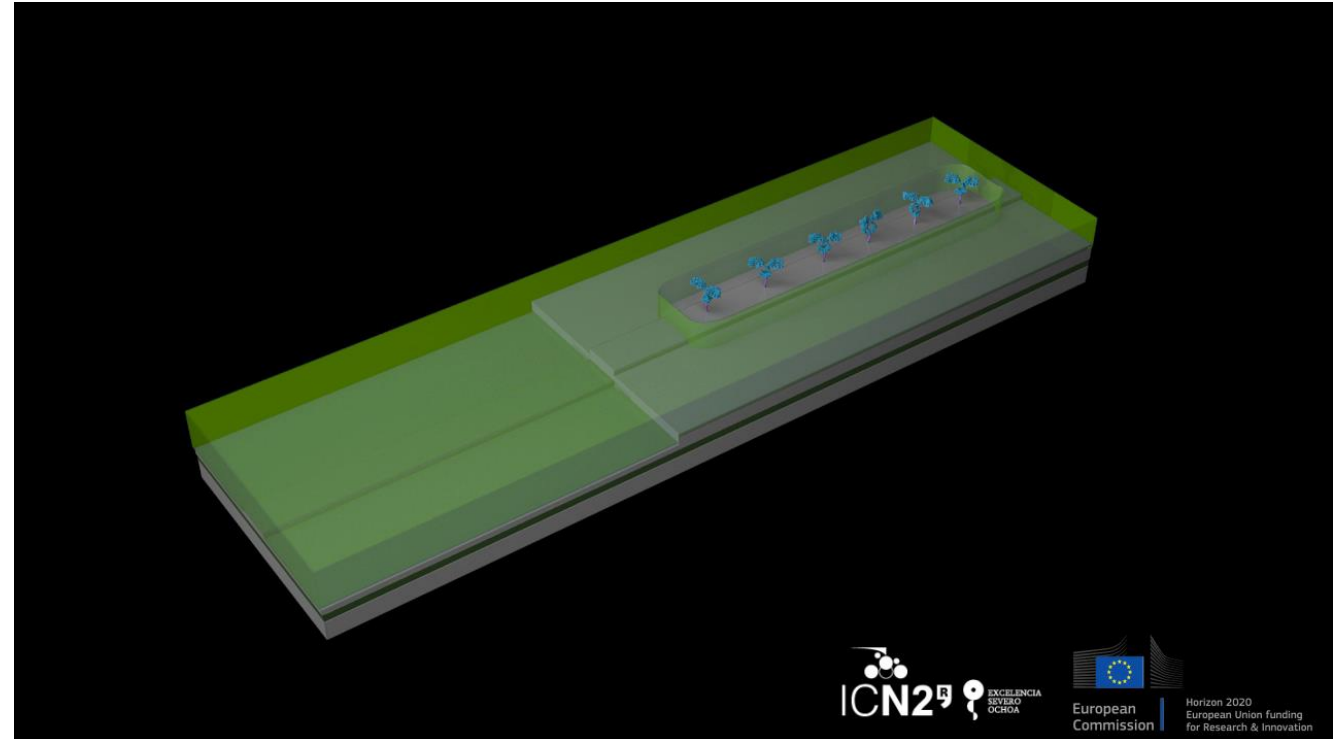
Combating COVID-19: ADVANCED NANOBIOSENSING PLATFORMS FOR POC GLOBAL DIAGNOSTICS AND SURVEILLANCE



Prof. Laura M. Lechuga

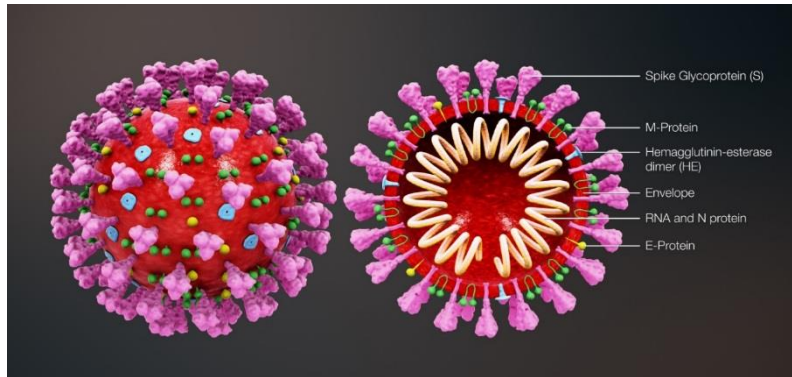
Nanobiosensors and Bioanalytical Applications group (NanoB2A)
Catalan Institute of Nanoscience and Nanotechnology (ICN2)
CSIC, BIST & CIBER-BBN
Barcelona, España

@nanob2a_group
nanob2a.icn2.cat



DIAGNOSTICS OF COVID-19

SARS-CoV-2



Diagnostics strategies

- Virus RNA detection
- Viral Antigen detection (intact virus)
- Serological test (immunological response)

Nucleic Acid Amplification Tests (RT-PCR)

Advantages: high sensitivity, specificity, well-established, high scalability.

Limitations: time consuming (2-5 h), reproducibility, trained personnel, limited to lab, complex instrumentation, price.



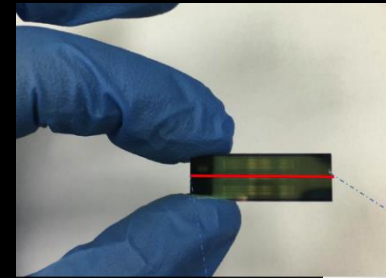
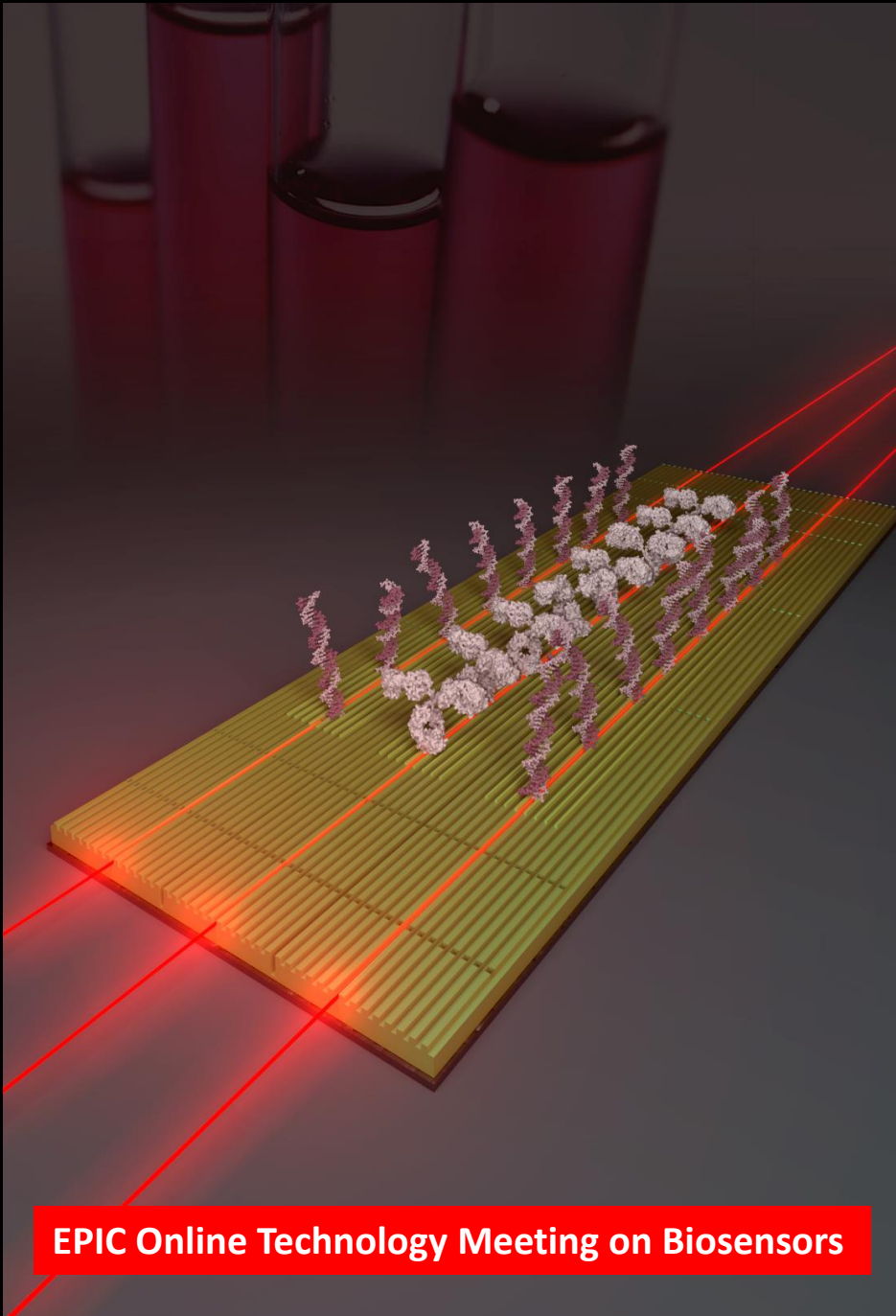
POC BIOSENSOR



- Easy diagnostics (out of specialized lab)
- Label-free, high sensitivity
- Fast diagnosis (min)
- Multiplexing capabilities
- User-friendly/minimum operation
- Minimum sample treatment/untreated samples

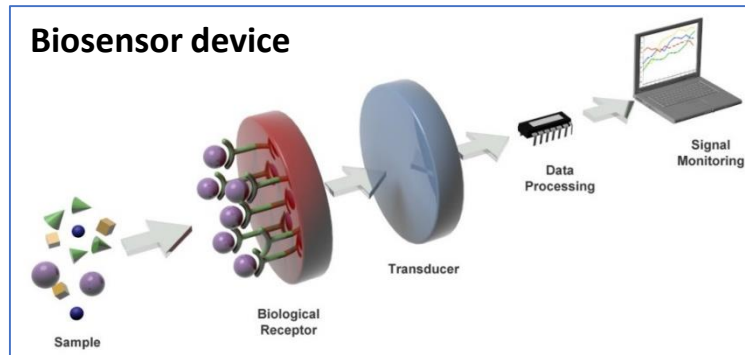
CONVAT PROJECT

A new **POC** nanophotonics **biosensor platform** based on Silicon Nitride interferometers capable to provide an **accurate and fast COVID-19 diagnosis** without requiring complex equipment.



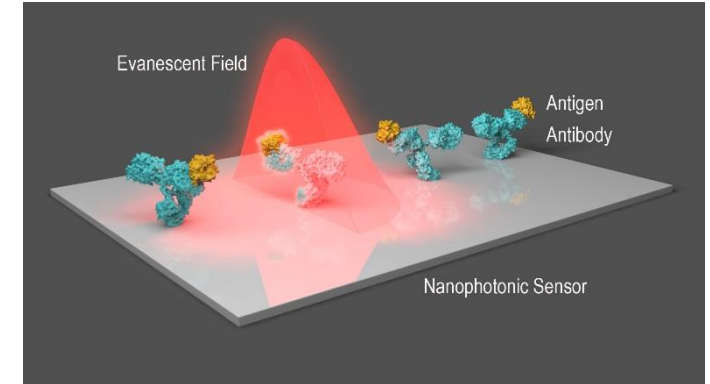
- Own production of antibodies and proteins
- Diagnostics of COVID-19 in human samples and clinical validation (antigen & RNA label-free detection)
- Surveillance of SARS-Cov-2 coronavirus in reservoir animals samples

Interferometric Biosensors



Evanescent wave optical Biosensor

- Immunity to electromagnetic interferences
- Label-free/ Real-time
- **HIGH SENSITIVITY**
- Multiplexing
- Miniaturization/integration lab-on-a-chip



EW detection:
Sensitive to surface
refractive index changes

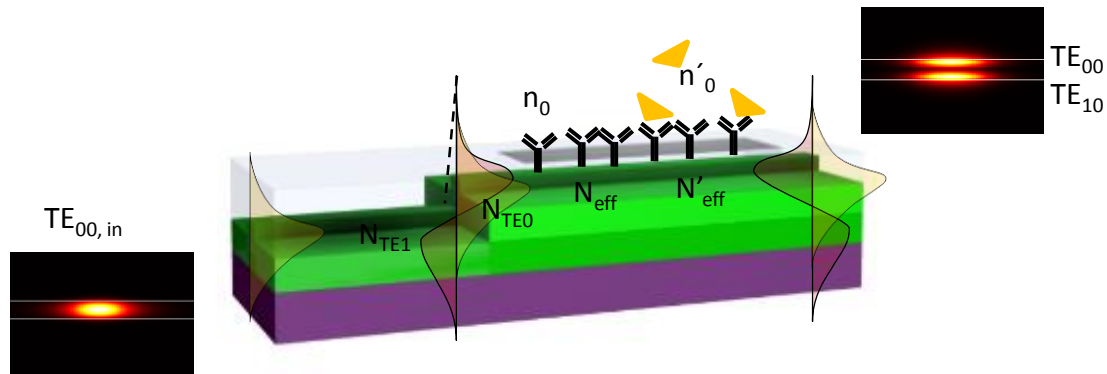
Evanescent wave biosensors	Bulk sensitivity (RIU)
Surface Plasmon Resonance (SPR)	$10^{-5} - 10^{-7}$
Grating couplers	$10^{-4} - 10^{-6}$
Interferometers	$10^{-7} - 10^{-9}$
Ring resonator	$10^{-5} - 10^{-7}$
Photonic crystal	$10^{-4} - 10^{-5}$



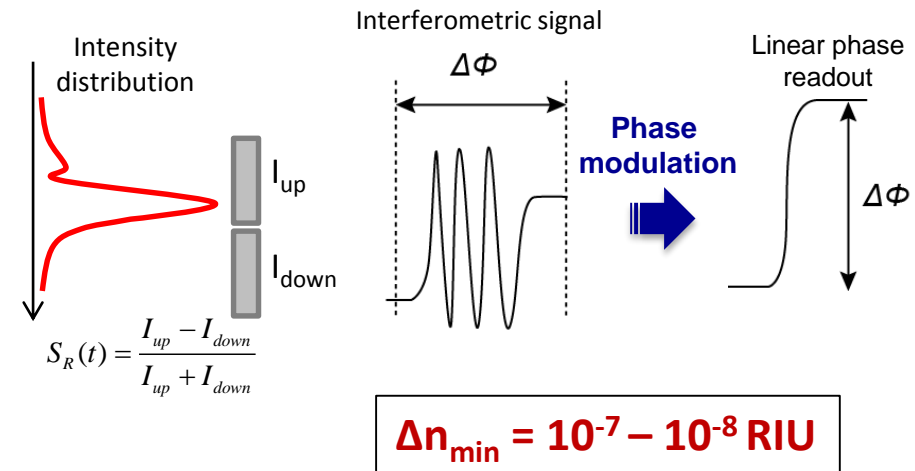
Mach-Zehnder

Bimodal Waveguide

Bimodal waveguide interferometer (BiMW)



$$\Delta n \rightarrow \Delta N_{\text{eff}} = (N_{\text{eff TE}_1} - N_{\text{eff TE}_0}) \rightarrow \Delta \phi \rightarrow \Delta C$$

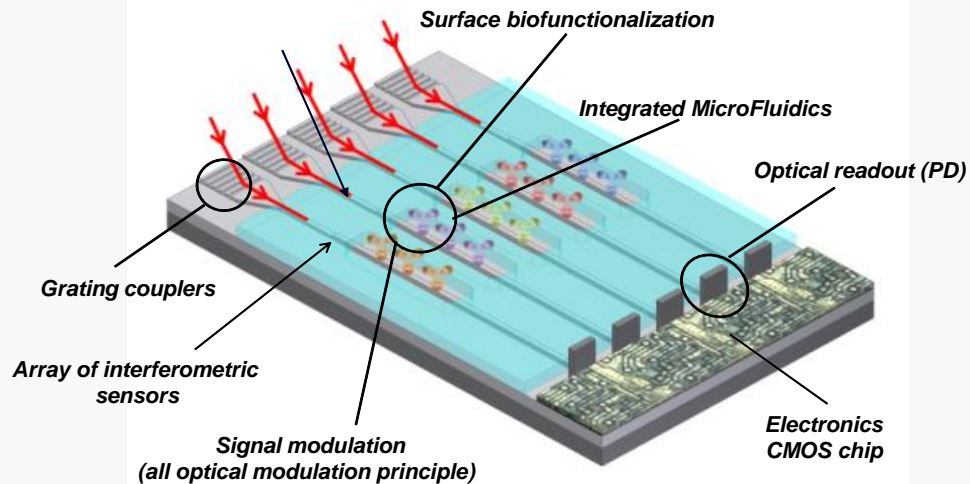
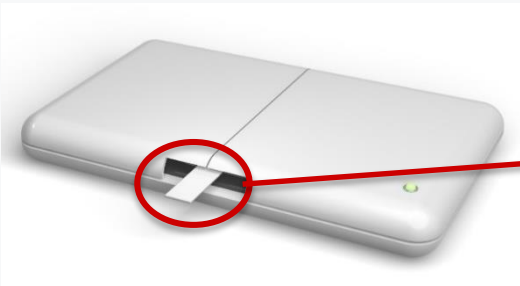


PRINCIPLE OF OPERATION

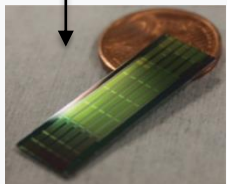
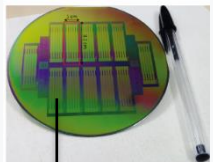
- Single channel waveguide interferometer
- Operated on interference of two light modes (fundamental and first order) of the same polarization
- No need anymore of Y-shape splitters (as in MZI or Young Interferometer)
- The modes propagate with different velocities and create an interference pattern at the exit, which intensity distribution depends on the refractive index of the cladding layer through the interaction with the evanescent field.

Bimodal waveguide interferometer (BiMW) POC biosensor

Portable POC Biosensor platform

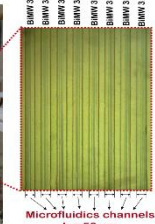
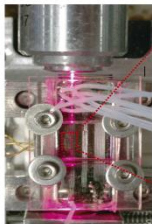


Sensor chip (SiN technology)

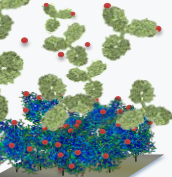
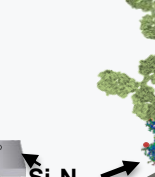
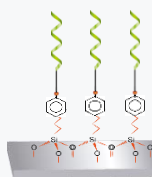


Fabrication
@IMB-CNM-CSIC

Polymer microfluidics

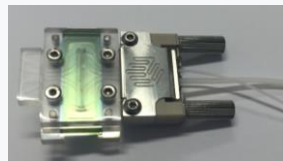


Surface Biofunctionalization



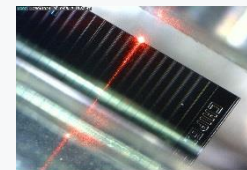
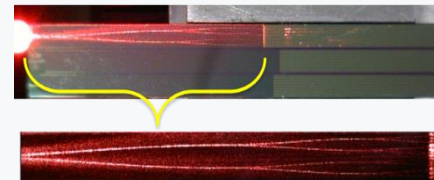
Si₃N₄

Cartridge development

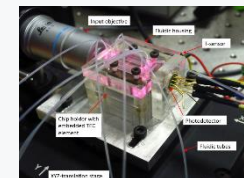


Packaging
& Storage

Light incoupling & Modulation



Optical readout & Signal processing



EPIC Online Technology Meeting on Biosensors

Summary of Applications @NanoB2A Group

PROTEIN BIOMARKERS



Early detection Colorectal cancer
Gluten consumption
Hormone alteration
Doping control
Tuberculosis
Allergy diagnosis
Growth factors
Sintrom antibiotics

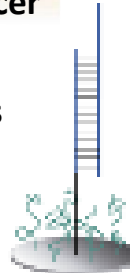


Urine, serum,
plasma, tears

NUCLEIC ACIDS



Single DNA cancer mutations
DNA Epigenetics
microRNAs biomarkers
Messenger RNA
Alternative splicing RNA



Urine, serum,
plasma, tissue

SMALL POLLUTANTS

Environmental water pollutants

Pesticides, Organo-halogenated compounds, antibiotics, biocides



Food contaminants

Pesticides residues:
canned food, oranges

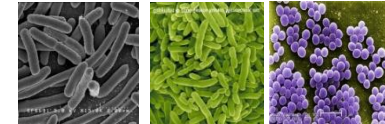
Toxins



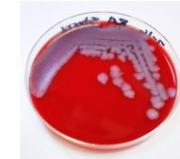
Wastewater, tap
water, ocean, food

PATHOGENIC BACTERIA

Nosocomial pathogens



- Chronic liver failure
- Sepsis



Antibiotic susceptibility of bacteria

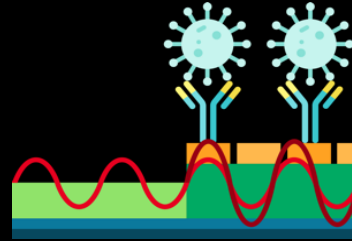


Water pathogens

Urine, serum,
plasma, ascetic fluid

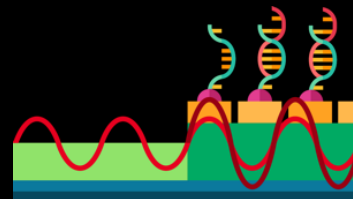
CONVAT PROJECT

(1) Antigen-directed Detection



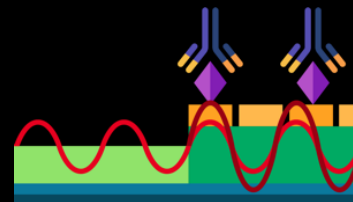
The biosensor will use **specific antibodies** for the **capture of complete units of the SARS-CoV-2 virus**. This process will be **monitored in real time** for a **rapid diagnosis** and will allow the **quantification of the viral load** in the sample.

(2) RNA Analysis

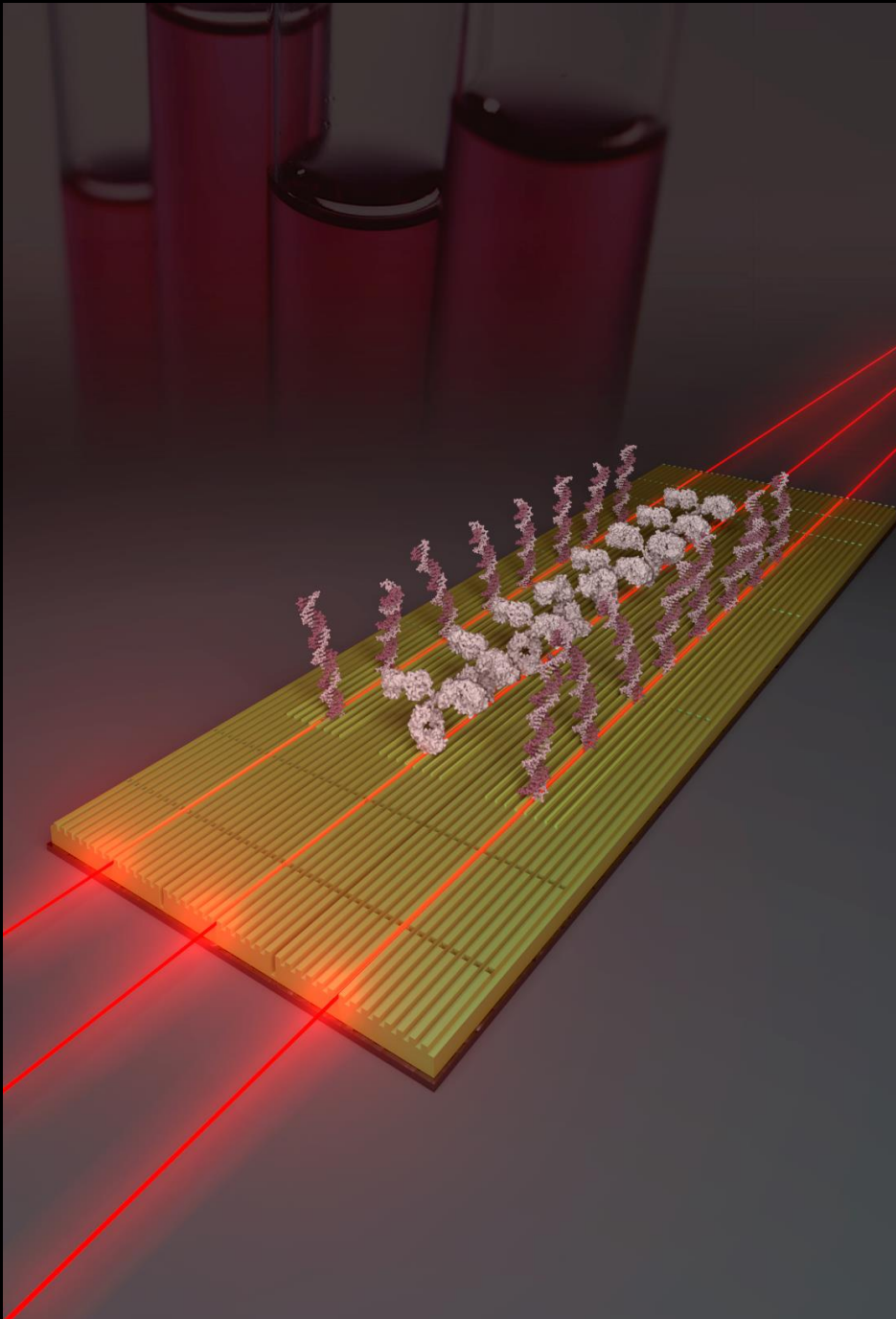


The biosensor will include **complementary DNA probes** that **hybridize to exclusive sequences of the SARS-CoV-2 RNA**. The sensor chip will integrate different DNA probes for similar virus to identify the **presence of other viral species in the same sample**.

(3) Serological Assays



Detection of antibodies in patients for serological testing will be carried out **using antigens of SARS-CoV-2**. This strategy will identify **asymptomatic individuals, patients with mild symptoms** and will be useful for **epidemiological studies**.

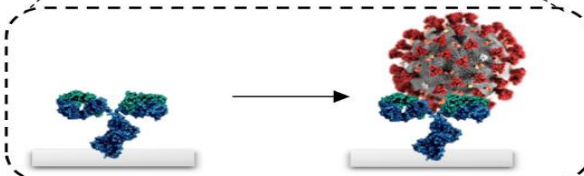
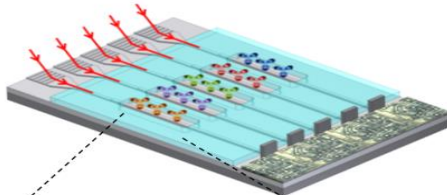


Summary of CoNVat approach for diagnostics and surveillance of Covid-2019

Rapid nCoV clinical screening

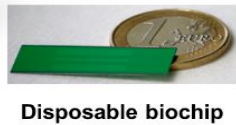
Human Sample collection
Sample introduction in the POC
Signal measurement

Direct nCoV detection



Antibody-based detection

Nanobiosensor platform



Disposable biochip



Sample collection & characterization

Patient selection



Animal reservoirs



Sample collection

- Nasal swap
- Pharyngeal swaps
- Sputum
- Saliva
- Faeces
- Urine
- ...

Sample collection

- Saliva
- Faeces

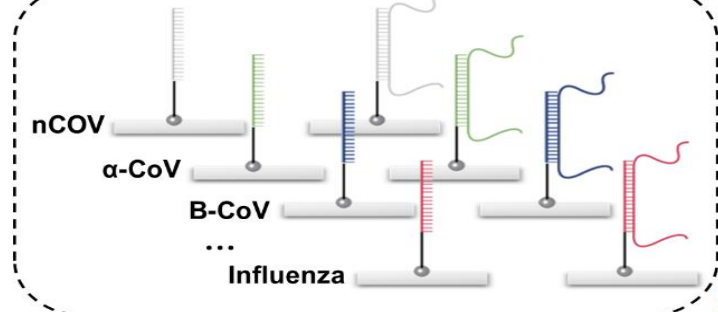
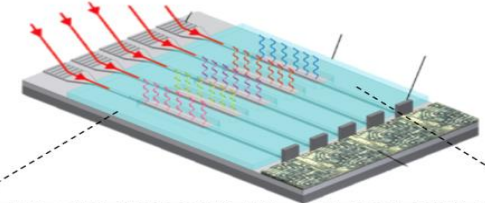
Multiplexed viral genomic analysis

Human & animal sample collection

Nucleic acid extraction

Signal measurement

Detection of nCoV RNA fragments

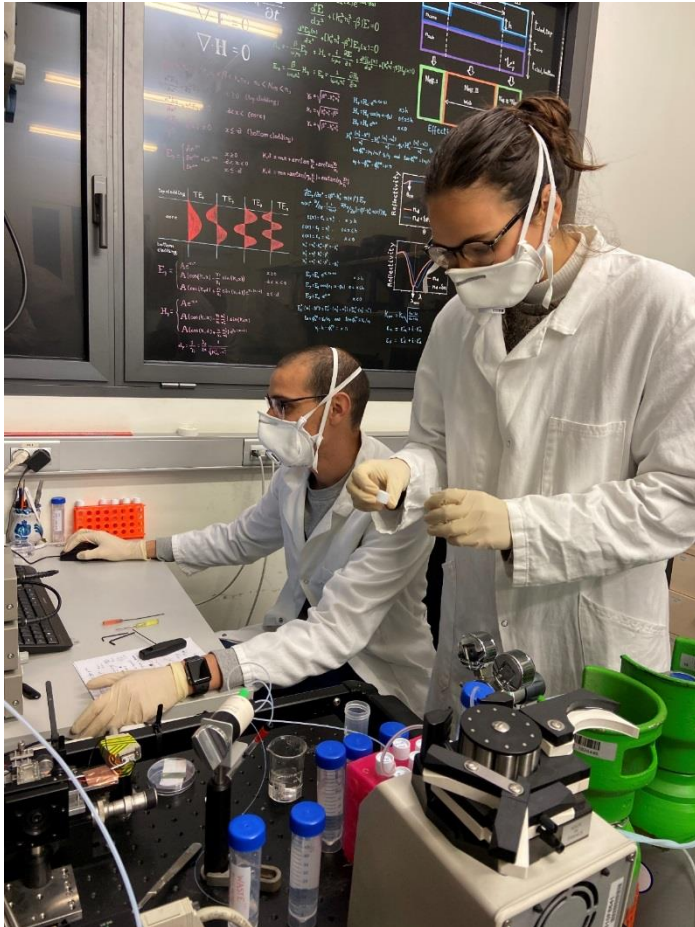


Complementary hybridization assays

**THANK YOU!!!
GRACIAS!!!**

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